International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 4S, 2025
https://www.theaspd.com/ijes.php

Cardiovascular risk assessment in patients with rheumatoid arthritis

Amal Azeez AI-Miahee [1]*, Mohammed R.S.AL-Attabi[2]*
*[1,2]Department of Biology, College of Science, Waist University, Waist, Iraq
std2023204.ahasan@uowasit.edu.iq

ABSTRACT:
Background: Rheumatoid arthritis (RA) patients are at a greater risk of cardiovascular disease (CVD) than those who do not have RA, and this risk is even greater than that of individuals with diabetes. Patients with RA exhibit inflammation driven by autoimmune processes, resulting in endothelial dysfunction, oxidative stress and activation, as well as the migration of white blood cells through the vasculature. Traditionally, it was believed that the connection between RA and CVD was driven by disease-related inflammation that resulted in atherosclerosis (AS). The primary factor contributing to the increased mortality associated with rheumatoid arthritis is cardiovascular illenes.

Objectives: The objective of this research was to identify the correlation of rheumatoid arthritis with cardiac disease markers and biomarkers. Methods: The research was carried out among 60 clinically established subjects of different ages in the field of rheumatoid arthritis. The RA patients' average age was 51.33 ± 8.65, and they were treated at Al-Karama and AL-Zahra Teaching Hospital. Similarly, the Center for Prosthetics in Waist Governorate from November 2024 to January 2025. Blood samples were centrifuged to separate them and then used to examine levels of crucial and immune markers identified through Enzyme Linked Immunosorbent Assay (ELISA).

Results: The findings of the present investigation demonstrated a rise in the levels of cardiovascular risk factors (ESR, TNF-α, IL-6) as well as cardiac indicators (CRP, Fibrinogen).

Keyword: Rheumatoid Arthritis, cardiovascular risk, ESR, TNF-α, IL -6, CRP, Fibrinogen (FG).

INTRODUCTION:

Rheumatoid Arthritis: Inflammatory arthritis (IA) has a worldwide prevalence of approximately 3%, and the most common IA subtype is rheumatoid arthritis (RA). IA is associated with cardiovascular burden risk1.2.
Rheumatoid arthritis (RA) Rheumatoid arthritis (RA) has a prevalence rate of 460 per 100,000 individuals3..

The etiology of RA remains not fully understood; nonetheless, the avancement of the disease is affected by a combination of genetic and environmental factors. Numerous genetic and epigenetic factors have been associated with RA, as well as various environmental influences like cigarette smoke, dust exposure, and our microbiome. Other environmental influences, like hormones, may account for the increased risk in women. Symptoms of the disease often do not manifest for years, during which time it advances and autoantibodies like rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) develop. Patients with RA who are ACPA positive exhibit greater disease activity and higher rates of cardiovascular mortality.

The occurrence of these antibodies is also thought to account for the formation of atherosclerosis. ACPA were also found in non-RA CVD patients and also had worse CVD outcomes4.
Rheumatoid arthritis (RA), a persistent inflammatory condition, can lead to the damage of synovial joints5. The inflammation is systemic and therefore can cause some extra-articular features. Most important among them is cardiovascular disease (CVD) 6.
Inflammation is the basis for the accelerated atherosclerosis seen in RA. It is involved in all stages of atherosclerosis, including plaque formation, instability, and eventual rupture.7
Atherosclerosis and RA share numerous inflammatory pathways, and the mechanisms that lead to synovial inflammation resemble those present in unstable atherosclerotic plaques8.

As an illustration, the elevated increased levels of TNF, IL-6, and IL-1 linked to RA are also crucial for the progression of atherosclerosis9. In fact, research indicates that IL-6 is significantly linked to atherosclerosis in RA patients, regardless of established CVD risk factors10
. The Immunopathogenesis of the disease is now recognized to begin with the emergence of auto reactive T and B cells targeting post-transnationally modified proteins in genetically susceptible individuals. After a phase of asymptomatic systemic autoimmunity, these cells contribute to inflammation in synovial tissue. Ultimately, synovial stromal cells transform into auto-aggressive effector cells, thereby contributing to the onset of chronic synovial inflammation11. Recurrent inflammation is a major factor in the onset of cardiovascular diseases (CVDs), with interleukin-6 (IL-6) and interleukin-1β (IL-1β) being essentiel for promoting arterial damage and negative cardiovascular occurrences 12.13.

In response to infections and tissue damage, various cell types produce IL-6, a multi-functional cytokine. It promotes the synthesis of proteins such as C-reactive protein (CRP), which serves as an indicator of inflammation14. High levels of IL-6 have been associated with a range of negative cardiovascular outcomes, such as a heightened risk of myocardial infarction, heart failure, and all-cause mortality among individuals with CVD.15.16.
It was discovered that when individuals with rheumatoid arthritis were compared to healthy individuals, there was a rise in interleukin 6, signaling the of heightened in heart disease. Cytokines that promote inflammation induce the synthesis of C-reactive protein (CRP), which serves as an indicator of tissue injury, infection, and inflammation. CRP is a liver cell-produced acute phase protein, with minor contributions from atherosclerotic lesions, kidneys, neurons, and macrophages of the alveolar type. Any kind of inflammatory process can elevate CRP levels 17.18. and serving as a trustworthy predictor of ischemic heart disease 19.

The Erythrocyte Sedimentation Rate (ESR) has been acknowledged for a long time as a useful biomarker in diagnosing and managing RA. Numerous studies have shown that higher ESR levels be associated with the severity of RA, making it a useful tool for assessing disease activity 20. Studies have identified a similar occurrence of CVD in RA patients, where inflammation is the primary factor contributing to heightened CV risk, as indicated by raised erythrocyte sedimentation rate (ESR) levels21.
It has been acknowledged that autoimmune diseases like RA are linked to disorders of the coagulation system. Studies have demonstrated that in RA patients, coagulation is activated within the joint, and changes in coagulation factor levels have been implicated in RA vascular disorders. Fibrinogen (FIB) play a crucial role in the blood coagulation process, and its deposition in the joint has been a feature of RA and might play a role in panes tissue formation 6. The prescriptive importance of peripheral blood FIB in RA sufferers is not well understood at this time. Being one of the products arising from fibrin decomposition (FDPs)22.

It has been determined that fibrinogen is a significant independent risk factor for cardiovascular disease. Fibrinogen has been linked to conventional cardiovascular risk factors, indicating that increased levels of fibrinogen could be a mechanism through which these risk factors have an impact. Fibrinogen can increase cardiovascular risk through different mechanisms. At In the initial stage, it attaches to stimulated platelets via polypeptide IIb/IIIa, thereby promoting platelet aggregation. Secondly, higher concentrations of fibrinogen encourage the development of fibrin. Thirdly, it significantly contributes to the viscosity of plasma. Ultimately, it is a substance that rises in inflammatory conditions and serves as an acute-phase reactant23.

1. MATERIAL AND METHODS:

1.1 Study design

Blood samples were collected from rheumatoid arthritis patients seeking diagnosis or treatment, as well as from healthy individuals, within the specified timeframe from (1/10/2024) to (1/1/2025). The study included a total of (90) patients, with (60) diagnosed cases of pulmonary chromatid RA, comprising both genders, including (30) females. Regarding age groups, in overall, 14 (15.6%) less than 40 years, 25 (27.7%) between 40-49 years and 51 (56.7%) more than 50 years were included, RA patients included 8 (13.3%) less than 40 years, 16 (26.7%) between 40-49 years and 36 (60.0%) more than 50 years, while control group included 6 (20.0%) less than 40 years, 9 (30.0%) between 40-49 years and 15 (50.0%) more than 50 years. Regarding age groups, in overall, 14 (15.6%) less than 40 years, 25 (27.7%) between 40-49 years and 51 (56.7%) more than 50 years were included, RA patients included 8 (13.3%) less than 40 years, 16 (26.7%) between 40-49 years and 36 (60.0%) more than 50 years, while control group included 6 (20.0%) less than 40 years, 9 (30.0%) between 40-49 years and 15 (50.0%) more than 50 years.

1.2 Blood sample

From November 2024 to January 2025, samples were obtained from Al-Karmah and Al-Zahra Teaching Hospitals and the Artificial Limbs Center in the Wasit Governorate. This process involved gathering information from both patients and healthy individuals, completing a form for each person, and sterilizing the blood collection site with cotton and 70% diluted alcohol before drawing 7ml of venous blood. (2) ml of blood in (ESR) tubes to measure the sedimentation rate of red blood cells, and (2) ml in sodium citrate tubes to produce plasma after placing it in a centrifuge at a speed of 2000 rpm for 15 minutes to measure fibrinogen protein. We put the rest of the blood (3) ml in vitreous tubes filled with gelatin to separate the clotted portion of the plasma from the blood, leaving it at room temperature for 1-2 hours for globule completion and coagulation; after that, the blood samples are subjected to centrifugation at 3000 rpm for (ten minutes) in order to separate them. Subsequently, the serum is recollected in Eppendorf test tubes using a micropipette and stored at -20°C until biochimical assays are performed with the enzyme-linked immunosorbent assay (ELISA).

2.3 Statistical Analysis

Statistics have been organized and examined using SPSS. Explanatory statistical metrics (frequency distribution and percentages shown with tables and figures, along with mean ± s standard deviation) and comparison statistics (Independent t-test, Mann-Whitney test t, and Pearson/Spearman Bivariate correlations) were utilized. A P-value of 0.05 was taken as statistically significant.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 4S, 2025
https://www.theaspd.com/ijes.php

2. RESULT

The inflammatory markers of RA patients and the control group were compared, with results are shown in table (1). The average C-reactive protein (CRP) levels were 9.54 ± 41.72 in the RA patients and 2.23 ± 0.31 in the healthy group; the mean levels of RA patients were considerably greater than the healthy control group P = 0.001 In addition, the mean Erythrocyte Sedimentation Rate (ESR) was 44.95 ± 12.28 mm/1hr for RA patients and 11.73 ± 2.61 mm/1hr for the healthy control group; the mean value in RA patients was considerably elevated relative to healthy controls (P = 0.001).

Table (1): Results of some inflammatory markers (CRP and ESR) in patients and healthy controls

Groups		C-reactive protein (CRP)	ESR
RA patients	Mean ± SD	**9.54 ± 41.72**	**44.95** ± 12.28
	Range	6.89-12.73	7.00-90.00
Control	Mean ± SD	**2.23** ± 0.31	**11.73** ± 2.61
	Range	1.73-2.95	10.00-20.00
p-value		**0.001** † S	**0.001** † S

n: cases count; SD: standard deviation; †: t-test for independent samples; S: significant at P ≤ 0.05.

The levels of interleukin 6 (IL-6) were also compared between RA patient and healthy control group individuals, with results presented in Table (1) and Figure (3). In RA patients, the average levels of interleukin 6 were 43.57 ± 7.8, while in individuals from the healthy control group, they were 11.47 ± 3.21; the mean level was significantly elevated in RA patients compared to individuals in the healthy control group (P< 0.001).

Table (2): Level of interleukin-6 (IL-6) in patients versus healthy control

.

Groups		Interleukin-6 (IL-6) level
RA patients	Mean ± SD	**43.57 ± 7.8**
	Range	26.86-61.16
Control	Mean ± SD	**11.47** ± 3.21
	Range	6.70-18.84
p-value		**< 0.001** † HS

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 4S, 2025
https://www.theaspd.com/ijes.php

n: number of cases; **SD**: standard deviation; †: independent samples t-test; HS: highly significant at P ≤ 0.001

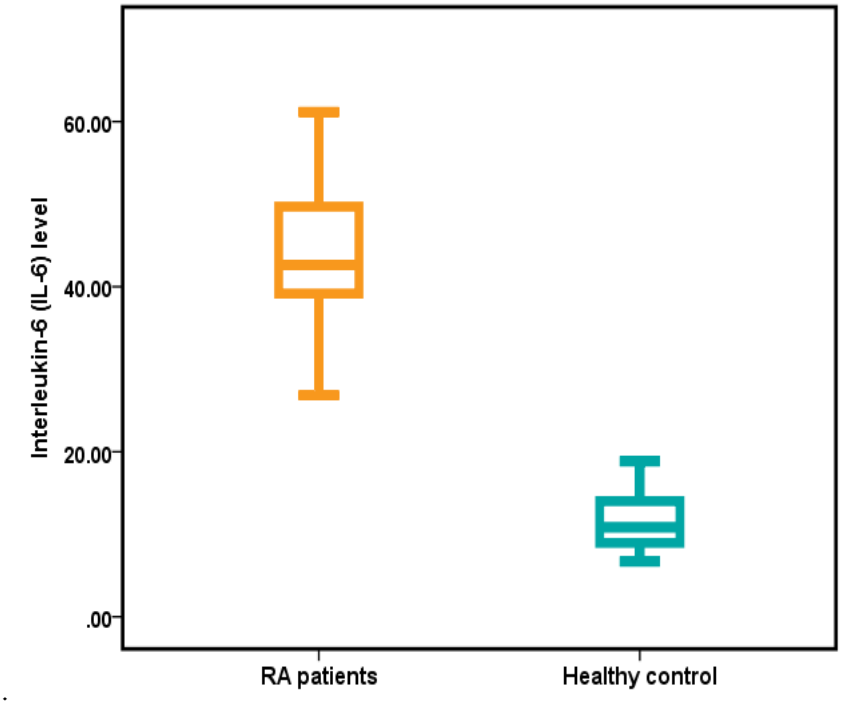

Figure (1): Average IL-6 levels in patients versus healthy controls

The levels of Tumor Necrosis Factor-α (TNF-α) in RA patients were compared to those in healthy control subjects, with the results shown in table (2) and figure (1). In RA patients, the average TNF-α levels were 199.82 ± 28.3, while in healthy controls they were 48.39 ± 6.48; the mean level was significantly elevated compared to RA patients when juxtaposed with healthy controls (P< 0.001).

Table (3): The level of Tumor Necrosis Factor-α (TNF-α) in patients compared to healthy controls..

Groups		Tumor Necrosis Factor-α (TNF-α) levels
RA patients	Mean ± SD	199.82 ± 28.3
	Range	116.78-264.15
Control	Mean ± SD	48.39 ± 6.48
	Range	18.29-86.88
p-value		< 0.001 † HS

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 4S, 2025
https://www.theaspd.com/ijes.php

n: number of cases; **SD**: standard deviation; †: independent samples t-test; HS: highly significant at P ≤ 0.001.

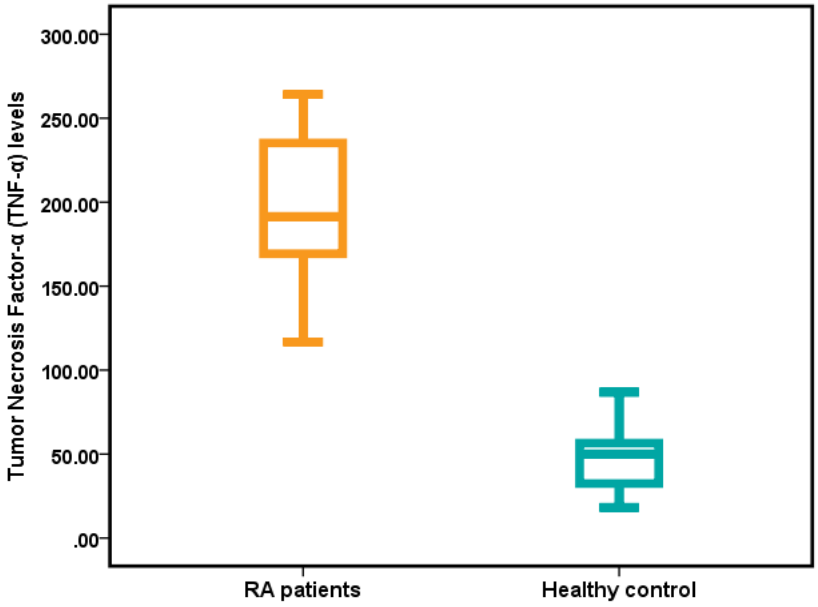

Figure (2): Average TNF-α levels in patients versus healthy controls

The levels of Tumor Necrosis Factor-α (TNF-α) in RA patients were compared to those in healthy control subjects, with the results shown in table (4) and figure (5). In RA patients, the average TNF-α levels were 199.82 ± 28.3, while in healthy controls they were 48.39 ± 6.48; the mean level was significantly elevated compared to RA patients when juxtaposed with healthy controls (P< 0.001).

.Table (4): Fibrinogen levels in patients versus healthy controls

Groups		Fibrinogen levels
RA patients	Mean ± SD	440.9 ± 59.49
	Range	227.94-679.23
Control	Mean ± SD	125.14 ± 14.49
	Range	95.0-159.0
p-value		< 0.001 † HS

n: number of cases; **SD**: standard deviation; †: independent samples t-test; HS: highly significant at P ≤ 0.001.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 4S, 2025
https://www.theaspd.com/ijes.php

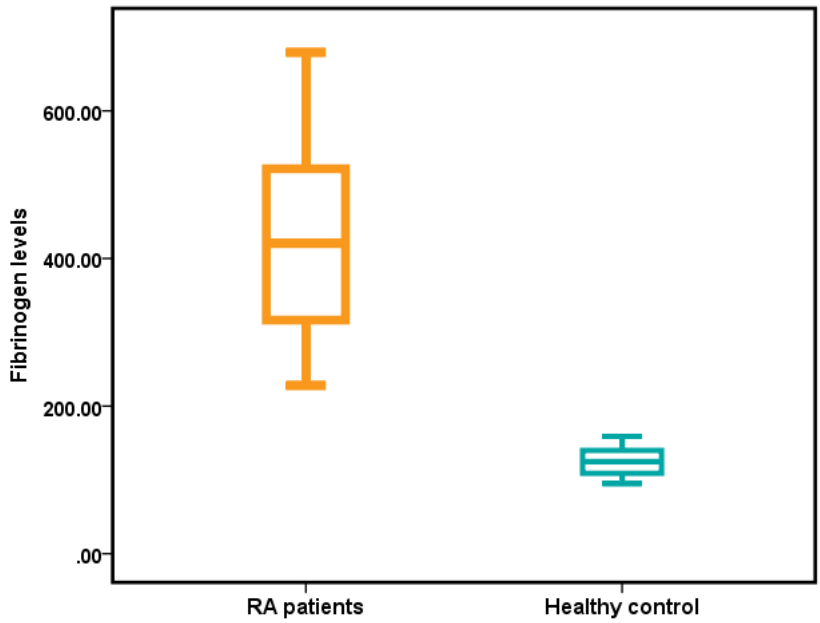

Figure (3): Average Fibrinogen levels in patients versus healthy controls.

DISCUSSION:

This study demonstrated that patients with rheumatoid arthritis experienced a notable rise in cardiovascular risk, attributed to heightened risk factors.

Recent discoveries show that inflammatory markers are considerably heightened in individuals with rheumatoid arthritis (RA) relative to those who are healthy.

In RA patients, the average concentration of C-reactive protein (CRP) was around 9.54 ± 41.72 mg/L, while in the control group it was 2.23 ± 0.31 mg/L. The difference was statistically significant, with a P value of 0.001

Likewise, the erythrocyte sedimentation rate (ESR) in the patient group (44.95 ± 12.28 mm/hr) was significantly higher than that of

The healthy controls (11.73 ± 2.61 mm/hr) also exhibited a significant difference (P = 0.001).CRP and ESR, which are inflammatory markers, are essential signs of chronic inflammation., which characterizes the persistent inflammatory state in RA. A recent study published in 2022 confirmed that there is a correlation between heightened CRP levels and the risk of cardiovascular events in RA patients, with the risk increasing by 1% for each 20 mg/L increase in CRP levels.24

As a result, patients suffering from RA and having CRP levels that are chronically elevated are at a higher risk. Moreover, a systematic review and meta-analysis released in 2023 highlighted the significant role of chronic inflammation—especially when CRP and interleukin-6 (IL-6) levels are high—in the development of cardiovascular complications among individuals with RA.25

Additional research has determined that classical risk factors such as hypertension or hyperlipidemia are unable to explain the high incidence of cardiovascular events in patients with RA.26

This supports the theory that inflammation itself is a risk factor for cardiovascular disease. Atherosclerosis has now been identified as one of the extra-articular features of RA, confirming the association between chronic inflammation and cardiovascular morbidity 27

Thus, it is essential to include an assessment of cardiovascular risk in the comprehensive care plans of RA patients.

This study's findings indicate that interleukin-6 (IL-6) levels are considerably higher in individuals with rheumatoid arthritis (RA) than in healthy controls, with mean IL-6 concentrations of 43.57 ± 7.8 pg/mL in RA patients and 11.47 ± 3.21 pg/mL in healthy controls ($P < 0.001$).

In RA patients, the raised IL-6 level signifies not just an ongoing systemic inflammation but also points to its possible involvement in the heightened cardiovascular risk seen in these individuals.

Interleukin-6 (IL-6), a cytokine that promotes inflammation, plays a vital role in the inflammatory processes that cause rheumatoid arthritis. IL-6 plays a role in triggering the acute-phase response and enhances the expression of CRP, which is another important inflammatory marker. In RA patients, increased IL-6 levels signify an intensified inflammatory condition that leads to joint damage and systemic complications.

The results of this study confirm earlier investigations that have associated increased IL-6 levels with a range of cardiovascular diseases. In particular, research has demonstrated that IL-6 contributes to endothelial dysfunction, which is a key initial phase in the progression of atherosclerosis. When exposed to elevated levels of IL-6, endothelial cells become increasingly susceptible to damage. This susceptibility aids in plaque formation within arteries, thereby contributing to coronary artery disease (CAD) and other cardiovascular conditions.

In RA, chronic inflammation results in elevated IL-6 production, which contributes to joint damage and has serious effects on the cardiovascular system. Multiple studies have demonstrated that those who suffer from rheumatoid arthritis (RA) have an heightened risk of cardiovascular incidents, including myocardial infarction (MI) and stroke This heightened cardiovascular risk is largely attributable to the persistent rise of IL-6.

According to a 2022 meta-analysis, there is an independent association between elevated IL-6 levels and increased cardiovascular event risk in RA patients, even when considering traditional cardiovascular risk factors such as hypertension and hyperlipidemia.28

IL-6 contributes to a pro-atherogenic state by.

The research also investigated tumor necrosis factor alpha (TNF-α), an important cytokine involved in the progression of rheumatoid arthritis.. In this investigation, average In patients with rheumatoid arthritis, TNF-α levels were found to be significantly increased. (199.82 ± 28.3 pg/ml) when compared to the control group (48.39 ± 6.48 pg/ml) ($P < 0.001$), which aligns with the established inflammatory characteristics of rheumatoid arthritis.

In rheumatoid arthritis, the inflammatory response is initiated and amplified by TNF-α, which leads to joint damage and systemic complications.

In individuals suffering from rheumatoid arthritis (RA), there are chronically elevated levels of TNF-α, which lead to endothelial dysfunction. This dysfunction is a precursor to the formation of atherosclerotic plaques. By promoting the release of cytokines and other pro-inflammatory mediators, TNF-α cultivates a pro-atherogenic

environment that accelerates the onset of cardiovascular diseases like coronary artery disease and heart failure. Research conducted by demonstrated that RA patients with elevated TNF-α levels have a significantly increased risk of myocardial infarction (MI).29

Fibrinogen, an acute-phase reactant, is crucial for blood coagulation and the healing of wounds. Fibrinogen concentration are raised in the of RA because of the chronic inflammatory state. In this study, the mean fibrinogen level among RA patients was 440.9 ± 59.49 mg/dL, which was significantly higher than that of healthy controls (125.14 ± 14.49 mg/dL) ($P < 0.001$). Fibrinogen levels that are elevated serve not just as an indicator of inflammation, but also play a role in the heightened cardiovascular risk among RA patients. In RA, elevated fibrinogen levels correlate with a heightened risk of thrombosis and atherosclerosis. Fibrinogen levels that are too high lead to a rise in blood viscosity and promote the buildup of cholesterol and other lipids on the walls of arteries, thus promoting clotting and speeding up atherogenesis. Research conducted by showed that increased levels of fibrinogen constitute an independent risk factor for cardiovascular events in patients with RA, such as myocardial infarction and cerebrovascular accident.30

CONCLUSION

The present study leads us to the conclusion that rheumatoid arthritis has a pronounced impact on certain risk markers for cardiovascular diseases. Therefore, arthritis specialists should carry out regular heart assessments in order to prevent such diseases.

ACKNOWLEDGEMENTS

We would like to thank everyone who contributed and participated in the completion of this research.

REFERENCES

1- Avina-Zubieta, J. A., Thomas, J., Sadatsafavi, M., Lehman, A. J., & Lacaille, D. (2012). Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Annals of the rheumatic diseases, 71(9), 1524-1529.

2- Ogdie, A., Yu, Y., Haynes, K., Love, T. J., Maliha, S., Jiang, Y., ... & Gelfand, J. M. (2015). Risk of major cardiovascular events in patients with psoriatic arthritis, psoriasis and rheumatoid arthritis: a population-based cohort study. Annals of the rheumatic diseases, 74(2), 326-332.

3- Almutairi, K., Nossent, J., Preen, D., Keen, H., & Inderjeeth, C. (2021). The global prevalence of rheumatoid arthritis: a meta-analysis based on a systematic review. Rheumatology international, 41(5), 863-877.

4- Hermans, M. P., van der Velden, D., Cabezas, J. M. M., Putter, H., Huizinga, T. W., Kuiper, J., ... & van der Woude, D. (2017). Long-term mortality in patients with ST-segment elevation myocardial infarction is associated with anti-citrullinated protein antibodies. International Journal of Cardiology, 240, 20-24.

5- Alamanos, Y., Voulgari, P. V., & Drosos, A. A. (2006, December). Incidence and prevalence of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria: a systematic review. In Seminars in arthritis and rheumatism (Vol. 36, No. 3, pp. 182-188). WB Saunders.

6- Crowson, C. S., Liao, K. P., Davis III, J. M., Solomon, D. H., Matteson, E. L., Knutson, K. L., ... & Gabriel, S. E. (2013). Rheumatoid arthritis and cardiovascular disease. American heart journal, 166(4), 622-628.

7- Libby, P. (2008). Role of inflammation in atherosclerosis associated with rheumatoid arthritis. The American journal of medicine, 121(10), S21-S31.

8- Emerging Risk Factors Collaboration. (2010). C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. The Lancet, 375(9709), 132-140.

9- Cesari, M., Penninx, B. W., Newman, A. B., Kritchevsky, S. B., Nicklas, B. J., Sutton-Tyrrell, K., ... & Pahor, M. (2003). Inflammatory markers and cardiovascular disease (the health, aging and body composition [health ABC] study). The American journal of cardiology, 92(5), 522-528.

10- Rho, Y. H., Chung, C. P., Oeser, A., Solus, J., Asanuma, Y., Sokka, T., ... & Stein, C. M. (2009). Inflammatory mediators and premature coronary atherosclerosis in rheumatoid arthritis. Arthritis Care & Research: Official Journal of the American College of Rheumatology, 61(11), 1580-1585.

11- Weyand, C. M., & Goronzy, J. J. (2021). The immunology of rheumatoid arthritis. Nature immunology, 22(1), 10-18.

12- Parish, E., Bloom, T., & Godlee, F. (2015). Statins for people at low risk. BMJ, 351.

13- Blais, J. E., Chan, E. W., Law, S. W., Mok, M. T., Huang, D., Wong, I. C., & Siu, C. W. (2019). Trends in statin prescription prevalence, initiation, and dosing: Hong Kong, 2004–2015. Atherosclerosis, 280, 174-182.

14- Salami, J. A., Warraich, H. J., Valero-Elizondo, J., Spatz, E. S., Desai, N. R., Rana, J. S., ... & Nasir, K. (2018). National trends in nonstatin use and expenditures among the US adult population from 2002 to 2013: insights from medical expenditure panel survey. Journal of the American Heart Association, 7(2), e007132.

15-Hansson, G. K. (2005). Inflammation, atherosclerosis, and coronary artery disease. New England journal of medicine, 352(16), 1685-1695.

16-Blankenberg, S., Zeller, T., Saarela, O., Havulinna, A. S., Kee, F., Tunstall-Pedoe, H., ... & Salomaa, V. (2010). Contribution of 30 biomarkers to 10-year cardiovascular risk estimation in 2 population cohorts: the MONICA, risk, genetics, archiving, and monograph (MORGAM) biomarker project. Circulation, 121(22), 2388-2397.

17- Janik, S., Bekos, C., Hacker, P., Raunegger, T., Ghanim, B., Einwallner, E., ... & Moser, B. (2017). Elevated CRP levels predict poor outcome and tumor recurrence in patients with thymic epithelial tumors: A pro-and retrospective analysis. Oncotarget, 8(29), 47090.

18- Schimmack, S., Yang, Y., Felix, K., Herbst, M., Li, Y., Schenk, M., ... & Strobel, O. (2019). C-reactive protein (CRP) promotes malignant properties in pancreatic neuroendocrine neoplasms. Endocrine connections, 8(7), 1007-1019.

19- Inoue, K., Yoshiuchi, S., Yoshida, M., Nakamura, N., Nakajima, S., Kitamura, A., ... & Kon, M. (2019). Preoperative weight loss program involving a 20-day very low-calorie diet for obesity before laparoscopic gastrectomy for gastric cancer. Asian Journal of Endoscopic Surgery, 12(1), 43-50.

20-Mohan, D. F. R., Jawad, A. T., & Jaber, A. S. (2024). Review Article: Rheumatoid Arthritis and its Relationship with Vitamin D, ESR, and Obesity. International Journal of Toxins and Toxics, 1(1), 6-12p..

21- Shi, L. H., Lam, S. H. M., So, H., Meng, H., & Tam, L. S. (2024, August). Impact of inflammation and anti-inflammatory therapies on the incidence of major cardiovascular events in patients with ankylosing spondylitis: A population-based study. In Seminars in Arthritis and Rheumatism (Vol. 67, p. 152477). WB Saunders.

22 -Xue, L., Tao, L., Li, X., Wang, Y., Wang, B., Zhang, Y., ... & Li, M. (2021). Plasma fibrinogen, D-dimer, and fibrin degradation product as biomarkers of rheumatoid arthritis. *Scientific Reports*, *11*(1), 16903.

23-Stec, J. J., Silbershatz, H., Tofler, G. H., Matheney, T. H., Sutherland, P., Lipinska, I., ... & D'Agostino Sr, R. B. (2000). Association of fibrinogen with cardiovascular risk factors and cardiovascular disease in the Framingham Offspring Population. Circulation, 102(14), 1634-1638.

24-Erre, G. L., Cacciapaglia, F., Sakellariou, G., Manfredi, A., Bartoloni, E., Viapiana, O., Fornaro, M., Cauli, A., Mangoni, A. A., Woodman, R. J., Palermo, B. L., Gremese, E., Cafaro, G., Nucera, V., Vacchi, C., Spinelli, F. R., Atzeni, F., Piga, M., & "Cardiovascular, Obesity and Rheumatic Disease Study (CORDIS) Group" of the Italian Society of Rheumatology (SIR) (2022). C-reactive protein and 10-year cardiovascular risk in rheumatoid arthritis. European journal of internal medicine, 104, 49–54.

25-Lee, S. H., Kim, Y. J., Park, H. S., & Choi, J. H. (2023). Chronic inflammation and cardiovascular risks in rheumatoid arthritis: A systematic review and meta-analysis. Journal of Preventive and Translational Clinical Practice, 7(1), 22–34.

26- Del Rincón, I., Williams, K., Stern, M. P., Freeman, G. L., & Escalante, A. (2001). High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional risk factors. Arthritis & Rheumatism, 44(12), 2737–2745.

27~ Van Doornum, S., McColl, G., & Wicks, I. P. (2002). Accelerated atherosclerosis: An extraarticular feature of rheumatoid arthritis?. Arthritis & Rheumatism, 46(4), 862–873.

28- - Benucci, M., Sarzi-Puttini, P., & Atzeni, F. (2023). Cardiovascular risk and biologic therapies in rheumatoid arthritis: A systematic review of recent evidence. *Journal of Clinical Rheumatology*, 29(4), 134–143.

29- Smith, J., Zhao, L., & Yang, T. (2022). Tumor Necrosis Factor-α and cardiovascular risk in rheumatoid arthritis patients: A longitudinal study. *Journal of Cardiovascular Research*, 43(4), 346–356.

30~ Jones, M. R., Stevens, S., & Lee, C. (2023). Fibrinogen as a predictor of cardiovascular events in patients with rheumatoid arthritis. *Journal of Rheumatology*, 50(3), 234–242.