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Detection of Some Physiological biomarker of Reumatoide Arthrites In Wasit Province \ Iraq

Zahra Karem Hady[1*] and Haider Hafudh Humaish [2]
[1]Department of Biology, Collage of Education for Pure Science , Wasit University , Iraq
[2]Department of Biology, Kut Technical Inshitate , Middle Technical University , Iraq
*Email: std2022304.zahraatya@uowasit.edu.iq

ABSTRACT: Rheumatoid arthritis (RA) is a multifaceted inflammatory disease with a significant hereditary component to its pathophysiology. Most of the population is vulnerable to this illness due to genetic factors. Predisposition to RA has been demonstrated to be influenced by genetic variables. Variation (or polymorphism) of the genes encoding numerous proteins known to be highly implicated in driving the inflammatory process in RA has been discovered in studies.The prevalence of RA was estimated to impact approximately 0.5 to 1% of the population worldwide with women being twice as likely as males to have the disease and the incidence of RA peaks in the fifth decade of life . Risk factors can be identified by studying reumatoide arthritis , where statistically significant differences are found in statistical analysis of some biomarkers in RA (Cathepsin K and G , Anti-Cyclic Citrullinated Peptides (ACCP) and Antinuclear Antibody (ANA), in addition to decreased But there was significant decrease of HDL level in RA patients in compared to healthy control.while increase to othere lipid profile (Triglycerides, Cholesterol, VLDL, LDL). 90 subjects of both genders were collected, including 60 patients and 30 from the control group. The results showed that the level of Reumatoide Arthrites had significant differences compared to the control group at $p \leq (0.05)$.

Keywords: Reumatoide Arthrites; Cathepsin K and G, ACCP, ANA, Lipid Profile, HDL, LDL, VLDL, CHOL, TG

1. INTRODUCTION

Rheumatoid Arthritis (RA) is a systemic disease characterized by a complex pathogenesis involving interactions between various cell types located in synovial compartments and peripheral blood, rather than resulting from a single pathogenic factor (1). The extra-articular manifestations in RA patients most commonly and severely impact the heart, lungs, larynx, and vascular systems. Involvement with extra-articular organs positively correlates with the severity of the disease, contributes to increased mortality, and is influenced by genetic and environmental factors (2). Clinical features of RA include swollen and tender joints, morning joint stiffness, elevated level of C-reactive protein or erythrocyte sedimentation rate. However, these features are not specific for rheumatoid arthritis, since similar features are also seen in other types of arthritis such as psoriatic arthritis and some inflammatory connective tissue diseases (3).

Exposure to smoking and specifically to tobacco may account for up to 30% of environmental risk in RA patients (4) The effect of 14 smoking on the pulmonary system may attribute to high inflammation of the pleural cavity with patients who experience symptoms from extra-articular manifestations in the lungs. Further evidence also indicates that diet, the health of the micro biome, and exposure to silica dust, are primary environmental risk factors for the development and severity of RA (5)

can be classified into 4 stages To RA. Early stage RA stage I: Is characterized by synovitis, or an inflammation of the synovial membrane, causing swelling of involved joints and pain upon motion, in moderate RA, stage II, there is a spread of inflammation in synovial tissue, affecting joint cavity space across joint cartilage , stage III, is marked by the formation of pannus in the synovium, loss of joint cartilage exposes bone beneath the cartilage,Stage IV Is called terminal or end stage RA ,the inflammatory process has subsided and the formation of fibrous tissue and or fusing of bone results in ceased joint function. This stage may be associated with the formation of subcutaneous nodules(6), At stage 4, there's no longer inflammation in the joint. This is end-stage RA, when joints no longer work, people may still experience pain, swelling, stiffness, and mobility loss, there may be reduced muscle strength (7)

2. MATERIALS AND METHODS

2.1 **Study Subjects:** This study was conducted at the Department of Biology - College of Science / Wasit University in cooperation with Al-Zahra Teaching Hospital of the Wasit Health Department, during the period from November, 2024 to March, 2025 - . The study included 90 samples, whose ages ranged from 18 to 70 years, 60 patients of both gender, who were clinically diagnosed with RA (based on RF, age, gender and Duration of disease) by a specialized physician and 30 healthy control. and verbal consent was obtained from the participants and they all agreed to contribute to the study. Samples (immunological) were excluded.

2.2: Methods: 5 ml of venous blood was drawn for both healthy and sick patients, , 5ml of blood was placed In gel tubes to obtain blood serum for measurement of indicators of Reumatoide Arthrites.

Blood samples were examined using the America-made Fine device, according to the manufacturer's instructions (Fine).The values of blood parameters were calculated for both patients and healthy subjects,by and the readings is recorded. Where the levels of (Cathepsin K and G ; ACCP; ANA and Lipid Profile(HDL;LDL,VLDL,CHOL,TG) were calculated.

2.3 **Statistical analysis :** The statistical analysis of the current study was based on (SPSS) version 26, which was based on the value of (Mean ± SD) to detect the effect of variation factors in the study parameters, using (ANOVA) method was used to find the least significant difference. (LSD) is used to compare the two groups (patients and control) within the tests studied under the probability level ($P \geq 0.05$),

RESULTS AND DISCUSSION

3.1. Result of ANA and ACCP : The results of the current study of RA, as shown in Table 1 As for our results for (ANA) and (ACCP) there is a significant difference, Anti-ccp with concentrations ≥100 IU/ml were considered as positive and with concentrations > 100 IU/ml were considered as negative. Also the mean of Anti-CCP were 125.53 ± 24.52, and 49.80 ± 12.97, in RA patients and healthy control group respectively; the mean was higher in patients with RA patients in compared to healthy control and the difference was significant (P= 0.001), table (1). Regarding to qualitative results: 33 (55.0%) of patients with RA were positive Anti-ccp, while all healthy control was negative and the difference was significant ($p < 0.05$). Furthermore ANA with concentrations ≥ 26 IU/ml were considered as positive and with concentrations < 26 IU/ml were considered as negative. Also the mean of ANA were 48.57 ± 11.62, and 23.07 ± 2.22, in RA patients and healthy control group respectively; the mean was higher in patients with RA patients in compared to healthy control and the difference was significant (P= 0.001). Regarding to qualitative results: 59 (98.3%) of patients with RA were positive ANA, while 5 (16.7%) of healthy control was positive and the difference was significant ($p < 0.05$).

Table (1)Diagnosis of rheumatoid arthritis of Antinuclear Antibody and Anti-CCP Antibody in RA patients and Healthy control

Parameters	RA patients	Healthy control	*P*
Anti-CCP Antibody (Quantitative results)			
Mean ± SD	125.53 ± 24.52	49.80 ± 12.97	0.001 † S
Range	28.00 –225.00	11.00 –99.00	
Anti-CCP Antibody (Qualitative results)			
Positive, *n* (%)	33 (55.0%)	0	0.001 ¥ S
Negative, *n* (%)	27 (45.0%)	30 (100.0%)	
Anti-nuclear Antibody (Quantitative results)			
Mean ± SD	48.57 ± 11.62	23.07 ± 2.22	0.001 † S
Range	22.60 –73.50	18.40 –26.90	
Anti-nuclear Antibody (Qualitative results)			
Positive, *n* (%)	59 (98.3%)	5 (16.7%)	0.001 ¥ S
Negative, *n* (%)	1 (1.7%)	25 (83.3%)	

Anti-CCP antibodies appear very early, even before the onset of symptoms(8).Studies have shown that a high titer of Anti-CCP antibody is a risk factor for radiographic progression and worsening disease activity in RA patients (9). Generally ,as mentioned in the above studies the level of Anti-CCP has become a key serologic marker in RA disease . It can be" used as a test for early diagnosis of RA; for the differential diagnosis between RA and other rheumatic or immune

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diseases; for prediction of prognosis; and for evaluation of treatment outcome"(10). The elevated ANA titers in RA patients may reflect increased B-cell activation and autoantibody production, processes that are central to RA pathogenesis and perpetuate joint and systemic inflammation (11).

The elevated ANA titers in RA patients may reflect increased B-cell activation and autoantibody production, processes that are central to RA pathogenesis and perpetuate joint and systemic inflammation (11). Moreover, recent literature has highlighted the utility of ANA testing in identifying RA patients at higher risk of developing complications such as secondary Sjögren's syndrome or interstitial lung disease (12). While ANA is not a specific marker for RA diagnosis, its presence in nearly all patients in this study suggests that it may have adjunctive value, particularly in clinical settings where seronegative RA is suspected or when autoimmune overlap syndromes are being considered. However, ANA testing should be interpreted with caution and in conjunction with other serological markers such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies, which possess greater diagnostic specificity for RA (13).

3.2. Result of Kathepsin (K and G) The comparison of Kathepsin (K and G) markers between RA patient and control group has been carried out and the results were demonstrated in table (2). Mean levels of Kathepsin K were 4.18 ± 0.91, and 2.75 ± 0.31 , in RA patients and healthy control group respectively; the mean levels was higher in RA patients in compared to healthy control and the difference was significant (P = 0.001). Also the mean of Kathepsin G were 3.74 ± 0.61, and 2.18 ± 0.21, in RA patients and healthy control group respectively; the mean was higher in patients with RA patients in compared to healthy control and the difference was significant (P = 0.001).

Table (2)Results of Kathepsin (K and G) markers in Patients and healthy controls

Groups		Kathepsin K	Kathepsin G
RA patients	Mean ± SD	4.18 ± 0.91	3.74 ± 0.61
	Range	2.40-7.80	2.40-5.80
Control	Mean ± SD	2.75 ± 0.31	2.18 ± 0.21
	Range	2.20-3.40	1.60-3.10
p-value		0.001 † S	0.001 † S

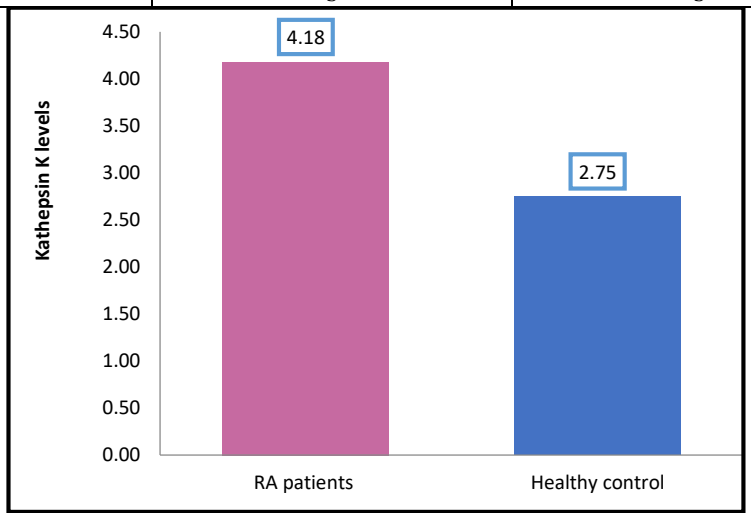

Figure (1): The means level of Kathepsin K in patients and control groups

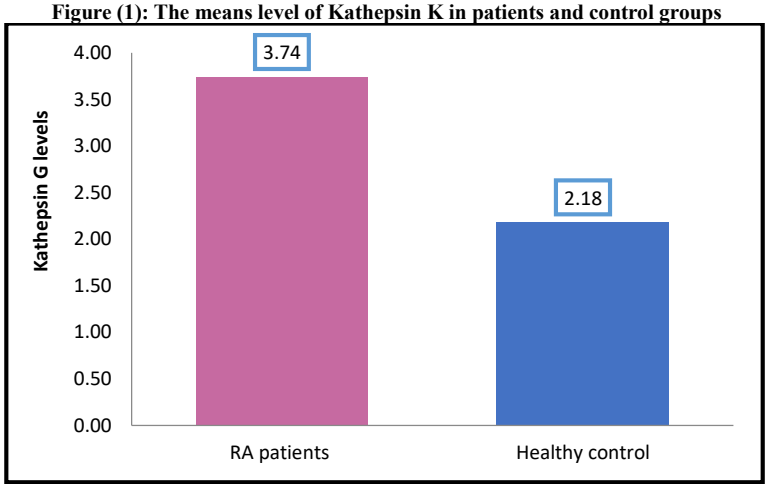

Figure (2): The means level of Kathepsin G in patients and control groups

The comparison of Cathepsin K and Cathepsin G levels between rheumatoid arthritis (RA) patients and healthy controls provides meaningful insights into the pathophysiological role of these proteolytic enzymes in RA. The data from Table (2) clearly demonstrate that both Cathepsin K and Cathepsin G levels are significantly elevated in the RA group compared to the control group, with P = 0.001 for both markers. This highly significant difference underscores their potential involvement in RA-related inflammation and joint destruction. Cathepsins are lysosomal proteases that play a crucial role in protein degradation, extracellular matrix remodeling, and immune response regulation. In the context of RA, Cathepsin K—a cysteine protease—is primarily expressed in osteoclasts and is known for its potent collagenolytic activity, particularly type I collagen degradation in bone. The elevated mean level of Cathepsin K (4.18 ± 0.91 in RA vs. 2.75 ± 0.31 in controls) suggests enhanced osteoclastic activity and supports the well-documented bone erosive nature of RA.(14). Cathepsin K plays a critical role in osteoclast-mediated bone resorption, while Cathepsin G is implicated in neutrophil-driven synovial inflammation, both of which are active early in RA pathogenesis.(15).

Similarly, Cathepsin G, a serine protease found in the azurophilic granules of neutrophils, contributes to tissue injury through degradation of cartilage matrix proteins and activation of pro-inflammatory cytokines, such as IL-1β and TNF-α. The observed increase in Cathepsin G levels (3.74 ± 0.61 in RA vs. 2.18 ± 0.21 in controls) further reinforces the neutrophil-mediated inflammatory response seen in RA pathogenesis.(16).

3.3. Results of lipid profile (Triglycerides, Cholesterol, VLDL, LDL and HDL) in patients and healthy controls

The comparison of lipid profile (Triglycerides, Cholesterol, VLDL, LDL and HDL) between patients and control group has been carried out and the results were demonstrated in table (3).Mean levels of serum triglycerides were 113.3 ± 17.11 mg/dl, 56.7 ± 15.5 mg/dl, in RA patients and healthy control group respectively;

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the mean levels was higher in patients group in compared to healthy control and the difference was significant (P= 0.001). The mean levels of serum cholesterol were 136.05 ± 23.2 mg/dl, 66.7 ± 9.58 mg/dl, in RA patients and healthy control group respectively; the mean levels was higher in RA patients in comparison with healthy control and the difference was highly significant (P < 0.001). Regarding the mean levels of serum Very-low-density lipoprotein (VLDL) were 27.18± 3.10 mg/dl and 20.07 ± 2.34 mg/dl, in RA patients and healthy control group respectively; the mean levels was higher in RA patients in compared to other group and the difference was significant (P= 0.018). The mean levels of serum low-density lipoprotein (LDL) were 84.3± 11.2 mg/dl and 38.21 ± 7.8 mg/dl, in RA patients and healthy control group respectively; the mean levels was higher in RA patients in comparison with healthy control and the difference was highly significant (P < 0.001). But there was significant decrease of HDL level in RA patients in compared to healthy control, (P > 0.05).

Table (3): Results of lipid profile (Cholesterol, Triglycerides, VLDL, LDL and HDL) in patients and healthy controls.

Groups	Chole (mg/dl)	TG (mg/dl)	VLDL (mg/dl)	LDL (mg/dl)	HDL(mg/dl)
RA patients	**136.05 ± 23.2**	**113.3 ± 17.11**	**27.18±** 3.10	**84.3±** 11.2	**35.79 ± 4.82**
	34.0-178.0	10.0-150.0	19.80-30.90	40.70-104.9	22.40-49.1
Control	**66.7** ± 9.58	**56.7** ± 15.5	**20.07** ± 2.34	**38.21** ± 7.8	**45.7** ± 2.32
	22.0-100.0	12.00-100.00	15.70-25.60	12.0-50.50	40.90-49.50
p-value	**0.001****	**0.001****	**0.018****	**0.001****	**0.001****

Chronic inflammation in RA leads to changes in lipid metabolism, resulting in higher triglyceride levels. This is often mediated by increased production of inflammatory cytokines, such as TNF-α and IL-6, which can promote the synthesis of triglycerides in the liver (17). Elevated cholesterol levels in RA patients could also contribute to the cardiovascular risk commonly seen in this population, making it a potential target for therapeutic intervention. (18). Elevated VLDL contributes to the accumulation of atherogenic lipoproteins in the circulation, increasing the risk of atherosclerosis and cardiovascular events in RA patients , the elevated LDL levels in RA patients could be a marker of an ongoing inflammatory process that predisposes them to cardiovascular diseases , HDL is widely known for its protective effects against cardiovascular disease, as it facilitates reverse cholesterol transport, removing cholesterol from peripheral tissues and arteries. Reduced HDL levels in RA patients could be indicative of an impaired ability to protect against atherosclerosis (19). However, some studies suggest that the relationship between RA and HDL is complex, as inflammation may alter the composition and functionality of HDL particles, rendering them less effective in preventing cardiovascular disease (20).

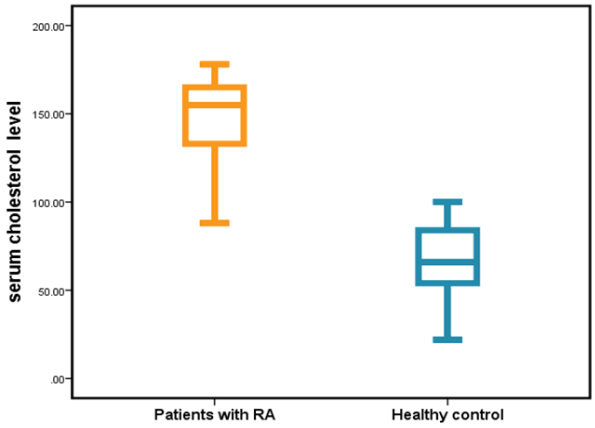

Figure (3)The means level of serum Cholesterol in patients and control groups.

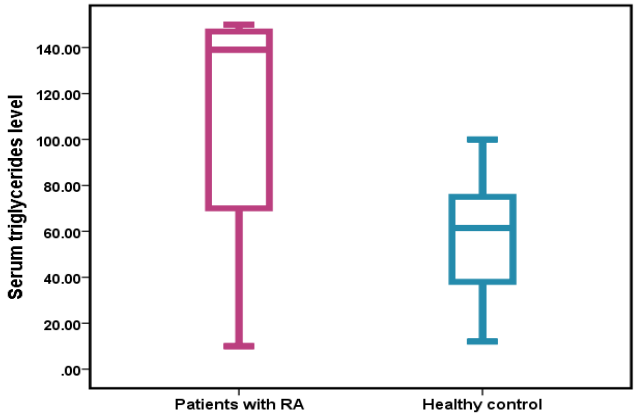

Figure (3-6): The means level of serum Triglycerides in patients and control groups

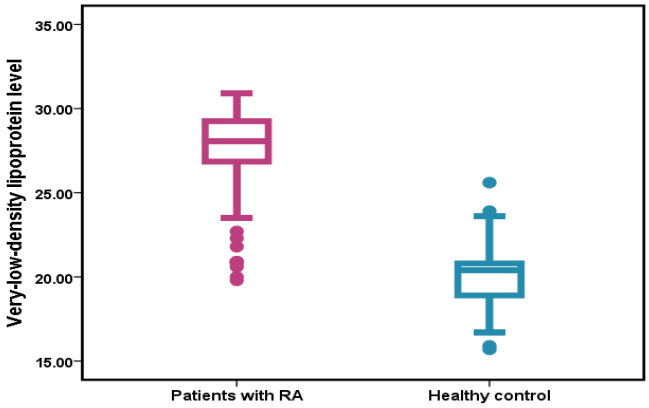

Figure (3-7): The means level of serum VLDL in patients and control groups

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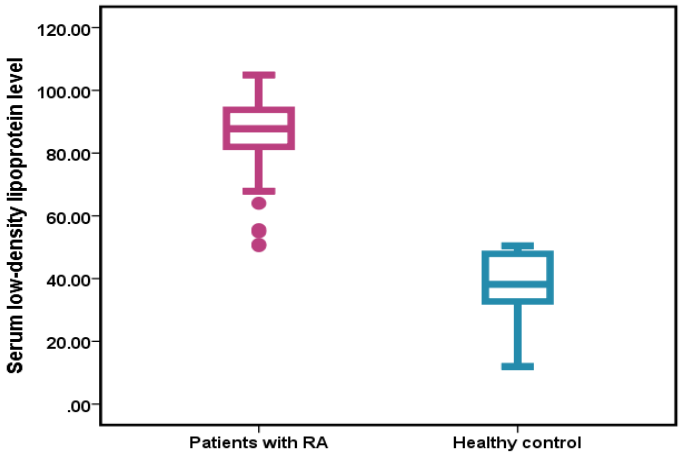

Figure (3-8): The means level of serum LDL in patients and control groups

3. CONCLUSION

The present study revealed that the levels of some blood parameters (Cathepsin K and G ; ACCP; ANA and Lipid Profile(LDL,VLDL,CHOL,TG).) was higher from the normal average. HDL decreased in patients suffering from Reumatoide Arthraites disease of all stages.

REFERENCES

1- McInnes, I.B. and Schett, G.,(2011). The pathogenesis of rheumatoid arthritis. New England Journal of Medicine, 365(23), pp.2205-2219.
2- Cojocaru, M., Cojocaru, I. M., Silosi, I., Vrabie, C. D., & Tanasescu, R. (2010). Extraarticular manifestations in rheumatoid arthritis. Maedica, 5(4), 286–291.
3- Smolen, J. S.; Aletaha, D. ;and McInnes, I. B.(2016). Rheumatoid arthritis. Lancet (London, England) 388, 2023-2038
4- Deane, K. D.; Demoruelle, M. K.; Kelmenson, L. B.; Kuhn, K. A.; Norris, J. M.; and Holers, V. M. (2017). Genetic and environmental risk factors for rheumatoid arthritis. Best practice & research Clinical rheumatology, 31(1), 3-18..
5- Badsha, H. (2018). Role of diet in influencing rheumatoid arthritis disease activity. The Open Rheumatology Journal,12(1), 19-28. doi: 10.2174/1874312901812010019.
6- Mikhail, A.; Brown. C.; Williams, J.A. (2017).Renal association clinical practice guideline on anaemia of chronic kidney disease. BMC Nephrol.;18:345.
7- Farid, S. S.; Azizi, G.; and Mirshafiey, A. (2013). Anti-citrullinated protein antibodies and their clinical utility in rheumatoid arthritis. International journal of rheumatic diseases, 16(4), 379-386
8- Peng, X., Wang, Q., Li, W., Ge, G., Peng, J., Xu, Y., Yang, H., Bai, J. and Geng, D., (2023). Comprehensive overview of microRNA function in rheumatoid arthritis. Bone Research, 11(1), p.8.
9- Syversen, S. W.; Goll, G. L.; van der Heijde, D.; Landewé, R.; Lie, B. A.;Ødegård, S.; and Kvien, T. K. (2010). Prediction of radiographic
10- Alfatlawi, R. B.; Al-Mashhadi, H. G.; Hameed, W. S.; and Aljazaeri, T. D.(2020). Comparative study between anti-ccp and rheumatoid factor as diagnostic value of rheumatoid arthritis patients. Health, 23(S6), 604-608
11- Kumar S, Zhang Y.(2024) B cell hyperactivity and autoantibody production in rheumatoid arthritis: mechanisms and therapeutic implications. Front Immunol. 15:1145002.
12- Park J, Kim S, Choi Y.(2025) Anti-nuclear antibodies and risk of interstitial lung disease in rheumatoid arthritis: a prospective cohort study. Clin Exp Rheumatol. 43(2):222–230.
13- Eisenberg R, Hernandez D, Watts R.(2024) Serological markers in early rheumatoid arthritis: role of ANA in the context of RF and anti-CCP. J Autoimmun. 138:103058.
14- Abdulrahaman, Y.; Osaro, E.; Uko, E. K.;Isaac, I. Z.; Bello, Z.; Liman, H. M. (2013). Packed cell volume, Reticulocyte count and index among patients with chronic kidney disease in Sokoto, North-western Nigeria. Journal of Medical and Health Sciences, 2319-9865.
15- Zhao L, et al.(2024) Role of Cathepsin K in early RA joint damage. Clin Rheumatol. 43(3):487–495.15- Etim, E. A. (2018). Effect of maintenance hemodialysis on red cell indices and erythrocyte sedimentation rate in northeast Nigeria. Age (years), 50(58), 0-01.
16- Zhang, Z., Liu, Y., & Wang, L. (2024). Inflammatory cytokines and lipid metabolism in rheumatoid arthritis. Autoimmunity Reviews, 23(1), 37-44.
17- Feldmann, M., Maini, R. N., & Taylor, P. C. (2023). Mechanisms of action of TNF inhibitors in rheumatoid arthritis. Nature Reviews Rheumatology, 19(3), 141-151.
18- Lei Q, Yang J, Li L, et al.(2023) .Lipid metabolism and rheumatoid arthritis. Front Immunol. 14:1190607.
19- Mikuls, T. R., & Liao, K. P. (2023). Dyslipidemia and cardiovascular risk in patients with rheumatoid arthritis. Arthritis Research & Therapy, 25(1), 15-23.
20- McInnes, I. B., & Schett, G. (2023). The pathogenesis of rheumatoid arthritis. New England Journal of Medicine, 378(11), 1026-1039.