



Estimation of some functional testing of Liver , kidney and some of lipid profiles of women suffering from rheumatoid arthritis

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Abstract

The present study was conducted in Basrah city/Iraq on women suffering rheumatoid arthritis. The study aimed to evaluating some biochemical parameters such as liver enzymes, kidney function and lipid profiles in serum of female patients . In this study, 90 samples of blood were collected from women: 60 samples from women with rheumatoid arthritis and 30 samples from non-patient women who were considered a healthy group. The samples were obtained from Basra General Hospital. The results obtained from the functional tests of the liver indicated a significant decrease in the level of Aspartate Aminotransferase (AST) enzyme in the serum of patients compared to healthy group, while the Alanine Aminotransferase (ALT) enzyme did not show any level of significance. While, the level of Alkaline phosphatase (ALP) enzyme recorded a significant increase in patients compared to the healthy female. Moreover, the results of the kidneys functional tests showed no significant differences in the concentration of creatinine and total protein between patients and healthy female, while a significant increase in the concentration of Urea was found in the patients compared to healthy female. The lipid profiles, showed that there were no significant differences in the cholesterol concentration between patients and healthy female. However, the concentration of triglycerides increased significantly in arthritis patients compared to healthy female. The present study concluded that it appears that there are no abnormalities in liver function in patients with rheumatoid arthritis, depending on the concentration of liver enzymes, while the significant increase in Urea concentration is an indicator of renal impairment in rheumatic patients. In addition, the results of the lipid profile test showed a significant increase in the concentration of triglycerides in the serum of patients, which indicates that lipid profile changes are associated with rheumatoid arthritis and can be considered as an important risk factor in rheumatoid arthritis patients.

Keywords: Liver enzymes, kidneys functions, Lipid profiles, Rheumatoid Arthritis.

1. Introduction

Rheumatoid arthritis (RA) is a common chronic inflammatory autoimmune disease. It takes the shape of a devastating and irremediable arthropathy and thus causes progressive disability and systemic complications (Heo *et al.*, 2017). Although the main causes of the disease are unknown, it has been found that oxidative stress, genetic and hormonal factors, viral and

bacterial factors and environmental stimuli can be generally recognized as potential causes that lead to the development of this disease (Weinblatt & Kuritzky, 2007). Rheumatism is considered one of the most prevalent diseases in the world, with an estimated incidence of 0.8-1% in the population. Although rheumatoid arthritis usually develops at the age of 40-60 years, it may also develop at any age, and females are at a higher risk of developing rheumatoid arthritis than males by 1:3 (American College of Rheumatology, 2013).

Although liver injury is not common in patients with rheumatoid arthritis, it has been proven that liver enzyme disorders occur in about 5-77% of RA patients (Kojima *et al.*, 2002). In the study by Olago-Rakuomi *et al.* (2017), 107 patients with rheumatism participated and the prevalence of abnormal liver function tests in rheumatic patients was determined. The study concluded that the prevalence of abnormal liver function tests was observed in 57% of patients, and the most abnormal tests were associated with ALP enzyme in 15% of patients and bilirubin pigment in 34.6% of patients. It was noted that high ALP enzyme was associated with high body mass index and disease duration. In the study (Ajlan & Baqir, 2011), they concluded that there is a strong relationship between liver enzyme changes and coronary heart disease, and that these indicators may be added to the list of factors causing the disease, its development and the possibility of complications.

Renal impairment is common among patients with rheumatoid arthritis, although the relationship between chronic inflammation and the incidence of kidney disease is not often clear in rheumatic patients (Karstila *et al.*, 2007). The study by Kochi *et al.* (2016) was conducted to evaluate the relationship between the levels of acute proteins phase and the chronic kidney disease in RA patients. 345 patients participated in the study, and Glomerular filtration rate and proteinuria were measured. The study concluded that about 14% of RA patients developed chronic kidney disease, which indicates that inflammation is an indicator of the risk of exacerbation of chronic kidney disease in patients with rheumatism.

Some studies indicated changes in the lipids profile in patients with rheumatoid arthritis. In the study by Turesson *et al.* (2015) on the effect of high total cholesterol and triglycerides on increasing the risk of RA, 290 patients with rheumatism (151 men and 139 women) and 1160 healthy individuals participated. The study showed that women with rheumatism had higher levels of total cholesterol compared to healthy subjects, and these levels were statistically associated with smoking, menopause, and the presence of rheumatoid factor (RF), while in men, total cholesterol had no significant effect on the development of arthritis. Moreover, the study found that triglycerides were not associated with the development of arthritis in both men and women. The present study aims to evaluate some biochemical parameters represented by liver enzymes, kidney function and lipid profiles in the serum of patient women and the relationship of these parameters to inflammation.

2. Materials and Methods

2.1 Samples collection

60 samples of blood were obtained from women with rheumatoid arthritis, which have attended the Joint Consultant at Basra General Hospital. And 30 samples of blood were obtained from healthy women after making sure that they were not diagnosed with rheumatoid arthritis.

2.2 Preparation of serum

From each woman, 5mL of blood was drawn from the vein of the elbow using a clean medical syringe, then the blood was collected in a gel tube and left for 20 minutes. Then the samples were centrifuged at 3000 rpm for 15 minutes to obtain the blood serum. The obtained serum was divided and collected in 1.5 mL Eppendorf tubes, and the samples were stored at -20°C in deep freeze until tests were carried out.

2.3 Estimation of biochemical concentrations

The concentration of liver enzymes (ALT, AST and ALP) was estimated using the measurement kits supplied by the French companies Randox and Biolabo. These kits were used for Cholesterol, Triglycerides, Creatinine, and Total protein tests. The examination kit supplied by the Egyptian company Spectrum was used for the examination of urea, following the leaflet attached to each kit.

3. Statistical analysis

Statistical analysis of the data was carried out using the T-test and the analysis of variance (ANOVA) test for the least significant difference LSD at the probability level of $P < 0.05$. The standard deviation was calculated using the SPSS program version 21.

4. Results

4-1 Liver enzymes

The results of the current study showed that there was no significant difference at the probability level of $P < 0.05$ in the concentration of ALT enzyme in patients with rheumatoid arthritis (13.28 ± 5.48 U/L) compared with healthy group (12.26 ± 6.02 U/L). The table also showed that the concentration of AST enzyme decreased significantly in the patients (17.01 ± 5.90 U/L) compared with healthy group (36.40 ± 10.64 U/L). In addition, arthritis caused a significant increase in the concentration of ALP enzyme in patients (13.10 ± 7.89 U/100 mL) compared with healthy subjects (2.72 ± 1.87 U/100 mL), as shown in Table (1).

Table 1: The concentration of liver enzymes in the serum of patients and healthy subjects

Parameters	mean $\pm$ standard deviation	
	Patient group, number = 60 samples	healthy group, number = 30 samples
ALT U/L	13.28 ± 5.48	12.26 ± 6.02
AST U/L	17.01 ± 5.90 *	36.40 ± 10.64
ALP U/100ml	13.10 ± 7.89 *	2.72 ± 1.87

* Significant difference at the probability level of $P < 0.05$ in the groups

4-2 kidneys functions

With regard to the results obtained from table (2) showed that there was no significant difference at the probability level of ($P < 0.05$) in the concentration of creatinine and total proteins between rheumatic patients and the healthy group, as the concentration of creatinine in the group of patients was (1.56 ± 0.48 mg/dL) compared to its concentration in the healthy group (1.38 ± 0.35 mg/dL). The total protein concentration in the group of patients was (13.07 ± 2.30 mg/dL) compared to its concentration in the healthy group (12.82 ± 2.30 mg/dL). However, its same table appeared a significant increase in the urea concentration was

observed in the patients (79.21 ± 20.75 mg /dL)) compared with healthy female (63.32 ± 14.90 mg/dL) .

Table 2: The concentration of creatinine, total protein and urea in the serum of the patient group compared to the healthy group

Parameters	mean $\pm$ standard deviation	
	Patient group, number = 60 samples	healthy group, number = 30 samples
Creatinine mg/dL	1.56 ± 0.48	1.38 ± 0.35
Total protein mg/dL	13.07 ± 2.30	12.82 ± 2.65
Urea mg/dL	79.21 ± 20.75 *	63.32 ± 14.90

* Significant difference at the probability level of $P < 0.05$ in the groups

4-3 Lipid profiles

The results of lipid profiles shown in Table (3) that there was no significant difference in cholesterol concentration in the patients (219.50 ± 76.93 mg/dL) compared with healthy female (202.22 ± 90.12 mg/dL). The concentration of triglycerides increased significantly in the patients (219.98 ± 59.57 mg/dL)) compared to its concentration in the healthy female (135.40 ± 34.16 mg/dL).

Table 3: The concentration of cholesterol and triglycerides in the serum of the patients group compared to the healthy group

Parameters	mean $\pm$ standard deviation	
	Patient group, number = 60 samples	healthy group, number = 30 samples
Cholesterol mg/dL	219.50 ± 76.93	202.22 ± 90.12
Triglycerides mg/dL	219.98 ± 59.57 *	135.40 ± 34.16

* Significant difference at the probability level of $P < 0.05$ in the groups

5. Discussion

The liver is one of the largest lymphoid organs in the human body. It serves as a primary line of defense and plays an important role in modulating the inflammatory response in autoimmune diseases. The liver produces many enzymes, the most important of which are alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP), which are indicators of vital and functional disorders of the liver (Tiegs & Lohse, 2010).

The results of the present study of women with rheumatoid arthritis showed that there were no significant differences in the concentration of ALT in the serum of patients and healthy subjects, while significant differences were found in the concentration of both AST and ALP enzymes. The results of the present study are not in agreement with the results of previous studies (Tawfeeq&Ali, 2012; Karlsson Sundbaum *et al.*, 2019) which reported an increase in the concentrations of ALT and AST in rheumatic patients compared to healthy subjects. However, our results are in agreement with another study by Thompson *et al.* (1990) which indicated that the concentration of ALT enzyme did not increase in the patients and was within the normal ranges.

The results of this study showed a significant increase in the concentration of ALP enzyme in the patients compared to healthy subjects, and these results agreed with the results of other studies (Selmi1 *et al.*, 2011; Olago-Rakuomi *et al.*, 2017). Indeed, the increase in the liver enzymes may be due to liver disorders caused by take disease-modifying and anti-rheumatic drugs. Study by Amital *et al.* (2009), he was found that 45% of rheumatic patients receiving methotrexate MTX and other treatments caused increase in the concentration of ALP enzyme and albumin.

Many physiological factors, including gender, age, high triglycerides, body mass index, blood sugar level and insulin resistance, may contribute to the elevation of some liver enzymes in the serum (Chen *et al.*, 2018; Al-Akabi *et al.*, 2019). Moreover, the reason for the lack of a significant difference in the concentration of ALT enzyme between patients and healthy subjects may be due to the enzyme that is higher in males than in females, and this is likely associated with hormonal differences between the two sexes (Sohn *et al.*, 2013).

With regard to the results obtained from the functional tests of the kidneys, the results showed that there were no significant differences in the concentrations of creatinine and total proteins in the patients compared to the healthy subjects. The results of the present study are not in agreement with another study (Isaacs *et al.*, 2014) which reported that there was an increase in the concentration of creatinine in the rheumatic patients treated with Tofacitinib, and the study attributed this to the effect of this treatment on the inflammatory condition.

The results of the present study revealed a significant increase in urea concentration in the patients compared to the healthy group. These results are in agreement with the results of the study by Hannawi *et al.* (2018). However, the results of this study do not agree with the results of another study (Choe & Kim, 2015) which concluded that there was a decrease in the concentration of uric acid in the rheumatic patients after being treated with leflunomide by increasing renal excretion of urea.

The cause of the high concentration of urea in the serum may be attributed to the stimulation of the production of inflammatory cytokines such as (TNF- α , IL-6, IL-1 β) by the monocytes in the body when inflammation occurs. This is because urea is an important stimulant for the production of cytokines in the body, which indicates that urea contributes to the systemic inflammations such as rheumatism, as it was believed to have an important role as an antioxidant factor (Lyngdoh *et al.*, 2011).

The results of lipid profile tests showed that there were no significant differences in the concentration of total cholesterol in the patients compared to the healthy subjects, while the triglyceride concentration significantly increased in the patients compared to the healthy

subjects. The results of the present study agree with the results of the study by (Rodríguez-Carrio *et al.*, 2017). Although the relationship between lipid profiles and rheumatoid arthritis is not clearly identified, many studies indicate changes in lipid profiles in patients with active rheumatism, especially in lipoproteins, total cholesterol and triglycerides (Chapman *et al.*, 2011; Robertson *et al.*, 2013).

The cause of the high triglycerides may be attributed to the decrease in the antioxidants of the body and the dysfunction of high-density lipoprotein HDL (Toms *et al.*, 2011). The results of this study are disagreement with the results of another study (Khadim & Al-Fartusie, 2021) they found a significant increase in the different lipid compounds in the serum of the patients compared to the healthy subjects, and they attributed the cause of this to the effect of non-steroidal anti-inflammatory treatments. In the study by Charles-Schoeman *et al.* (2018), they concluded that lipids serum decreases in the case of chronic inflammation in patients with active rheumatism, and lipids may increase after the therapeutic response to Sarilumab treatment.

6. Conclusion

This study concluded that patients suffering from rheumatoid arthritis don't effect the liver function, depending on the concentration of liver enzymes (ALP, AST and ALT). Although there was a significant increase in the concentration of ALP enzyme, it remained within the normal limits of the enzyme concentration in the serum, which range between 41-133 U/L. Also the results showed a significant increase in the concentration of urea in the serum of the patients above the normal range of (7-20 mg/dL) and this is an indication of kidney dysfunction in rheumatic patients caused by inflammation. With respect to lipid profiles, the study revealed a significant increase in the concentration of triglycerides in the serum of patients above the normal limits, which is estimated at (150 mg/dL). This indicates that changes in lipid profiles are associated with rheumatoid arthritis. Therefore, high triglycerides can be considered as an important risk factor in rheumatoid arthritis patients.

References

- Ajlan, S. K. & Baqir, Y. A. (2011). Changes of Liver Enzymes in Coronary Heart Disease. *Karbala J. Med.*,4(1,2) : 994-1001.
- Al-Akabi , D. F. , Kata, F. S. , Khosho, E. Z. (2019). Estimation of biochemical and immunological parameters alteration in women with polycystic ovary syndrome in Basrah.*EJBPS*,6(5) : 607-611.
- American College of Rheumatology.(2013). Rheumatoid arthritis. Available at: http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.asp. Updated August 2012. Accessed December 9, 2013.
- Amital, H., Arns, Y., Chodick, G., and Shalev, V. (2009). Hepatotoxicity rates do not differ in patients with rheumatoid arthritis and psoriasis treated with methotrexate. *Rheumatology (Oxford, England)*, 48(9):1107–1110. doi: 10.1093 / rheumatology /kep176.
- Chapman, M. J., Ginsberg, H. N., Amarencu, P., Andreotti, F., Borén, J., Catapano, A. L., Descamps, O. S., Fisher, E., Kovanen, P. T., Kuivenhoven, J. A., Lesnik, P., Masana, L., Nordestgaard, B. G., Ray, K. K., Reiner, Z., Taskinen, M. R., Tokgözoğlu, L., Tybjaerg-

- Hansen, A., Watts, G. F., and European Atherosclerosis Society Consensus Panel (2011). Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. *European heart journal*, 32(11): 1345–1361. <https://doi.org/10.1093/eurheartj/ehr112>.
- Charles-Schoeman C., St. John G., Leher H., Kimura T., van Hoogstraten H., Nurmohamed M.T., González-Gay M.A. and Keystone E.C.(2018). The Relationship between Lipid Profile Changes and Inflammation across the Phase 3 Sarilumab Rheumatoid Arthritis (RA) Developmental Program. *Arthritis Rheumatol.*; 70 (suppl 10).
- Chen, K. W., Meng, F. C., Shih, Y. L., Su, F. Y., Lin, Y. P., Lin, F., Lin, J. W., Chang, W. K., Lee, C. J., Li, Y. H., Hsieh, C. B., and Lin, G. M. (2018). Sex-Specific Association between Metabolic Abnormalities and Elevated Alanine Aminotransferase Levels in a Military Cohort: The CHIEF Study. *International journal of environmental research and public health*, 15(3): 545. [PubMed PMID: 29562671].
- Choe, J. Y., and Kim, S. K. (2015). Association between serum uric acid and inflammation in rheumatoid arthritis: perspective on lowering serum uric acid of leflunomide. *Clinica chimica acta; international journal of clinical chemistry*, 438: 29–34. doi: 10.1016 /j.cca .2014 .07.039.
- Hannawi S., Salmi I. and Hannawi H. (2018). Factors contribute to the level Uric acid in rheumatoid arthritis. *Annals of the Rheumatic Diseases* 77 (Suppl 2) : 1367-1367. <http://dx.doi.org/10.1136/annrheumdis-2018-eular.4249>.
- Heo R., You D.G., Um W., Choi K.Y., Jeon S., Park J.S., Choi Y., Kwon S., Kim K., Kwon I.C., Jo D.G., Kang Y.M. and Park J.H.(2017). Dextran sulfate nanoparticles as a theranostic nanomedicine for rheumatoid arthritis. *Biomaterials*,131:15-26. doi: 10.1016/j.biomaterials.2017.03.044.
- Isaacs, J. D., Zuckerman, A., Krishnaswami, S., Nduaka, C., Lan, S., Hutmacher, M. M., Boy, M. G., Kowalski, K., Menon, S., and Riese, R. (2014). Changes in serum creatinine in patients with active rheumatoid arthritis treated with tofacitinib: results from clinical trials. *Arthritis research & therapy*, 16(4): R158. <https://doi.org/10.1186/ar4673>.
- Karlsson Sundbaum, J., Eriksson, N., Hallberg, P., Lehto, N., Wadelius, M., and Baecklund, E. (2019). Methotrexate treatment in rheumatoid arthritis and elevated liver enzymes: A long-term follow-up of predictors, surveillance, and outcome in clinical practice. *International journal of rheumatic diseases*, 22(7): 1226–1232. doi: 10.1111/1756-185X.13576.
- Karstila, K., Korpela, M., Sihvonen, S., and Mustonen, J. (2007). Prognosis of clinical renal disease and incidence of new renal findings in patients with rheumatoid arthritis: follow-up of a population-based study. *Clinical rheumatology*, 26(12): 2089–2095. <https://doi.org/10.1007/s10067-007-0625-y>
- Khadim, R. M. and Al-Fartusie, F. S. (2021). Evaluation of Liver Function and Lipid profiles in Iraqi patients with Rheumatoid Arthritis. In *Journal of Physics: Conference Series* , 1853(1): 012040). doi:10.1088/1742-6596/1853/1/012040.

- Kochi, M., Kohagura, K., Shiohira, Y., Iseki, K. and Ohya, Y. (2016). Inflammation as a Risk of Developing Chronic Kidney Disease in Rheumatoid Arthritis. *PloS one*, 11(8): e0160225. <https://doi.org/10.1371/journal.pone.0160225>.
- Kojima, H., Uemura, M., Sakurai, S., Ann, T., Ishii, Y., Imazu, H., Yoshikawa, M., Ichijima, K. and Fukui, H. (2002). Clinical features of liver disturbance in rheumatoid diseases: clinicopathological study with special reference to the cause of liver disturbance. *Journal of gastroenterology*, 37(8): 617–625. <https://doi.org/10.1007/s005350200098>.
- Lyngdoh, T., Marques-Vidal, P., Paccaud, F., Preisig, M., Waeber, G., Bochud, M. and Vollenweider, P. (2011). Elevated serum uric acid is associated with high circulating inflammatory cytokines in the population-based Colaus study. *PloS one*, 6(5): e19901. <https://doi.org/10.1371/journal.pone.0019901>
- Olago-Rakuomi, A., Oyoo, G.O., Kamau, E., Genga, E., Okalebo, F. and Ogutu E. (2017). Prevalence of abnormal liver function tests in rheumatoid arthritis. *Afr J Rheumatology*, 5(1): 70-75 .
- Robertson, J., Peters, M. J., McInnes, I. B. and Sattar, N. (2013). Changes in lipid levels with inflammation and therapy in RA: a maturing paradigm. *Nature reviews. Rheumatology*, 9(9): 513–523. <https://doi.org/10.1038/nrrheum.2013.91>
- Rodríguez-Carrio, J., Alperi-López, M., López, P., López-Mejías, R., Alonso-Castro, S., Abal, F., Ballina-García, F. J., González-Gay, M. Á. and Suárez, A. (2017). High triglycerides and low high-density lipoprotein cholesterol lipid profile in rheumatoid arthritis: A potential link among inflammation, oxidative status, and dysfunctional high-density lipoprotein . *Journal of clinical lipidology*, 11(4):1043–1054 . e2. <https://doi.org/10.1016/j.jacl.2017.05.009>
- Selmi, C., De Santis, M., and Gershwin, M. E. (2011). Liver involvement in subjects with rheumatic disease. *Arthritis research & therapy*, 13(3): 226. <https://doi.org/10.1186/ar3319>
- Sohn, W., Jun, D. W., Kwak, M. J., Park, Q., Lee, K. N., Lee, H. L., Lee, O. Y., Yoon, B. C. and Choi, H. S. (2013). Upper limit of normal serum alanine and aspartate aminotransferase levels in Korea. *Journal of gastroenterology and hepatology*, 28(3): 522–529. <https://doi.org/10.1111/j.1440-1746.2012.07143.x> .
- Tawfeeq, H. R. and Ali, J. M. (2012). Assessment of Liver Enzymes Activity in Patients with Rheumatoid Arthritis in Nineveh province. *Tikrit Journal of Pharmaceutical Sciences* ,8: 138-144.
- Thompson, P. W., Houghton, B. J., Clifford, C., Jones, D. D., Whitaker, K. B. and Moss, D. W. (1990). The source and significance of raised serum enzymes in rheumatoid arthritis. *The Quarterly journal of medicine*, 76(280): 869–879. PMID: 1977186 .
- Tiegs, G. and Lohse, A. W. (2010). Immune tolerance: what is unique about the liver. *Journal of autoimmunity*, 34(1): 1–6. <https://doi.org/10.1016/j.jaut.2009.08.008>
- Toms, T. E., Panoulas, V. F., Douglas, K. M., Nightingale, P., Smith, J. P., Griffiths, H., Sattar, N., Symmons, D. P. and Kitas, G. D. (2011). Are lipid ratios less susceptible to

change with systemic inflammation than individual lipid components in patients with rheumatoid arthritis? *Angiology*. 62(2):167-75 . doi: 10.1177/0003319710373749.

Turesson, C., Bergström, U., Pikwer, M., Nilsson, J. Å. and Jacobsson, L. T. (2015). High serum cholesterol predicts rheumatoid arthritis in women, but not in men: a prospective study. *Arthritis research & therapy*, 17(1): 284. doi.org/10.1186/s13075-015-0804-1.

Weinblatt, M. E., & Kuritzky, L. (2007). RAPID: rheumatoid arthritis. *The Journal of family practice*, 56(4 Suppl), S1–S8. PMID: 17403322.