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Impact of Rheumatoid Arthritis on Some Immunological Aspects and Lipid Profile of Type 2 Diabetes in Nasiriyh City, Iraq

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Abstract

Background: Rheumatoid arthritis A systemic autoimmune disease causes polyarthritis and organ damage. Insulin resistance is associated with inflammatory indicators. Glycated hemoglobin (HbA1c), a biomarker for continuous glucose monitoring, and 1,5-ahydroglucitol are found in the blood in high but consistent amounts under normal conditions. Disease-modifying anti-rheumatic drugs raise lipid levels. The aim of study was to evaluate whether or not there is a relationship between rheumatoid arthritis and diabetes mellitus, using many immunological and biochemical criteria.

Methods: Current research on rheumatoid arthritis and diabetes mellitus was conducted at Al-Nasriyah Education Hospital with one hundred blood samples collected from patients. Divided into four groups, this study employed immunological (1,5-anhydroglucitol) and biochemical (random blood sugar, total triglyceride, and total cholesterol) data.

Result: In the current study, the control group had more 1,5-anhydroglucitol than the patients. significant increases in random blood sugar, triglyceride, total cholesterol, and HbA1c in patients with only diabetes and patients with both diseases, as well as a significant difference between rheumatoid patients and controls.

Conclusion: Patients with type 2 diabetes mellitus who have low 1,5-ahydroglucrtol levels may be strong predictors of diabetes mellitus. Rheumatoid arthritis patients may have an effect on lipid profiles, HbA1c percentages, and 1,5-ahydroglucrtol levels, which should be evaluated throughout the illness.

Keywords: Rheumatoid arthritis, Diabetes mellitus, 1,5-Anhydroglucitol, HbA1c, lipid profile.

1. Introduction

Rheumatoid arthritis, also known simply as RA, is a systemic autoimmune condition that causes inflammatory polyarthritis as well as organ failure. Particularly, immunological abnormality-driven persistent synovitis causes aberrant bone and cartilage metabolism and increased IL-6 and tumor necrosis factor (TNF) production. Permanent joint deterioration results (1). In RA patients, peripheral insulin resistance, which is associated with inflammatory indicators and normalizes after glucocorticoid therapy to reduce inflammation (2), Pancreatic beta cell activity was observed to be compromised in prior studies of RA patients who were not diabetic (3). Since insulin resistance has been hypothesized to link rheumatoid arthritis (RA) and type 2 diabetes mellitus (T2DM), their metabolic interaction is currently being researched (4). Insulin resistance develops when insulin fails to activate insulin receptors (IRs). Inflammatory cytokines influence the expression of IRs on the surfaces of adipose tissue, muscle, synovial cells, and T lymphocytes (5).

Glycated hemoglobin (HbA1c), a biomarker for continuous glucose monitoring, measures blood glucose levels over the past 60 to 90 days. Human hemoglobin (Hb) chain N-terminal valine and glucose non-enzymatically form this stable protein in serum. As a result, short-term changes in glucose do not affect its concentration (6). Patients with splenectomy or iron deficiency anemia have lower RBC counts, which increase the glycation rate of Hb and contribute to the high value of HbA1c (7). HbA1c is highly specific but less sensitive in the diagnosis of gestational diabetes mellitus (8). Gestational diabetes occurs when pregnant women with no history of diabetes have high blood sugar (9).

Monosaccharide 1,5-ahydroglucitol (1,5AG) is another hyperglycemia biomarker. Normal blood contains high yet constant amounts of 1,5-AG. Hyperglycemia reduces 1,5-AG plasma levels by limiting renal tubular reabsorption. Low serum 1,5-AG concentrations may suggest short-term hyperglycemia during the preceding 1-2 weeks (10). In healthy patients, proximal tubules reabsorb 99.9% of 1,5-AG filtered out by the glomerulus. Glucose and 1,5-AG reabsorption compete. 1,5-AG does not help normoglycemic patients with blood glucose levels below the glycosuria threshold (11). Glucose is reabsorb via sodium glucose cotransporter 2 (SGLT2) in the proximal renal tubules and glucose transporter 1 (SGLT1) downstream. After hyperglycemia, glucose excretion will exceed the capabilities of SGLT2 and SGLT1 to reabsorb glucose; therefore, the 1,5-AG/mannose/fructose cotransporter (SGLT4) will begin glucose reabsorption. If glucose enters tubules, 1,5-AG reabsorption is prevented. SGLT4 resorbs 99.9% of 1,5-AG when glucose is not present; however, this reabsorption mechanism is shared with glucose, inhibiting 1,5-AG resorption (12).

Patients with type 2 diabetes had significantly higher levels of triglycerides (TG) but lower levels of high-density lipoprotein cholesterol (HDL-C) (13). According to the findings of a number of studies, insulin resistance and insulin hypersecretion both originate in dysfunctional adipose tissue; hence, both diseases are capable of coexisting with one another (14). Adipocyte enlargement induces liver and muscle insulin resistance and adipocyte insulin secretion. This chain reaction also causes inflammation, fatty acid release, and reduced insulin action on triglyceride lipolysis. Increasing lipids is a side effect of both conventional synthetic (CS) and biological (b) disease-modifying anti-rheumatic medications (DMARDs) (15). Lipoproteins are complex entities composed of cholesterol ester and TGs (16). The outer layer of these particles is composed of phospholipids, apolipoproteins, and unbound cholesterol, which aid in the formation and operation of lipids (17). High visceral adipose tissue has been linked to metabolic syndrome, hypertension, and increased fasting glucose in RA patients (18). The aim of this study was to evaluate whether or not rheumatoid arthritis and diabetes mellitus have any sort of connection to one another. Measures 1,5-AG, RBS, HbA1c, TC, and TG are included.

2. Material and method

2.1. Study design

The current research for rheumatoid arthritis and diabetes mellitus was conducted at Al-Nasiriyah Education Hospital in Thi-Qar Province and lasted from September 2022 until February 2023. (100) blood samples were collected from patients divided into (4) groups (rheumatoid arthritis, diabetes, rheumatoid arthritis and diabetes, and control); each group had (25) patients. Five milliliters of the patient's venous blood were extracted and analyzed in an EDTA and gel tube. Two milliliters of blood were used with EDTA to measure HbA1c, while three milliliters of blood were used with a gel tube to measure immunological and biochemical parameters. Immunological parameters (1,5-anhydroglucitol) and biochemical parameters (random blood sugar, total cholesterol, and total triglyceride) were measured after allowing the blood to clot. The gel tube was separated and centrifuged at 4000 rpm for 5 minutes before being divided into two tubes and stored at -20°C until used.

Samples of blood from all participants in the four groups were taken for measurement of random blood sugar (RBS) (mg/dl), total triglyceride (TG) (mg/dl), and total cholesterol (TC) (mg/dl). The measurements were carried out using a full-automatic clinical chemistry analyzer (Dirui, CS-T180). HbA1c (%) was measured by the usage of a full-automatic clinical chemistry Cobas c 111 analyzer (Roche) belonging to the medical laboratory techniques. 1,5-anhydroglucitol (1,5-AG) usage in Sandwich-ELISA. Type of study is empirical study.

3. Statistical Analysis

All of the data from the current study were statistically evaluated by utilizing Microsoft Windows EXCEL (version 2019) and SPSS version 26 (Statistical Package of Social Science), based on one-way ANOVA and the least significant difference at p values of <0.05 and <0.01.

4. Result

The current study demonstrates an increase in 1,5-anhydroglucitol in the control group compared to the patients' groups, a significant increase in the level of RBS and percentage of HbA1c in patients with only diabetes and a significant increase in patients with both diseases, and a significant difference in HbA1c percentage between rheumatoid patients and control, while there is a non-significant difference between rheumatoid and control in the level of RBS at a p value of < 0.05 as shown in Table 1.

Table 1: Assessment of RBS, Hba1c, and 1,5-AG in all categories

Immune Parameters	Rbs	1,5-Ag	Hba1c
Groups	Mean ± Sd		
Rheumatoid	111.5 ± 25.4^{c}	11.7 ± 2.59^{b}	5.35 ± 0.46^{c}
Diabetic	229.9 ± 48.5^{a}	10.9 ± 2.98^{b}	9.38 ± 2.05^{a}
Ra & Dm	174.3 ± 55.5^{b}	11.2 ± 2.68^{b}	8.12 ± 1.92^{b}
Control	89.46 ± 9.47^{c}	15.2 ± 3.67^{a}	4.48 ± 0.37^{d}
P. Value	< 0.01**	< 0.01**	< 0.01**
Lsd	29.4	1.69	0.80

A significant increase in the level of TG was found in patients who had both diseases, and a significant increase was found in diabetic patients only and rheumatoid patients compared to the control group. Additionally, the level of TC rose significantly in patients who had both diseases, with a significant increase in diabetic patients only and rheumatoid patients, also noted a significant increase in rheumatoid and diabetic patients compared to the control group at p values < 0.05, as shown in Table 2.

Table 2: Evaluation of lipid profile parameters in studded groups

Lipid Profile Group	Tg Mg/Dl Mean ± Sd	Tc Mg/Dl
Rheumatoid	120.6 ± 32.2[c]	170.6 ± 38.1[b]
Diabetic	155.6 ± 35.3[b]	179.5 ± 40.5[b]
Ra & Dm	180.5 ± 49.8[a]	181.5 ± 59.5[a]
Control	89.17 ± 17.9[d]	142.0 ± 23.1[c]
P. Value	< 0.01[**]	< 0.01[**]
Lsd	22.0	23.7

5. Discussion

The present study describes the relationship between 1,5-anhydroglucitol, random blood sugar, HbA1c, triglyceride level, and cholesterol level in patients with rheumatoid arthritis (RA) and diabetes mellitus type 2 (T2DM). Resistance to insulin, a key component of the metabolic syndrome, is usually present in RA patients, particularly those with severe and active illness (19).

The current study found an increase in 1,5-anhydroglucitol in the control group compared to the patients' groups. The study agrees with Shimizu et al. (1999), finding that the concentration of 1,5-AG in the serum was significantly lower in the DM group compared to the concentration found in the control group (20). The result also agrees with Ajlan & Qasim (2020) finding that serum 1,5-AG concentrations are reduced in diabetic patients (21). The mechanism of competition between 1,5-AG and glucose at the site of reabsorption in the proximal renal tubules is responsible for the decrease in the level of 1,5-AG in serum (22). According to the significantly elevated RBS, the current study found that the majority of the included patients had significant hyperglycemia. Because of their severe hyperglycemia, these individuals' 1,5-AG levels in their blood decreased.

The current findings show a significant increase in RBS and HbA1c levels in patients with just diabetes, then a significant increase in patients with both diseases. There is also a significant difference in HbA1c percentage between rheumatoid arthritis patients and the control group, whereas the level of RBS does not differ significantly between the rheumatoid and the control groups. The result agrees with the finding of Noah et al. (2020), showing that individuals with T2DM exhibited a significant increase in RBS when compared to healthy controls (23). The current

study also agrees with the finding by Hadi & Enayah (2022), which indicates a significant difference in the RBS and HbA1c percentages between patients with T2DM and the control group (24). Hyperglycemia is frequently seen in individuals who are in critical condition, and its presence is proportional to the extent of the disease (25). An increase in the number of white blood cells in the bloodstream or tissues is one of the hallmarks of inflammation. High levels of pro-inflammatory cytokines are another indicator of inflammation. In many cases, problems such as organ dysfunction and tissue damage are brought about by excessive stimulation of the inflammatory process. In addition to this, visceral adipocytes are responsible for the secretion of adipocyte-specific cytokines such as leptin and adiponectin and inflammatory cytokines such as tumor necrosis factor (TNF) and interleukin-6 (IL-6). Induction of hepatic and systemic insulin resistance can be caused by increased adipose tissue outflow into the portal vein, synthesis of chemokines, and production of IL-6 (26). The current study discovered that HbA1c levels were elevated in T2DM patients and RA patients due to many reasons, like the influence of biologic agents on the glucose metabolism of RA patients. This is complicated, so it is difficult to interpret changes in HbA1c values as direct effects of anti-inflammatory agents (27).

According to the findings of the current study, individuals who suffered from both disorders had significantly higher levels of TG and TC when compared to the group that served as the control, a significant increase in patients with only diabetes, and then a significant increase in patients with rheumatoid arthritis. This study's findings agree with Khadim & Al-Fartusie, (2021), the lipid profile values of rheumatoid arthritis patients appeared to be higher than those of the control group (28). In individuals with RA, the inflammatory mediators that are released into the blood change lipid metabolism. This leads to dyslipidemia, which is caused by an increase in the release of free fatty acids (FFA) from adipose tissue, an increase in the synthesis of FFA and triglycerides in the liver, and a decrease in the activity of lipoprotein lipase (29). The study also agrees with Jedda et al. (2021), showing that in the study, patients with T2DM had significantly different levels of total cholesterol and total triglycerides than the control group (30). Another study agrees with the result by Majid et al. (2018), who suggest significant differences in TC and TG in patients with T2DM (31), The current study finds that an increase in inflammation leads to an elevated lipid profile.

Conclusion Patients who have hyperglycemia and low 1,5-anhydroglucitol levels may have a useful marker for diabetes by monitoring 1,5-AG. Rheumatoid arthritis patients' lipid profiles, HbA1c percentages, and 1,5-ahydroglucrtol levels should be monitored throughout the disease. Patients with T2DM and RA have a greater impact on their lipid profiles.

Recommended

Monitoring daily 1,5-anhydroglucitol and RBS to found if the relation is more close. Take more rheumatoid arthritis patient and monitor the HbA1c.

References

1. McInnes IB, Schett G. Pathogenetic insights from the treatment of rheumatoid arthritis. Lancet. 2017;389(10086):2328–37.

2. van den Oever IAM, Baniaamam M, Simsek S, Raterman HG, van Denderen JC, van Eijk IC, et al. The effect of anti-TNF treatment on body composition and insulin resistance in patients with rheumatoid arthritis. Rheumatol Int. 2021;41:319–28.

3. Tejera-Segura B, López-Mejías R, de Vera-González AM, Jiménez-Sosa A, Olmos JM, Hernández JL, et al. Relationship between insulin sensitivity and β-cell secretion in nondiabetic subjects with rheumatoid arthritis. J Rheumatol. 2019;46(3):229–36.

4. Cai W, Tang X, Pang M. Prevalence of metabolic syndrome in patients with rheumatoid arthritis: An updated systematic review and meta-analysis. Front Med. 2022;9.

5. De Oliveira PG, Farinon M, Sanchez-Lopez E, Miyamoto S, Guma M. Fibroblast-like synoviocytes glucose metabolism as a therapeutic target in rheumatoid arthritis. Front Immunol. 2019;10:1743.

6. Chehregosha H, Khamseh ME, Malek M, Hosseinpanah F, Ismail-Beigi F. A view beyond HbA1c: role of continuous glucose monitoring. Diabetes Ther. 2019;10:853–63.

7. Huang Z, Liu Y, Mao Y, Chen W, Xiao Z, Yu Y. Relationship between glycated haemoglobin concentration and erythrocyte survival in type 2 diabetes mellitus determined by a modified carbon monoxide breath test. J Breath Res. 2018;12(2):26004.

8. Renz PB, Chume FC, Timm JRT, Pimentel AL, Camargo JL. Diagnostic accuracy of glycated hemoglobin for gestational diabetes mellitus: a systematic review and meta-analysis. Clin Chem Lab Med. 2019;57(10):1435–49.

9. Al-seidi FA. The incidence of proteinuria among diabetic patients in relation to the level of glycated Hb, duration of the disease& types of treatment in Thi-Qar province. J THI-QAR Sci. 2016;5(4).

10. Selvin E, Rawlings A, Lutsey P, Maruthur N, Pankow JS, Steffes M, et al. Association of 1, 5-anhydroglucitol with cardiovascular disease and mortality. Diabetes. 2016;65(1):201–8.

11. Hassanein M, Shafi T. Assessment of glycemia in chronic kidney disease. BMC Med. 2022;20(1):1–9.

12. Suzuki S, Koga M. Glycemic control indicators in patients with neonatal diabetes mellitus. World J Diabetes. 2014;5(2):198.

13. Lorenzatti AJ, Toth PP. New perspectives on atherogenic dyslipidaemia and cardiovascular disease. Eur Cardiol Rev. 2020;15.

14. Ghaben AL, Scherer PE. Adipogenesis and metabolic health. Nat Rev Mol cell Biol. 2019;20(4):242–58.

15. Myasoedova E. Lipids and lipid changes with synthetic and biologic disease-modifying antirheumatic drug therapy in rheumatoid arthritis: implications for cardiovascular risk. Curr Opin Rheumatol. 2017;29(3):277–84.

16. Makkar R, Behl T, Kumar A, Uddin MS, Bungau S. Untying the correlation between apolipoproteins and rheumatoid arthritis. Inflamm Res. 2021;70:19–28.

17. Venetsanopoulou AI, Pelechas E, Voulgari P V, Drosos AA. The lipid paradox in rheumatoid arthritis: the dark horse of the augmented cardiovascular risk. Rheumatol Int. 2020;40(8):1181–91.

18. Yoshida T, Hashimoto M, Kawahara R, Yamamoto H, Tanaka M, Ito H, et al. Non-obese visceral adiposity is associated with the risk of atherosclerosis in Japanese patients with rheumatoid arthritis: a cross-sectional study. Rheumatol Int. 2018;38(9):1679–89.

19. Ferraz-Amaro I, González-Juanatey C, López-Mejias R, Riancho-Zarrabeitia L, González-Gay MA. Metabolic syndrome in rheumatoid arthritis. Mediators Inflamm. 2013;2013.

20. Shimizu H, Shouzu A, Nishikawa M, Omoto S, Hayakawa T, Miyake Y, et al. Serum concentration and renal handling of 1, 5-anhydro-D-glucitol in patients with chronic renal failure. Ann Clin Biochem. 1999;36(6):749–54.

21. Ajlan SK, Qasim SK. Evaluation Of Serum 1, 5-Anhydroglucitol Levels among Type 2 Diabetic Patients in Basrah. Univ Thi-Qar J Med. 2020;19(1):106–19.

22. Pramodkumar TA, Jayashri R, Gokulakrishnan K, Velmurugan K, Pradeepa R, Anjana RM, et al. Relationship of glycemic control markers-1, 5 anhydroglucitol, fructosamine, and glycated hemoglobin among Asian Indians with different degrees of glucose intolerance. Indian J Endocrinol Metab. 2016;20(5):690.

23. Noah K, Hmood F, Zainal I. Estimation and isolation of ceruloplasmin and some biochemical indicators in diabetes mellitus type II patients compared to healthy controls in Kirkuk Province, Iraq. Med J Babylon. 2020;17(1):49.

24. Hadi HS, Enayah SH. Effects of Covid-19 Infection on Some Pancreatic Functions in Diabetic Patients at Thi-Qar Province/Iraq. Univ Thi-Qar J Sci. 2022;9(2):66–74.

25. Joshi SC, Pozzilli P. COVID-19 induced diabetes: A novel presentation. Diabetes Res Clin Pract. 2022;110034.

26. Wondmkun YT. Obesity, insulin resistance, and type 2 diabetes: associations and therapeutic implications. Diabetes, Metab Syndr Obes targets Ther. 2020;13:3611.

27. Ng JM, Cooke M, Bhandari S, Atkin SL, Kilpatrick ES. The effect of iron and erythropoietin treatment on the A1C of patients with diabetes and chronic kidney disease. Diabetes Care. 2010;33(11):2310–3.

28. Khadim RM, Al-Fartusie FS. Evaluation of Liver Function and Lipid profiles in Iraqi patients with Rheumatoid Arthritis. In: Journal of Physics: Conference Series. IOP Publishing; 2021. p. 12040.

29. Popa C, van Tits LJH, Barrera P, Lemmers HLM, van den Hoogen FHJ, Van Riel P, et al. Anti-inflammatory therapy with tumour necrosis factor alpha inhibitors improves high-density lipoprotein cholesterol antioxidative capacity in rheumatoid arthritis patients. Ann Rheum Dis. 2009;68(6):868–72.

30. Jedda WAAL, Al-Ali ZAJR, Akram RS. Study the Interferon–γ, C-reactive Protein and Lipid Profile in Iraqi Diabetic Patients With and Without Hypertension. NVEO-NATURAL VOLATILES Essent OILS Journal| NVEO. 2021;8820–32.

31. Majid A, Sayer SA, Farhood HB. Study of some biochemical parameters for patients with type ii diabetes mellitus in thi-qar governorate, iraq. J Pharm Sci Res. 2018;10(11):2938–41.