Egyptian Journal of Medical Microbiology Volume 33 / No.4 / October 2024 83-89 Online ISSN: 2537-0979

ORIGINAL ARTICLE

Role of Interleukin-17 in the Pathogenesis and Progression of Coronary Artery Disease

[1]Douaa A. Kadhum*, [1]Muthana S. Mashkour, [1]Hanaa A. Ali, [2]Heshmatolah Parsian
[1]Department of Chemistry, Faculty of Science, University of Kufa / Najaf, 54001– Iraq
[2]Department of Physical Education and Sport Science, Shahre - e - Qods Branch, Islamic Azad University, Iran

Key words:
Artery disease, immune system ,IL-17 , atherogenic index, and lipid profile

Corresponding Author:
Douaa Abdul Hussain Kadhum
Department of Chemistry, Faculty of Science, University of Kufa / Najaf, 54001– Iraq
Tel. : 08724886008
douaa.kadhum@atu. edu.iq

ABSTRACT

Background: *Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide. Inflammation is a critical component of CAD pathogenesis, with interleukin-17 (IL-17) emerging as a key pro-inflammatory cytokine involved in various autoimmune and inflammatory diseases.* ***Objective:*** *This study investigates the role of IL-17 in CAD, examining its potential as a biomarker for disease severity and its mechanistic contribution to atherosclerosis.* ***Methodology:*** *A case-control study with 138 subjects, including 88 (CAD) patients, and 50 apparently healthy individuals age between 40-75 years, was conducted. IL-17 level were measured using (ELISA) technique.* ***Results:*** *higher serum IL-17 concentration was significantly observed in patients (20.0567±4.4118 pg/ml) compared with that found in the apparently healthy group (12.9072±4.0378pg/ml) ($P \leq 0.0001$). Serum IL-17 level had significant positive correlations with age, atherogenic index, lipid profile (Total cholesterol ,TG, LDL-C,VLDL-C . while showing significant negative correlations with high-density lipoprotein (HDL-C) levels in the CAD group. The results of the receiver operating curve (ROC) and AUC analysis for CETP as a potential diagnostic parameter showed a sensitivity of 79.10%, a specificity of 76%, and AUC 0.880 at a level of ≥ 16.0837pg/ml.*
Conclusion: *elevated levels of serum IL-17 in the bloodstream may serve as a predictive indicator of the likelihood of developing CAD. which in go to increase the danger of developing CAD.*

INTRODUCTION

The most common kind of heart illness is (CAD), which is defined by plaque accumulation restricting or obstructing the coronary arteries, preventing oxygen-rich blood from reaching the heart muscle[1-3]. This disorder, also referred to as atherosclerotic heart disease, is a key contributor to heart attacks and can result in a number of dangerous side effects, including angina (chest discomfort), strokes, and heart failure[3].

Approximately 15% of all deaths in affluent nations are related to CAD, making it a major cause of death worldwide[4]. The rate of death from CAD has reduced recently due to advancements in medical therapy, reperfusion methods, and better management of cardiovascular risk issues[4-5]. Appropriate therapy, lifestyle changes, and early detection are essential for controlling CAD and averting its potentially catastrophic outcomes**.**

Proinflammatory cytokine IL-17 is essential for immune responses to infections because it stimulates neutrophil recruitment and the combination of antimicrobial peptides [6]. Inflammatory and autoimmune disorders such multiple sclerosis, rheumatoid arthritis, and psoriasis can be brought on by dysregulated IL-17 levels[7]. Severe alcohol-associated hepatitis (SAH) patients had considerably higher levels of IL-17 in the context of alcohol-associated liver disease (ALD), and these levels certainly connected with Model for End-Stage Liver Disease (MELD) scores[8]. It is clear that IL-17 has two roles because it can both boost immune responses and lower immunological activity in illnesses that are already established[9]. Monoclonal antibodies directed against IL-17A and IL-17F are among the therapeutic approaches that target IL-17 and have demonstrated potential in the treatment of autoimmune and chronic inflammatory illnesses[6]. Gaining control over IL-17's protective immunity against pathogens while preventing immunopathology in illnesses requires an understanding of how its effects balance.

In the recognition of (CAD), narrowed coronary arteries are a hallmark, often attributed to the accumulation of plaque in the arteries, a process known as atherosclerosis[10-12]. This condition is closely related to inflammation, with immune cell-produced cytokines like interleukin-17 (IL-17) emerging as potential players in the pathogenesis of CAD[13]. The precise role of IL-17 in the onset, development, and progression of atherosclerosis and the consequent development of congestive heart failure is yet unknown, and research on the subject is still underway. Comprehending the role of IL-17 and additional inflammatory pathways in CAD is

essential for creating focused treatment strategies that can complement existing treatments and address the residual cardiovascular risk that persists despite conventional interventions[14]. Research from multiple studies supports the pro-atherogenic role of IL-17 in cardiovascular diseases. IL-17 can induce the release of adhesion molecules and pro-inflammatory cytokines from various cells in the artery wall, leading to the accumulation of immune cells and exacerbating inflammation[15]. Elevated IL-17 levels have been detected in patients with acute coronary syndrome, a complication of coronary heart disease (CHD)[16]. Moreover, studies indicate a potential correlation between IL-17 levels and the severity of coronary artery lesions, suggesting that IL-17 may contribute to plaque instability and rupture, increasing the risk of heart attacks. These findings underscore the significance of IL-17 in promoting vascular inflammation and atherosclerosis progression, highlighting its potential as a therapeutic target for preventing cardiovascular complications[17]. The aim of this study is to study the function of IL-17 in CAD is investigated in this work, along with its potential as a biomarker for the severity of the illness and its mechanistic involvement in atherosclerosis.

METHODOLOGY

Using a case-control research approach, data was collected from 138 subjects obtained from Center for Cardiac Surgery and Catheter Intervention at Al- Sadr Medical City between Mar., 2023 and Nov., 2023. The subjects, age ranged between 40 to 75 years, were divided into two groups: 88 patients with CAD and 50 apparently healthy as a control group. The Sandwich-ELISA method was employed to measure the amounts of serum IL-17 (Sunlong Biotech , China), and a SMART-120 chemistry analyzer was used to measure the levels of lipid profiles and other compounds in human serum. (AFLO / Germany, colorimetric enzymatic method). The BMI is expressed as kg/m^2, which is the result of dividing the weight (in kg) by the square of the height (in m)[18].

The coefficient represents the Atherogenic index. The ratio of non-high-density lipoprotein cholesterol (non-HDL-C) to high-density lipoprotein cholesterol (HDL-C) is known as the atherogenic coefficient (AC). It is an alternate diagnostic method that has been applied to forecast the likelihood of experiencing cardiovascular events[19]. AC = non-HDL-C / HDL-C Non- HDL-C = TC – HDL-C. Atherogenic index of Plasma (AIP) Atherogenic index of plasma (AIP) is an unconventional lipid ratio representing the logarithm of the molar ratio of TG to HDL-C[20].

AIP = log (TG/ HDL-C).

While Castelli's Risk Indexes (I & II) Castelli's risk indexes (I & II) also called cardiac risk indexes) are two lipid ratios, the CRI-I is the ratio of TC to HDL-C, while the CRI-II is the ratio of LDLC to HDL-C. They were reported by William Castelli, at the end of the past century [21].

CRI-I= TC/ HDL-C ratio CRI-II = LDL-C / HDL-C ratio.

At last Cholesterol Index Cholesterol index (C-index) is a simple index that predicts the probability of developing CAD with greater accuracy than the other indices.C- index= (LDL-C) – (HDL-C).

The questionnaire collected demographic data on gender, age, smoking status, sedentary lifestyle, and personal history of CAD for both patients and healthy controls. preserving quality of life for people suffering from a variety of chronic conditions, including diabetes, cirrhosis, end-stage disease, acute heart failure, stroke, cancer, structural weakness, and endocrine dysfunction.

Analytical Statistics

Statistical analysis was done using SPSS software, version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were provided as mean ± SD or as median and interquartile range in order to assess if the distribution was normal. The univariate analysis for anomalous distributions was carried out by an independent Kruskal Wallis Test for data that is continuous. The Pearson rank test was used to compare biomarkers in order to determine the association within the case study.

Analytical statistical research revealed significant variations in the parameters of category variables.. A P-value of 0.0001 was considered statistically significant for all hypothesis tests. Using receiver operating characteristic (ROC) analysis, an optimal threshold with high specificity and sensitivity for crucial instances were identified. It was discovered that all P values was and a P value of 0.0001 was considered statistically significant.

Ethical approval

Ethical approval for the investigation was acquired from the Kufa College of science, Kufa University (Approval number 1390 on 6/3/2023). After explaining the nature and objectives of the research to each patient, consent was taken from both patients and staff at the Center for Cardiac Surgery and Catheter Intervention at Al- Sadr Medical City Additionally, participants underwent a medical checkup by a specialized doctor to check for any indications or symptoms of heart problems, including troponin levels and electrocardiographic patterns.

RESULTS

Tables 1, 2, and 3 provide an overview of the study participants' clinical traits and metabolic markers. The comparison of anthropometric measurements and lipid profile parameters between the CAD collective and the healthy group is presented in Table 1. Figure 1

illustrates that the level of serum IL-17 was significantly increased in patients than in the control group. The mean ± SD of IL-17 in CAD patients was 20.0567±4.4118 pg/ml, while with the control group, it was 12.9072±4.0378 pg/ml. Patients were overweight.

.

with statistical differences in BMI between the study groups. Other results that are statistically significant include TC, TG, HDL-C, LDL-C, and VLDL- C levels, and atherogenic index as shown in Table 1.

Table 1: Demographic characteristics of the study participants in patients and healthy groups with p =0.0001.

Characteristics	Patients Mean ±SD	Control Mean ±SD	P-value
BMI (Kg/m^2)	27.74±4.20	25.03±2.31	0.004
Age years	52.22±12.269	51.32±10.260	0.067
History of Family Yes/No	62/26	----------	
Onset of diseases	2.92±1.59	----------	
IL-17 pg/ml	20.0567±4.4118	12.9072±4.0378	<0.0001
TC mg/ml	227.4476±76.71572	160.8959±68.59730	0.000
TG mg/ml	160.8959±68.59730	51.5274±36.49274	0.000
HDL-C mg/ml	24.0731±7.774	48.1409±7.62331	0.000
LDL-C mg/ml	178.6470±75.088	136.8607±68.175	0.001
VLDL-C mg/ml	10.4487±7.23854	8.1845±4.54163	0.025
AC	6.877±3.861	0.08712±0.467	0.000
AIP	4.18288±1.625.	0.16861±0.0275	0.000
CR-I	7.1949±3.57427	5.1979±1.67374	0.000
CR-II	5.8339±3.503	3.9581±1.621	0.002
C-Index	135.0134±73.95801	105.0092±60.94893	0.017

BMI; Body mass index, IL-17:Intrlukein, HDL; High-density lipoprotein, LDL; Low-density lipoprotein, ALP; Alkaline phosphatase. TC; total cholesterol ,TG :triglyceride ,VLDL :very low density lipoprotein . Coefficient Atherogenic coefficient AIP: Atherogenic index of Plasma, CR-I ,CR-II :cardiac risk index I,II , (C-index): Cholesterol index.

Table 2 shows the association between the parameters studied and serum IL-17 levels in patients as examined by Pearson correlation analysis (r). interleukin-17 (IL-17) displayed a weak positive correlation with BMI (r=0.236, p=0.025) but not with age, cholesterol, TG, HDL-C, LDL-C, VLDL-C, with IL-17 level in the CAD group.

Table 2: Correlations between IL-17 and parameters in patients and healthy groups.

Variables	Groups			
	CAD Patients		Controls	
	r	p	r	p
Age years	0.054	0.616	0.022	0.879
BMI Kg/m^2	0.236	0.025	-0.228	0.111
Total Cholesterol mg/ml	0.001	0.990	-0.091	0.529
TG mg/ml	0.001	0.990	-0.120	0.462
HDL-C mg/ml	-0.013	0.900	-0.023	0.889
LDL-C mg/ml	-0.026	0.805	-0.198	0.220
VLDL-C mg/ml	0.039	0.716	-0.120	0.462

HDL-C; High-density lipoprotein, LDL-C; Low-density lipoprotein,. TC; total cholesterol , TG :triglyceride ,VLDL-C :very low density lipoprotein .

The results of the receiver operating curve (ROC) and AUC analysis for IL-17 are shown in table 3 Figure1. Presented that the area under the curve (AUC) was 0.880 with a 95% CI of 0.824-0.937, sensitivity was 79.10 %, specificity was 76.00 %, and the cut-off point was = 16.0837 Pg/ml).

Table3: Receiver operating characteristic of IL-17 in patients with CAD

Variables	Cut-off concentration	Sensitivity %	Specificity %	AUC	95% CI of AUC	p-value
IL-17 (pg/mL)	**16.0837**	**79.10**	**76.00**	**0.880**	**0.824-0.937**	**<0.0001**

AC: Area Under the Curve, CI: Confidence Interval.

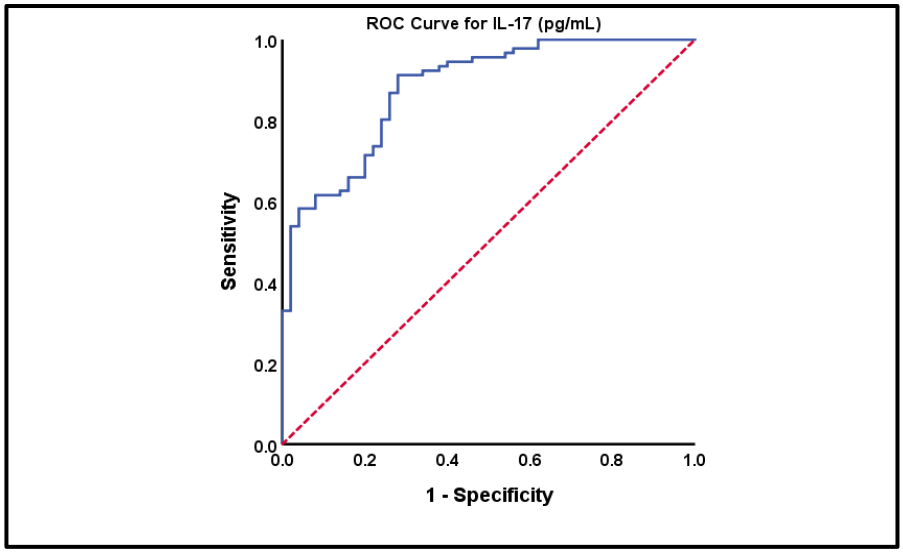

Fig. 1: Receiver operating characteristic (ROC) curve of IL-17 in CAD patients.

DISCUSSION

Globally, CAD continues to be the primary cause of mortality[19] Patients with more severe CAD had an increased chance of heart attack and cardiovascular death. There was also a strong correlation between the clinical outcome and severity of CAD[20] Finally, there was an increase in all-cause mortality as CAD severity increased.

Even if the coronary lesions were substantial, a large proportion of patients with CAD simply showed abnormal or absent sensations of chest tightness. Patients frequently did not pay enough attention to this, and they are also frequently missed in clinical work[21-22]. Consequently, by determining the predictors of severe CAD, it is meaningful to distinguish patients with high severity of CAD from those who are suspected of having CAD. This would significantly enhance CAD therapy, diagnosis, and prevention. In this investigation,We discovered a strong correlation between serum cytokine levels and severe CAD.

The present study showed that low-density lipoprotein (LDL), immunological and inflammatory reactions, endothelial dysfunction, and atheroma development within the intima are the pathophysiology of coronary atherosclerosis. the patients' BMI was substantially increased than the control groups. IL-17 levels were significantly greater in patients than in controls. The patients' total cholesterol (TC) values were higher than the controls' levels. TG levels were substantially higher in patients compared to controls. the patients' levels of high-density lipoprotein cholesterol (HDL-C) were lower than the controls'. Additionally, patients had greater levels of low-density lipoprotein cholesterol (LDL-C) than the patients. very low-density lipoprotein cholesterol (VLDL-C) levels were elevated in patients compeered to controls' levels.

The result of present study shows that IL-17 Levels have evaluated the connotation between interleukin-17 (IL-17) levels and CAD, indicating potential implications for cardiovascular danger[23]. The investigate has shown that interleukin-17 (IL-17) levels can be a susceptibility marker for coronary artery disease, potentially impacting patient risk[24]. The current investigation demonstrated the relationships between IL-17 levels and other variables in both healthy controls and CAD patients. A modest positive connection was seen between IL-17 and BMI in CAD patients, but not with age, and lipid profile. IL-17 did not significantly correlate with any of these indicators in healthy controls. This indicates that, whereas there were no discernible associations in healthy controls, there may be a relationship between IL-17 and BMI in CAD patients. These conclusions propose a potential association between IL-17 and BMI in CAD patients, while no significant correlations were experiential in

healthy controls for the parameters assessed. A previous study indicated that dysregulated production of IL-17 can lead to the pathogenesis of various inflammatory and autoimmune disorders, such as multiple sclerosis, rheumatoid arthritis, and psoriasis[25]. Moreover, IL-17's involvement in chronic inflammatory diseases like type II diabetes mellitus (T2DM) further highlights its complex function in immune responses and disease etiology[26]. IL-17 has been thoroughly investigated in a number of cardiovascular conditions, demonstrating its value as a predictive biomarker. Studies have demonstrated the critical function of IL-17 in inducing inflammation and playing a part in the expansion of diseases such as early-onset CAD[27], unstable angina (UA)[28], and atherosclerosis in individuals suffering from rheumatoid arthritis (RA)[29]. Inducing cytokines and chemokines, in addition to drawing in inflammatory cells such as monocytes, neutrophils, and natural killer cells, IL-17 is essential for immune responses[30]. Furthermore, IL-17 levels have been connected to the cardiovascular disease risk and comorbidities associated with obesity, and IL-17E and IL-17F may be useful biomarkers for determining the grade of inflammation[31].

Thus, during inflammation, IL-17 is vital for leukocyte adherence to blood vessel walls, which is necessary for the staffing of different immune cells implicated in the inflammatory response.

Our research consistently shows that CAD patients have significant levels of IL-17, which can be evaluated in comparison with the control group. Within the peripheral circulation, the majority of the patients in our research exhibited undetectable levels of circulating IL-17. Consequently, there are significant variations in the levels of circulating IL-17 in CAD patients compared with controls. These results support the idea that there is a link between an elevated risk of heart attack in the coronary heart and higher fat levels, as measured by BMI and other lipid markers. Patients with elevated triglycerides, cholesterol, and inflammatory markers highlight how critical it is to control these variables in order to decrease the risk of CAD[32–38].

CONCLUSION

It is become known that IL-17 plays a significant role in the inflammatory processes that underlie CAD, and focusing on this cytokine which may be beneficial for future treatment approaches.

The answers of our search indicated that elevated IL-17 levels aided in the development of CAD, pointing to IL-17 as a putative risk marker. To establish IL-17 as a therapeutic biomarker of CAD, more investigation is required.

Declarations:
Consent for publication: Not applicable

Availability of data and material: Data are available upon request.
Competing interests: The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.
This manuscript has not been previously published and is not under consideration in another journal.
Funding: Authors did not receive any grants from funding agencies.

REFERENCES

1. Hamdan M, Kossaify A. Silent myocardial ischemia revisited, another silent killer, emphasis on the diagnostic value of stress echocardiography with focused update and review. Advanced Biomedical Research. 2023; 12(1), 245-255.
2. Zheng Y, Yang H, Aliyu SH, Micallef C. Human fungal pathogen identification: methods and protocols. Cardiovascular Diabetology. 2022; 21(1), 29-35.
3. Wallhaus TR, Taylor M, DeGrado TR, Russell DC, Stanko P, Nickles RJ, Stone CK. Myocardial free fatty acid and glucose use after carvedilol treatment in patients with congestive heart failure. Circulation. 2001; 103(20), 2441-2446.
4. Ford TJ, Berry C, De Bruyne B, Yong ASC, Toth GG, Ruggeri S, ... Gall H. Assessment of vascular dysfunction in patients without obstructive coronary artery disease: why, how, and when. Cardiovascular Interventions. 2020; 13(16), 1847-1864.
5. Mijwil MM, Shukur BS, Mahmood ES. The most common heart diseases and their influence on human life: a mini-review. Journal of Advances in Medicine and Medical Research. 2022; 34(1), 26-36. doi:10.9734/jammr/2022/v34i1531396.
6. Kingston HG, Mills KH. IL-17 and IL-17-producing cells in protection versus pathology. Nature Reviews Immunology. 2022; 23(1), 38-54. doi:10.1038/s41577-022-00746-9.
7. 7. Akhter S, Tasnin FM, Islam MN, Rauf A, Mitra S, Emran TB, Thiruvengadam M. Role of Th17 and IL-17 cytokines on inflammatory and auto-immune diseases. Current Pharmaceutical Design. 2023; 29(26), 2078-2090.
8. Li N, Yamamoto G, Fuji H, Kisseleva T. Interleukin-17 in liver disease pathogenesis. Semin Liver Dis. 2021, 41(4), 507-515.
9. Bălănescu P, Bălănescu E, Bălănescu A. IL-17 and Th17 cells in systemic sclerosis: A comprehensive review. Rom J Intern Med. 2017, 55(4), 198-204.
10. Olveira A, Augustin S, Benlloch S, Ampuero J, Suárez-Pérez JA, Armesto S, Vilarrasa E,

Belinchón-Romero I, Herranz P, Crespo J, Guimerá F, Gómez-Labrador L, Martín V, Carrascosa JM. The essential role of IL-17 as the pathogenetic link between psoriasis and metabolic-associated fatty liver disease. Reproductive and Developmental Biology. 2023; 13(2), 419-424. doi:10.3390/life13020419.

11. Wang X, Kaiser H, Kvist-Hansen A, McCauley BD, Skov L, Hansen PR, Becker C. IL-17 pathway members as potential biomarkers of effective systemic treatment and cardiovascular disease in patients with moderate-to-severe psoriasis. Int J Mol Sci. 2022, 23(1), 555-560. https://doi.org/10.3390/ijms23010555.
12. Tanaka T, Sasaki N, Rikitake Y. Recent advances on the role and therapeutic potential of regulatory T cells in atherosclerosis. J Clin Med. 2021; 10(24):5907-5916. https://doi.org/10.3390/jcm10245907.
13. Henein MY, Vancheri S, Longo G, Vancheri F. The role of inflammation in cardiovascular disease. International Journal of Molecular Sciences. 2022; 23(21), e112906. doi:10.3390/ijms232112906.
14. Mahmoudi-Nejad S, Esm-Khani L, Mahmudi S, Khadem-Vatani K, Abdi Rad I, Bagheri M. Evaluation of interleukin-17 receptor (IL-17RA) gene expression in PBMCs of patients with premature coronary artery disease. Bratislavske Lekarske Listy. 2022, 123(10), 736–739. https://doi.org/10.4149/BLL_2022_118.
15. Jurkiewicz CL. Interleukin-17A influences the vulnerability rather than the size of established atherosclerotic plaques in apolipoprotein E-deficient mice. Biol. 2022; 17(1), 1104-1115. doi:10.1515/biol-2022-0072.
16. Ling S, You Z, Li Y, Zhang J, Zhao S, He Y, Chen X. The role of γδ T17 cells in cardiovascular disease. Journal of Leukocyte Biology. 2022; 112, 1649-1661. doi:10.1002/JLB.3MR0822-761RR.
17. Wang J, He L, Li W, Lv S. A role of IL-17 in rheumatoid arthritis patients complicated with atherosclerosis. Front Pharmacol. 2022, 13, 898-933. https://doi.org/10.3389/fphar.2022.828933.
18. Donini LM, Pinto A, Giusti AM, Lenzi A, Poggiogalle E. Obesity or BMI paradox? Beneath the tip of the iceberg. Front Nutr. 2020; 7, 53. https://doi.org/10.3389/fnut.2020.00053.
19. 19. Sujatha R, Kavitha S. Atherogenic indices in stroke patients: A retrospective study. Iranian Journal of Neurology. 2017; 16(2), 78-82.
20. Dharmaraj S, Rajaragupathy S, Denishya S. A descriptive study of atherogenic indices in patients admitted to a tertiary care hospital. Cureus. 2022; 14(12), e32231. doi:10.7759/cureus.32231.
21. Tien YT, Wang LJ, Lee Y, Lin PY, Hung CF, Chong MY, Huang YC. Comparative predictive efficacy of atherogenic indices on metabolic syndrome in patients with schizophrenia. Schizophrenia Research. 2023; 262, 95-101.
22. Musunuru K, Kathiresan S. Genetics of common, complex coronary artery disease. Cell. 2019; 177(1), 132-145. doi:10.1016/j.cell.2019.02.015.
23. Reynolds HR, Shaw LJ, Min JK, Page CB, Berman DS, Chaitman BR, Picard MH, Kwong RY, O'Brien SM, Huang Z, Mark DB, Nath RK, Dwivedi SK, Smanio PE, Stone PH, Held C, Keltai M, Bangalore S, Newman JD, Spertus JA, et al. Outcomes in the ISCHEMIA trial based on coronary artery disease and ischemia severity. Circulation. 2021; 144(13), 1024-1038. doi:10.1161/CIRCULATIONAHA.120.049755.
24. Chieffo A, Buchanan GL, Mauri F, Mehilli J, Vaquerizo B, Moynagh A, Mehran R, Morice MC. ACS and STEMI treatment: Gender-related issues. EuroIntervention. 2012; 8(suppl. P), 27–35. doi:10.4244/EIJV8SPA6.
25. Akhter S, Tasnim FM, Islam MN, Rauf A, Mitra S, Emran TB, Alhumaydhi FA, Khalil AA, Aljohani ASM, Al Abdulmonem W, Thiruvengadam M. Role of Th17 and IL-17 Cytokines on Inflammatory and Auto-immune Diseases. Curr Pharm Des. 2023, 29(26), 2078–2090. https://doi.org/10.2174/1381612829666230904150808.
26. Elahi R, Nazari M, Mohammadi V, Esmaeilzadeh K, Esmaeilzadeh A. IL-17 in type II diabetes mellitus (T2DM) immunopathogenesis and complications; molecular approaches. Mol Immunol. 2024, 171, 66–76. https://doi.org/10.1016/j.molimm.2024.03.009.
27. Oliveira DC, Oliveira CG, Mendes Jr EB, Silveira MM, Cabral JV, Ferreira E. Circulating interleukin-17A in patients with acute and chronic coronary syndromes. American Journal of Cardiovascular Disease. 2021; 11(6), 704-718.
28. Fang B. The comparison of IL-17 levels in patients with unstable angina before and after medical treatment. Human Antibodies. 2022; 30(1), 25-29. doi:10.3233/hab-210446.
29. Zhao R, Zhang YW, Yao JY, Qiao J, Song S, Zhang SX, Wang CH, Li XF. Genetic association between interleukin-17 and susceptibility to rheumatoid arthritis. BMC Med Genomics. 2023, 16(1), 277-290. https://doi.org/10.1186/s12920-023-01713-6.
30. Zhang S, Li Y, Chen G, Wang X, Wu B. Sarcandra glabra (Thunb.) Nakai alleviates DSS-induced ulcerative colitis by promoting restitution, restoring barrier function, and modulating IL-

17/Notch1/FoxP3 pathway in intestinal cells. J Ethnopharmacol. 2024, 328, 118-131.

31. Polak-Szczybyło E, Tabarkiewicz J. IL-17A, IL-17E and IL-17F as potential biomarkers for the intensity of low-grade inflammation and the risk of cardiovascular diseases in obese people. Nutrients. 2022; 14(3), 643-653. doi:10.3390/nu14030643.
32. Ebrahimi Chaharom F, Ebrahimi AA, Feghhi Koochebagh F, Babalou Z, Ghojazadeh M, Aghebati Maleki L, Nader N D. Association of IL-17 serum levels with clinical findings and systemic lupus erythematosus disease activity index. Immunological Medicine. 2023; 46(4), 175-181. doi:10.1080/25785826.2023.2202050.
33. TÜRKER ASLAN H, Ateş ÖF. Investigation of level of serum interleukin 17 in age-related macular degeneration. Sabuncuoğlu Şerefeddin Health Sciences. 2022; 4(2), 9-16. doi:10.55895/sshs.1145995.
34. Stepanova N, Driianska V, Rysyev A, Kholod V, Savchenko V, Kolesnyk M. # 2594 Elevated Serum Il-17 Level Is Associated With The Persistence Of Post-Covid Syndrome And Vaccination Status In Hemodialysis Patients. Nephrology Dialysis Transplantation. 2023; *38*(Supplement_1), gfad063c_2594.
35. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Kathrine Skibelund A. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. European heart journal. 2021; 42(36), 3599-3726.
36. Libby P. The changing landscape of atherosclerosis. Nature. 2021; 592(7855), 524-533. doi:10.1038/s41586-021-03392-8.
37. Kobiyama K, Ley K. Atherosclerosis: A chronic inflammatory disease with an autoimmune component. Circulation Research. 2018; 123(10), 1118-1120.
38. Tousoulis D, Oikonomou E, Economou EK, Crea F, Kaski JC. Inflammatory cytokines in atherosclerosis: current therapeutic approaches. European heart journal, 2016; 37(22), 1723-1732.