Assessment of Adiponectin Levels, Lipid Profile, and Oxidative Stress in Thyrotoxic Women in Kirkuk City

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Abstract

Background: Hyperthyroidism is the cause of thyrotoxicosis, a pathological condition caused by increased secretion of thyroid hormones in the blood, and it is important to note that hyperthyroidism and thyrotoxicosis

Aim: The current study aims was to evaluate the serum levels of adiponectin, lipid profile, malondialdehyde and glutathione in women with thyrotoxicosis and hyperthyroidism

Materials and methods: In this study conducted in Kirkuk, blood samples were collected from 110 women aged 25 to 45 years, divided into five groups representing different thyroid conditions and a control group. The participants were categorized as untreated hyperthyroidism, hyperthyroidism undergoing treatment, untreated thyrotoxic women, thyrotoxic women undergoing treatment, and healthy women without thyroid disorder. Blood samples were collected using a 5 ml syringe via vein puncture, and after clotting, the sera were separated through centrifugation. The collected samples were analyzed for adiponectin levels, lipid profile parameters (total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), as well as oxidative stress markers including malondialdehyde (MDA) and glutathione (GSH).

Results: The study found that women with thyrotoxicity and hyperthyroidism had lower cholesterol levels compared to the control group. Treatment improved cholesterol levels, triglyceride levels, HDL-c levels, LDL-C levels, and VLDL levels. HDL-c levels decreased, LDL-C levels increased, and VLDL levels decreased, but no significant improvement was observed after treatment.Adiponectin levels were significantly lower in the thyrotoxicity and hyperthyroidism groups (37.75±4.66 pg/ml and 39.55±5.67 pg/ml) compared to the control group (98.88±11.43 pg/ml), and they improved after treatment (45.66±5.99 pg/ml and 55.71±6.38 pg/ml). Glutathione levels were significantly lower in the thyrotoxicity and hyperthyroidism groups (64.60±3.99 IU/ml and 68.70±4.67 IU/ml) compared to the control group (90.56±10.73 IU/ml), with no significant improvement after treatment. MDA levels were significantly higher in the thyrotoxicity and hyperthyroidism groups (10.77±2.99 nmol/L and 10.44±3.15 nmol/L) compared to the control group (6.88±1.17 nmol/L), with no significant improvement after treatment.

Conclusions: Thyrotoxicity and hyperthyroidism women's lipid profiles and oxidative stress markers altered; treatment improved cholesterol, triglyceride, HDL-c, LDL-C, adiponectin, glutathione, MDA levels.

Keywords: Lipid; Adiponectin, Oxidative stress; Glutathione; thyrotoxicosis.

Introduction

Thyroid diseases are common, especially in women, and the incidence increases with age, so that about 10% of the population over the age of 65 suffers from thyroid dysfunction. Hyperthyroidism is an overactive thyroid tissue that causes overproduction of thyroid hormones (thyroxine, or "T4", and triiodothyronine, or "T3") (Yahya et al 2023). Thyrotoxicosis and hyperthyroidism are endocrine disorders characterized by excessive thyroid hormone production. These conditions can lead to various metabolic alterations and have been associated with changes in adiponectin levels, lipid profile, and oxidative stress markers. Adiponectin, a hormone secreted by adipose tissue, plays a crucial role in regulating glucose and lipid metabolism (De Guzman *et al.,* 2021). Alterations in adiponectin levels have been observed in thyroid disorders, suggesting its involvement in the pathophysiology of thyrotoxicosis and hyperthyroidism. Furthermore, thyroid hormones play a vital role in lipid metabolism, and dyslipidemia is commonly observed in individuals with these conditions (Devereaux et al., 2014). In addition to changes in adiponectin and lipid profile, thyrotoxicosis and hyperthyroidism have been linked to oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) production and antioxidant defense systems. Malondialdehyde (MDA) is a marker of lipid peroxidation, while glutathione (GSH) is an essential antioxidant involved in neutralizing ROS (Czarnywojtek et al., 2014) Assessing serum levels of adiponectin, lipid profile parameters, MDA, and GSH in women with thyrotoxicosis and hyperthyroidism can provide valuable insights into the metabolic and oxidative stress status associated with these conditions (Ahmad et al., 2018). Understanding the relationship between these factors may contribute to better management and monitoring of thyrotoxicosis and hyperthyroidism in women (Jafarzadeh et al., 2010). Therefore, this study aims to evaluate the serum levels of adiponectin, lipid profile parameters, MDA, and GSH in women diagnosed with thyrotoxicosis and hyperthyroidism, shedding light on their potential implications in the pathogenesis and clinical outcomes of these endocrine disorders.

Materials and methods

This study was conducted in Kirkuk, involving Kirkuk Teaching Hospital, Azadi Teaching Hospital, and private laboratories, from December 2022 to April 2023. A total of 110 blood samples were collected from women aged 25 to 45 years who were categorized into five groups: untreated hyperthyroidism women (25 samples), hyperthyroid women undergoing treatment (20 samples), untreated thyrotoxic women (25 samples), women with thyrotoxicity undergoing treatment (20 samples), and healthy women without thyroid disorder serving as the control group (20 samples).

Blood samples were collected from each participant and control person using a 5 ml syringe via vein puncture, and 5 milliliters of blood were collected. The blood samples were collected in plain tubes and allowed to clot for 30 minutes at 37°C. Subsequently, the tubes were centrifuged at 3000 rpm for 15 minutes. The resulting sera were carefully aspirated and transferred into Eppendorf tubes for further analysis.

The variables measured in this study included adiponectin levels, lipid profile parameters (such as total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), as well as markers of oxidative stress, namely malondialdehyde (MDA) and glutathione (GSH). These variables were selected to assess their association with thyrotoxicosis and hyperthyroidism.

Statistical analysis will be performed to compare the variables between the different groups and evaluate their significance in relation to thyrotoxicosis and hyperthyroidism. This analysis aims to provide insights into the potential metabolic and oxidative stress alterations associated with these endocrine disorders in women from Kirkuk.

Results

The results of the current study demonstrated a statistically significant decrease in cholesterol levels in women with thyrotoxicity and hyperthyroidism compared to the control group (135.7±9.6 mg/dL and 139.7±8.81 mg/dL vs. 193.5±17.66 mg/dL). Following treatment, there was a significant improvement in cholesterol levels in the thyrotoxicity and hyperthyroidism groups (150.1±11.8 mg/dL and 144.7±12.51 mg/dL) compared to their pre-treatment levels.

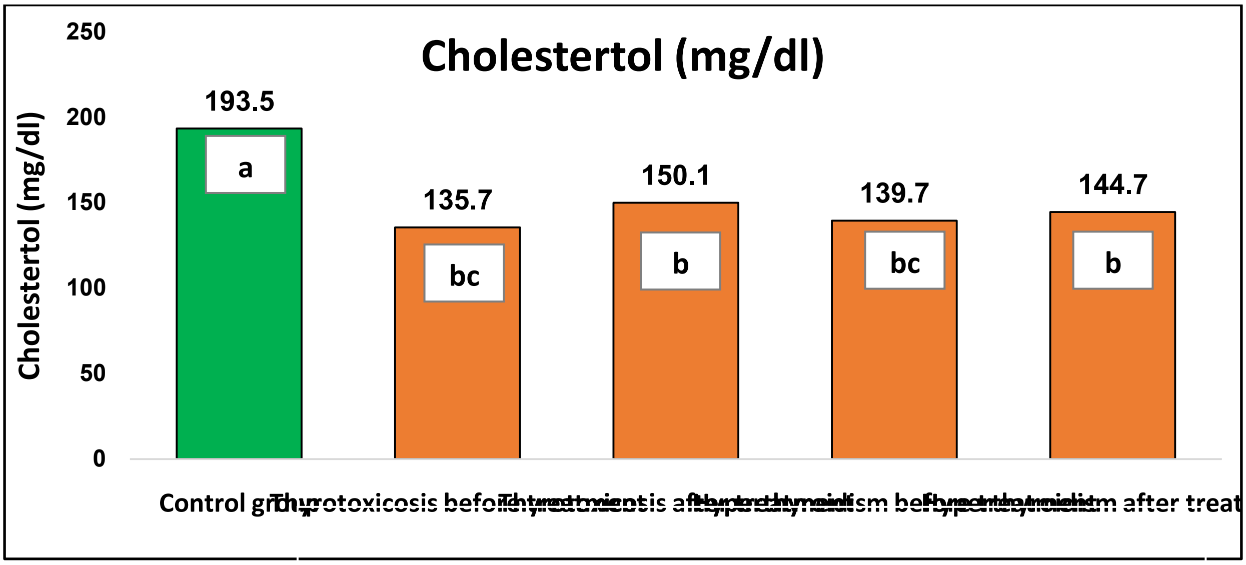

Figure 1:Cholesterol level in the studied groups.

Regarding triglycerides, a significant decrease was observed in women with thyrotoxicity and hyperthyroidism compared to the control group (90.6±8.66 mg/dL and 99.3±10.8 mg/dL vs. 145.7±11.69 mg/dL). After treatment, a significant improvement in triglyceride levels was observed in the thyrotoxicity and hyperthyroidism groups (103.5±9.54 mg/dL and 110.5±10.17 mg/dL) compared to their pre-treatment levels.

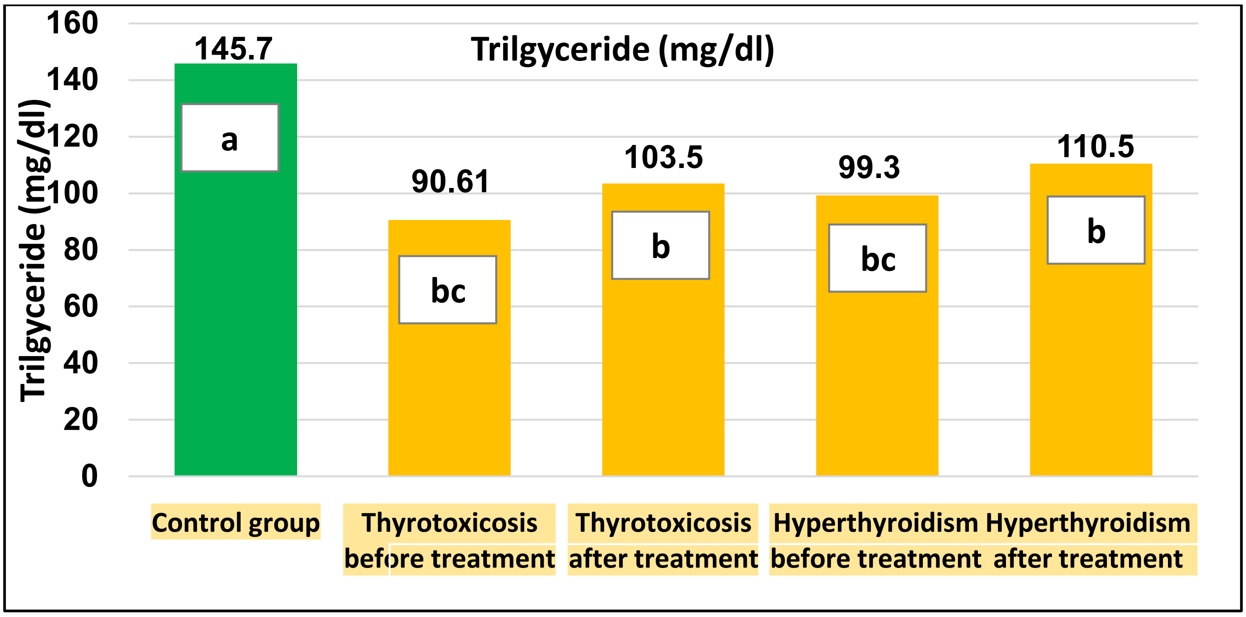

Figure 2: Triglycerides level in the studied groups.

The study also found a statistically significant decrease in high-density lipoprotein cholesterol (HDL-c) levels in women with thyrotoxicity and hyperthyroidism compared to the control group (40.6±8.66 mg/dL and 44.1±7.56 mg/dL vs. 70.5±10.19 mg/dL). After treatment, a significant improvement in HDL-c levels was observed in the thyrotoxicity and hyperthyroidism groups (46.6±6.77 mg/dL and 53.6±7.34 mg/dL) compared to their pre-treatment levels.

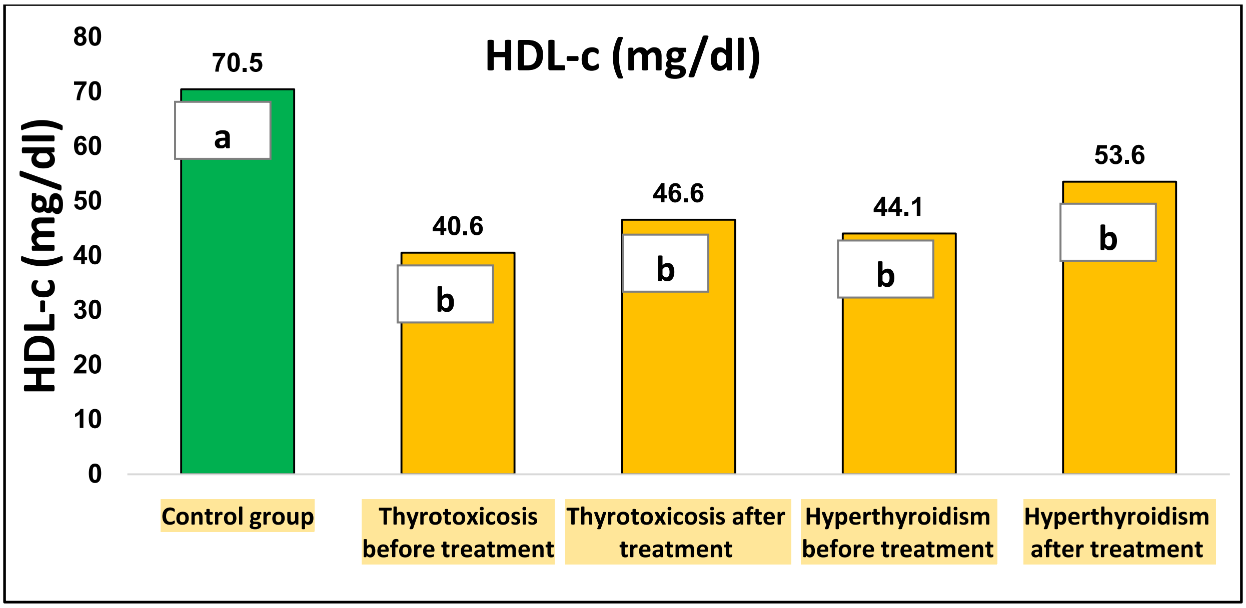

Figure 3: HDL-c level in the studied groups.

In contrast, there was a statistically significant increase in low-density lipoprotein cholesterol (LDL-C) levels in women with thyrotoxicity and hyperthyroidism compared to the control group (115.6±19.55 mg/dL and 110.5±18.7 mg/dL vs. 78.4±10.6 mg/dL). Following treatment, a significant improvement in LDL-C levels was observed in the thyrotoxicity and hyperthyroidism groups (95.6±14.17 mg/dL and 93.5±13.39 mg/dL) compared to their pre-treatment levels.

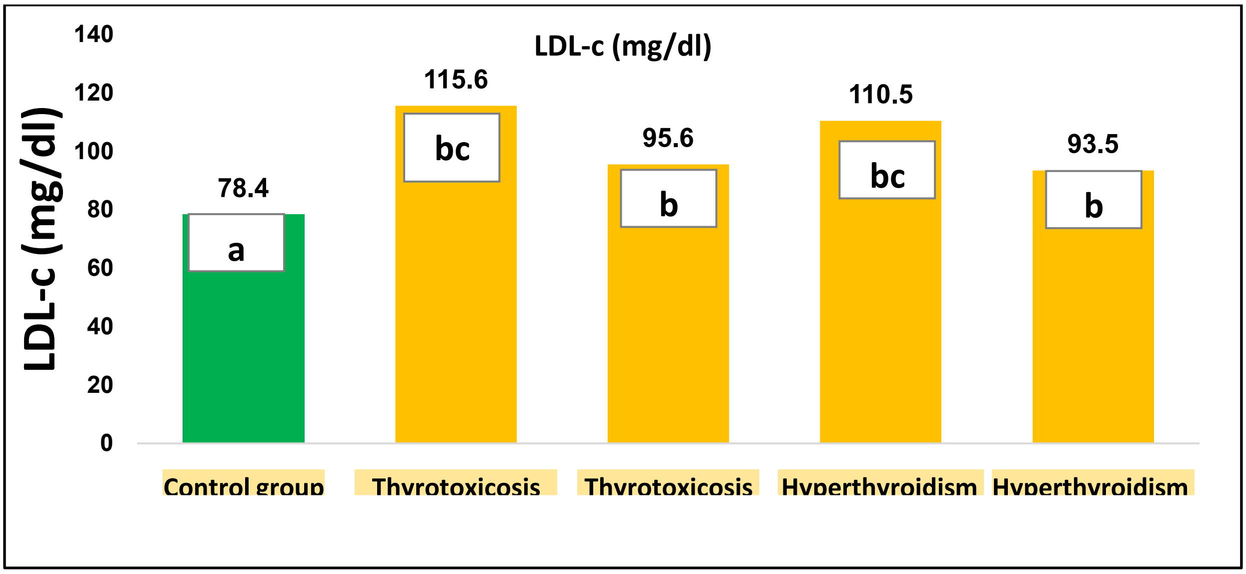

Figure 4: LDL-clevel in the studied groups.

Furthermore, very low-density lipoprotein (VLDL) levels were found to be significantly decreased in women with thyrotoxicity and hyperthyroidism compared to the control group (18.12±3.15 mg/dL and 19.86±3.7 mg/dL vs. 29.14±4.6 mg/dL). After treatment, there was no significant improvement in VLDL levels in the thyrotoxicity and hyperthyroidism groups.

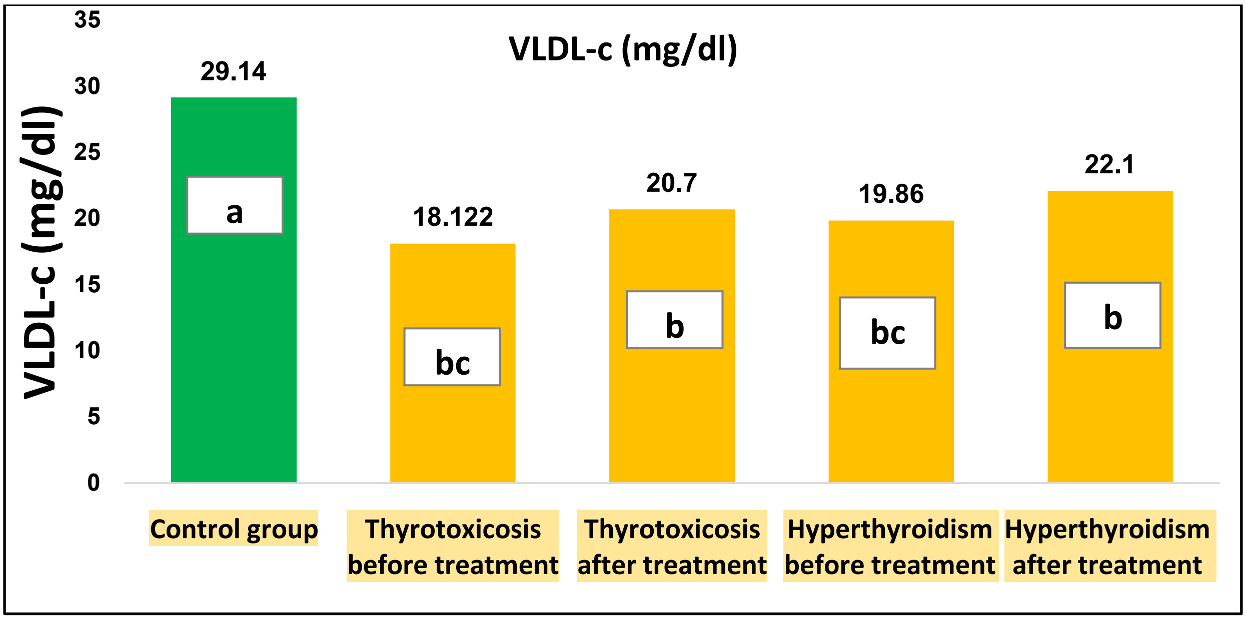

Figure 5: VLDL inlevel in the studied groups.

The study revealed a statistically significant decrease in adiponectin levels in women with thyrotoxicity and hyperthyroidism compared to the control group (37.75±4.66 pg/ml and 39.55±5.67 pg/ml vs. 98.88±11.43 pg/ml). Following treatment, there was a significant improvement in adiponectin levels in the thyrotoxicity and hyperthyroidism groups (45.66±5.99 pg/ml and 55.71±6.38 pg/ml) compared to their pre-treatment levels.

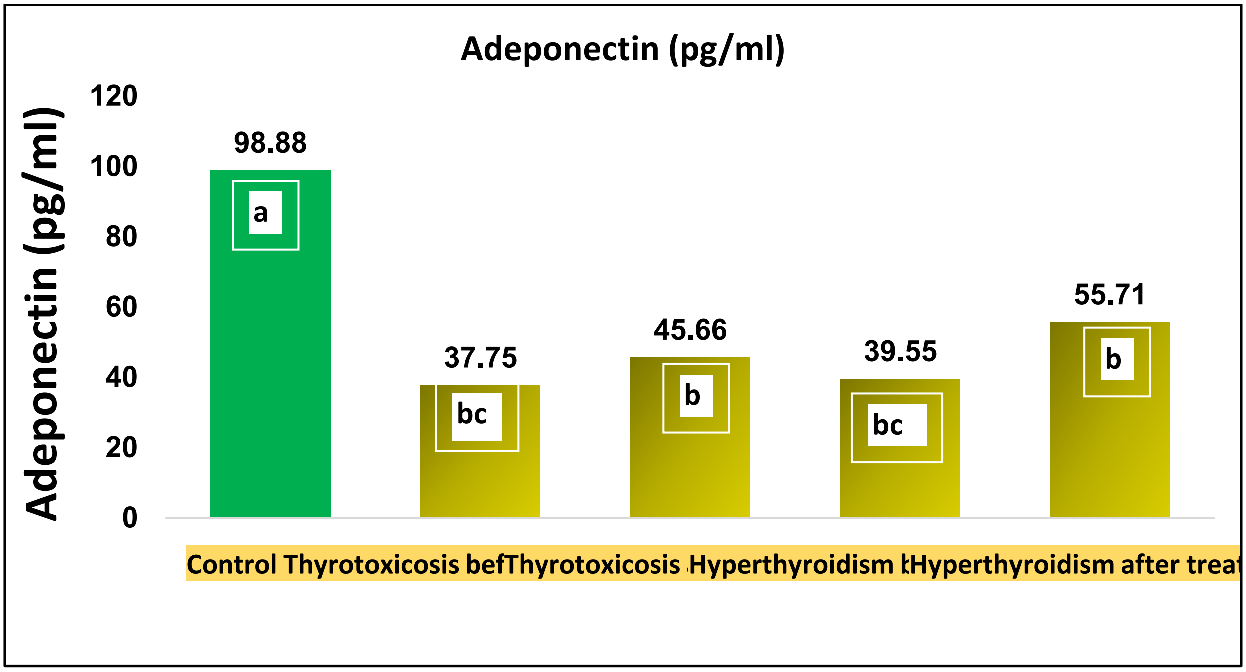

Figure 6:Adiponectin level in the studied groups.

Furthermore, glutathione levels were significantly decreased in women with thyrotoxicity and hyperthyroidism compared to the control group (64.60±3.99 IU/ml and 68.70±4.67 IU/ml vs. 90.56±10.73 IU/ml). There was no significant improvement in glutathione levels following treatment.

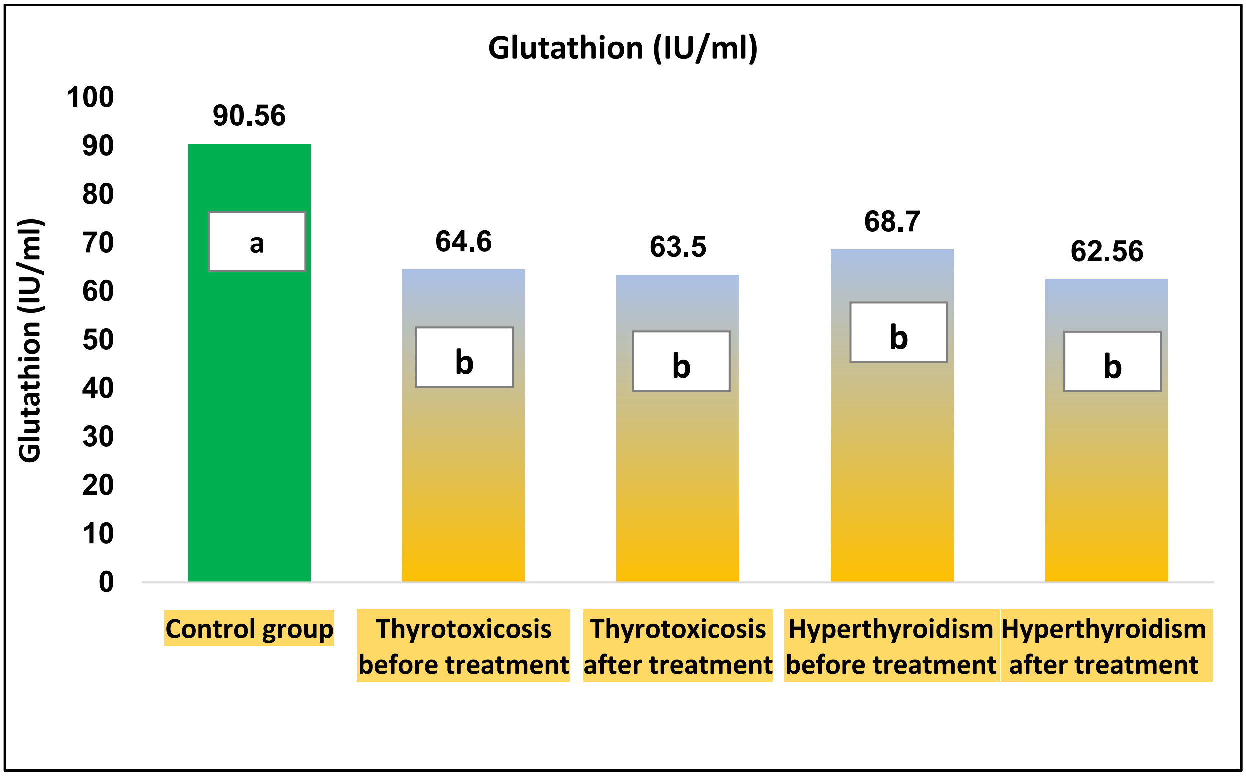

Figure7: Glutathione level in the studied groups.

Lastly, there was a statistically significant increase in malondialdehyde (MDA) levels in women with thyrotoxicity and hyperthyroidism compared to the control group (10.77±2.99 nmol/L and 10.44±3.15 nmol/L vs. 6.88±1.17 nmol/L). There was no significant improvement in MDA levels after treatment.

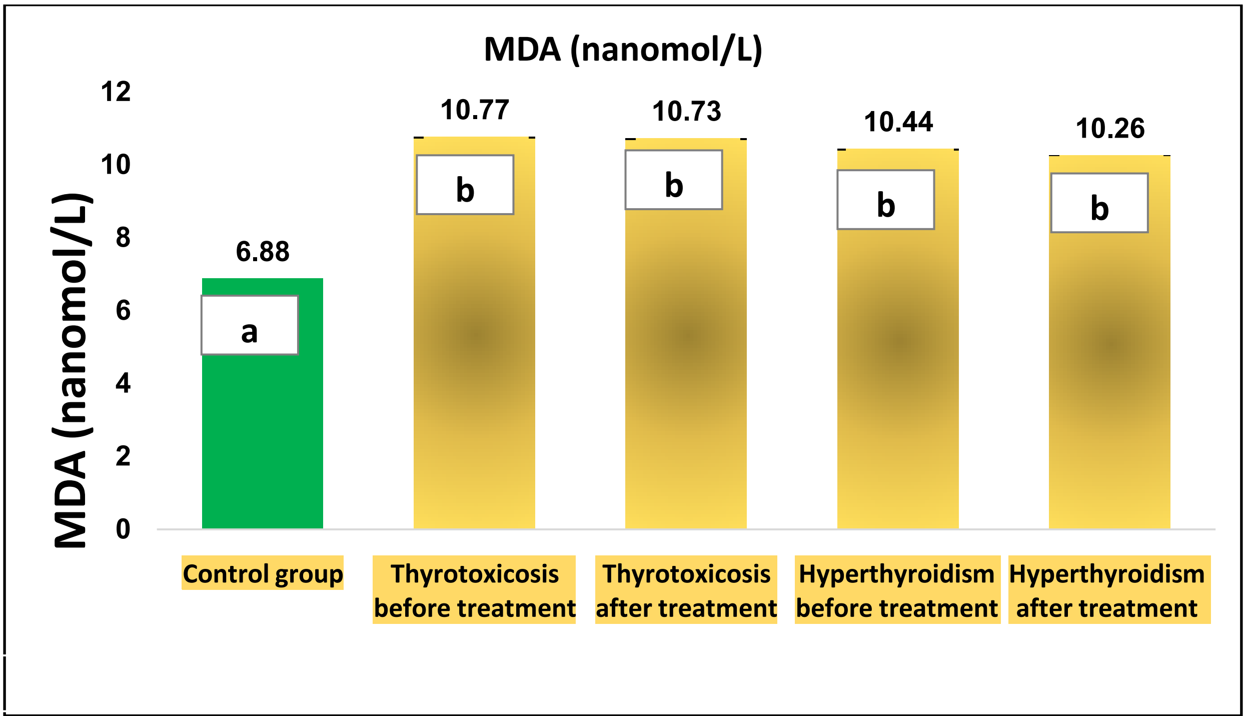

Figure 8:MDAlevel in the studied groups.

Discussion

Low cholesterol level in patients with thyrotoxicity and hyperthyroidism is an important and interesting consequence and one of the studies that indicated this decrease is a similar study that proved that targeted treatment for hyperthyroidism may contribute to improving cholesterol levels in these patients (Taub et al. 2013). Another study noted that the cholesterol rate in the thyrotoxicosis group that received treatment increased slightly compared to those that did not receive treatment, suggesting that targeted hyperthyroidism therapy may promote higher cholesterol levels to more normal levels (Iwenet al 2013).A study by Luxiaet al (2021) found that hyperthyroidism and thyroid poisoning are strongly associated with low blood lipids, including cholesterol levels. This is because hyperthyroidism and thyroid poisoning lead to increased production of thyroid hormone, which accelerates the metabolic rate and decreases the rates of lipid tests. The increased metabolic rate associated with hyperthyroidism can lead to the breakdown and use of stored fats, including cholesterol, leading to a decrease in blood lipid levels, including total cholesterol, LDL-C (low-density lipoprotein), and triglycerides. A similar study conducted by Alsalmiet al in 2013 indicated that targeted treatment for hyperthyroidism may contribute to improving triglyceride levels in these patients. Another study noted that the rate of triglycerides in the group of patients who received treatment had increased slightly compared to the group that did not receive treatment. This suggests that targeted therapy for hyperthyroidism may be involved in restoring triglyceride levels to more normal levels.Several studies have shown a strong association between hyperthyroidism, thyroid intoxication, and low blood lipids. When hyperthyroidism or thyroid poisoning occurs, this causes an increase in the production of thyroid hormone, which ultimately leads to an acceleration of the metabolic rate and a general decrease in the rates of fat tests in the blood. Potential mechanisms contributing to this decline include increased consumption of fat as an energy fuel due to increased metabolic rate caused by hyperthyroidism, which can cause low blood lipid levels, including total cholesterol and triglycerides (Akçay and Hatemi, 2001 and Akoh, C. C. 2017). In the current study, a relative decrease in the level of HDL-c (High Density Lipoproteins) was found in patients with thyrotoxicity compared to the group of healthy people. HDL-c is considered "good fat" because it plays an important role in removing LDL-c cholesterol from blood vessels and protecting the heart and blood vessels from cardiovascular disease. Rizoset al (2011) reported a reduction in the level of HDL-c in thyrotoxicosis patients and hyperthyroidism patients, especially those who did not receive treatment compared to the group of healthy people.Several studies have shown that the condition occurs as a result of excessive secretion of thyroid hormones from the thyroid gland. One of the most important side effects recorded in patients with thyrotoxicosis is an increase in the rate of body metabolism or cellular metabolism, which can affect the levels of lipids in the blood and a decrease in the level of LDL-c. However, the effect of thyrotoxicosis on blood lipid levels can be variable from person to person, and some studies indicate an increase in the level of high-density lipoproteins in some cases (Sadykova et al 2021).Visceral adipose tissue also releases inflammatory cytokines during the inflammatory process and contributes to raising serum CRP levels by increasing signaling (Wilke *et al.*, 2017). Similar results were also recorded in several studies (Aragão et al. 2007) that demonstrated a significant decrease in the level of adiponectin in the thyrotoxic group and hyperthyroidism patients compared to the control group and indicated a relationship between hyperthyroidism and low levels of adiponectin. A study conducted by Al-Sowdaniand his colleagues in the year (2014) in the city of Basra found that the levels of glutathione decreased significantly in individuals with hyperthyroidism compared to thecontrol group, and their results were close to our study and similar results were also recorded in several studies that proved a decrease in the level of glutathione in patients with hyperthyroidism, which can cause oxidative damage tocells, where glutathione helps to protect cells from oxidative stress by converting hydrogen peroxide into water and lipid peroxides into less harmful compounds (Maji *et al*., 2016).The decrease in glutathione levels indicates an imbalance between the production of reactive oxygen types and the antioxidant defense system, leading to oxidative damage and cellular dysfunction and this imbalance may contribute to the causes of complications associated with hyperthyroidism and its development (Londzin-Olesik, *et al*., 2020).The current study also indicated that there were no differences in the level of Glutathione between patients before and after treatment of hyperthyroidism, indicating that there was no direct effect of the treatment used on increasing the levels of glutathione in these patients. Malondialdehyde (MDA) is a product of lipid oxidation that is formed when the body is exposed to oxidative damage, according to several studies whose results coincided with our findings, where it was observed that the level of malondialdehyde was higher in patients with thyrotoxicity and hyperthyroidism compared to healthy individuals (Žarković et al., 2013). Hashim et al. (2018) reported that a significant level of MDA was observed in hyperthyroidism compared to healthy subjects as a result of an increase in oxidative stress and lipid peroxidation in hyperthyroid individuals.

A study conducted by Ahmed and colleagues in the year (2022) found that patients with hyperthyroidism and thyrotoxicosis were mainly characterized by increased production and release of thyroid hormones, which eventually led to metabolic abnormalities, including increased oxidative stress and high levels of malonedidehyde (MDA) in those patients compared to the control group, and the current study shows that there are no differences in the level of MDA Among patients before and after hyperthyroidism treatment and this may indicate that the treatment used for hyperthyroidism has no direct effect on reducing oxidative stress in these patients (Sultana *et al*., 2022).

In conclusion, women with thyrotoxicity and hyperthyroidism had altered lipid profiles and oxidative stress markers. Treatment improved cholesterol, triglyceride, HDL-c, and LDL-C levels, while VLDL levels did not significantly improve. Adiponectin levels were significantly lower in patient groups but improved after treatment. Glutathione levels were lower, and MDA levels were higher in patients, with no significant changes after treatment. Clinicians should monitor lipid profiles, adiponectin levels, and oxidative stress markers in these women and consider lifestyle modifications for better cardiovascular health. Further research is needed to explore underlying mechanisms and potential interventions.

References

Abdulazeez, M. I., Hamdi, A. Q., Mohammed, H. Y., & Ahmed, M. (2020). Dental trauma of permanent incisor teeth in children/Kirkuk city. studies, 22, 23.

Abdulqader, A. T., Al-Sammarie, A. M. Y., & Mustafa, M. A. (2022, May). A comparative environmental study of aqueous extracts of ginger and grapes to protect hepatocytes in Albino rabbits and a comparison of extracts in preserving Awassi lamb meat from oxidation. In IOP Conference Series: Earth and Environmental Science (Vol. 1029, No. 1, p. 012001). IOP Publishing.

Ahmad, N., Nagtilak, S., Sharma, A. K., Parashar, P., & Rastogi, A. (2018). Role of Circulating C Reactive Protein in Thyroid Disorders. *Journal of Medical Science And clinical Research*, *6*(2), 485-89.

Ahmed, A. H., Maulood, I. M., Sabah, A. S., & Abdullah, S. K. (2022). Association of Thyroid Hormones with Oxidative Stress Markers in Patient with Hyperthyroidism. *Diyala Journal of Medicine*, *22*(2), 18-28.

Akçay, T., & Hatemi, H. (2001). The effects of hyperthyroidism on lipid peroxidation, erythrocyte glutathione and glutathione peroxidase. *Turkish Journal of Endocrinology and Metabolism*, *1*, 17-19.

Akoh, C. C. (2017). *Food lipids: chemistry, nutrition, and biotechnology*. CRC press.

Ali, S. H., Armeet, H. S., Mustafa, M. A., & Ahmed, M. T. (2022, November). Complete blood count for COVID-19 patients based on age and gender. In AIP Conference Proceedings (Vol. 2394, No. 1, p. 020044). AIP Publishing LLC.

Al-Sowdani, K. H., AL-Maliki, A. D., Alawi, M. J., & AL-Salem, B. A. (2014). Effect of increase thyroid hormone on antioxidant enzymes activity and their related metals in hyperthyroid patients in Basrah Governorate/Iraq. *journal of kerbala university* .

Aragão, C. N., Souza, L. L., Cabanelas, A., Oliveira, K. J., &Pazos-Moura, C. C. (2007). Effect of experimental hypo-and hyperthyroidism on serum adiponectin. *Metabolism*, *56*(1), 6-11.

Badi, S., Hamed, A., Abualama, M., Mustafa, M., Abdulraheem, M., &Yousef, B. (2021). Knowledge, attitude, and practice of sudanese pharmacists toward COVID-19 in Khartoum State, Sudan: An online-based cross-sectional study. Libyan International Medical University Journal, 6(01), 19-26.

Choi, Y. H., Chung, J. H., Bae, S. W., Lee, W. H., Jeong, E. M., Kang, M. G., ... & Park, J. E. (2005). Severe coronary artery spasm can be associated with hyperthyroidism. *Coronary artery disease*, *16*(3), 135-139.

Czarnywojtek, A., Owecki, M., Zgorzalewicz-Stachowiak, M., Woliński, K., Szczepanek-Parulska, E., Budny, B., ... &Ruchała, M. (2014). The role of serum C-reactive protein measured by high-sensitive method in thyroid disease. *Archivumimmunologiae et therapiaeexperimentalis*, *62*, 501-509.

De Guzman, E., Shakeel, H., & Jain, R. (2021). Thyrotoxicosis: a rare presentation of molar pregnancy. *BMJ Case Reports CP*, *14*(7), e242131.

De Lemos, J. A., Drazner, M. H., Omland, T., Ayers, C. R., Khera, A., Rohatgi, A., ... & McGuire, D. K. (2010). Association of troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population. *Jama*, *304*(22), 2503-2512.

Devereaux, D., & Tewelde, S. Z. (2014). Hyperthyroidism and thyrotoxicosis. *Emergency Medicine Clinics*, *32*(2), 277-292.

Govindarajan, S., Mustafa, M. A., Kiyosov, S., Duong, N. D., Raju, M. N., &Gola, K. K. (2023). An optimization based feature extraction and machine learning techniques for named entity identification. Optik, 272, 170348.

Hashim, M. F., Ail, D. S., & Issa, A. Y. (2018). Evaluation of some biochemical parameters in serum patients with thyroid gland dysfunction. *Basrah Journal of Science*, *36*(C), 42-51.

Jafarzadeh, A., Poorgholami, M., Izadi, N., Nemati, M., &Rezayati, M. (2010). Immunological and hematological changes in patients with hyperthyroidism or hypothyroidism. *Clinical and Investigative Medicine*, E271-E279.

Kadham, S. M., Mustafa, M. A., Abbass, N. K., &Karupusamy, S. (2022). IoT and artificial intelligence–based fuzzy-integral N-transform for sustainable groundwater management. Applied Geomatics, 1-8.

Karupusamy, S., Mustafa, M. A., Jos, B. M., Dahiya, P., Bhardwaj, R., Kanani, P., & Kumar, A. (2023). Torque control-based induction motor speed control using Anticipating Power Impulse Technique. The International Journal of Advanced Manufacturing Technology, 1-9.

Keller, T., Zeller, T., Peetz, D., Tzikas, S., Roth, A., Czyz, E., ... &Blankenberg, S. (2009). Sensitive troponin I assay in early diagnosis of acute myocardial infarction. *New England Journal of Medicine*, *361*(9), 868-877.

Londzin-Olesik, M., Kos-Kudła, B., Nowak, A., Wielkoszyński, T., & Nowak, M. (2020). The effect of thyroid hormone status on selected antioxidant parameters in patients with Graves' disease and active thyroid-associated orbitopathy. *EndokrynologiaPolska*, *71*(5), 418-424.

Luxia, L., Jingfang, L., Songbo, F., Xulei, T., Lihua, M., Weiming, S., ... & Pei, S. (2021). Correlation between serum TSH levels within normal range and serum lipid profile. *Hormone and Metabolic Research*, *53*(01), 32-40.

Maji, B., Basu, P., Kunti, S., Mallik, S., & Mondal, A. K. (2016). Assessment of Oxidative Stress and Antioxidant Status in Hyperthyroidism. *Asian Journal of Pharmaceutical and Health Sciences*, *6*(1).

Mustafa, H. A., Asaad, M. M. K., Obayes, A. K., & Mustafa, M. A. (2022). Isolation and Identification of Some Types of Pathogenic Bacteria from the Prepuce (Foreskin) of Circumcised Children in Samarra City/Iraq. HIV Nursing, 22(2), 2776-2780.

Mustafa, M. A., Kadham, S. M., Abbass, N. K., Karupusamy, S., Jasim, H. Y., Alreda, B. A., ... & Ahmed, M. T. (2023). A novel fuzzy M-transform technique for sustainable ground water level prediction. Applied Geomatics, 1-7.

Rizos, C. V., Elisaf, M. S., &Liberopoulos, E. N. (2011). Effects of thyroid dysfunction on lipid profile. *The open cardiovascular medicine journal*, *5*, 76.

Sadykova, D. I., Susekov, A. V., Leontyeva, I. V., Zakirov, I. I., Slastnikova, E. S., Galimova, L. F., ... &Krinitskaya, N. V. (2021). Lipid metabolism disorders and thyrotoxicosis. *RossiyskiyVestnikPerinatologii i Pediatrii (Russian Bulletin of Perinatology and Pediatrics)*, *65*(6), 91-97.

Smithson, M., Asban, A., Miller, J., & Chen, H. (2019). Considerations for thyroidectomy as treatment for Graves disease. *Clinical Medicine Insights: Endocrinology and Diabetes*, *12*, 1179551419844523.

Sudha, I., Mustafa, M. A., Suguna, R., Karupusamy, S., Ammisetty, V., Shavkatovich, S. N., ... &Kanani, P. (2023). Pulse jamming attack detection using swarm intelligence in wireless sensor networks. Optik, 272, 170251.

Sultana, R., Shahin, A. D., &Jawadul, H. M. (2022). Measurement of oxidative stress and total antioxidant capacity in hyperthyroid patients following treatment with carbimazole and antioxidant. *Heliyon*, *8*(1), e08651.

Taub, R., Chiang, E., Chabot-Blanchet, M., Kelly, M. J., Reeves, R. A., Guertin, M. C., & Tardif, J. C. (2013). Lipid lowering in healthy volunteers treated with multiple doses of MGL-3196, a liver-targeted thyroid hormone receptor-β agonist. *Atherosclerosis*, *230*(2), 373-380.

Watanabe, N., Noh, J. Y., Hattori, N., Iwaku, K., Suzuki, N., Yoshihara, A., ... & Ito, K. (2021). Cardiac Troponin Is Elevated in Patients with Thyrotoxicosis and Decreases as Thyroid Function Improves and Brain Natriuretic Peptide Levels Decrease. *European Thyroid Journal*, *10*(6), 468-475.

Wilke, P., Masuch, A., Fahron, O., Zylla, S., Leipold, T., &Petersmann, A. (2017). Diagnostic performance of point-of-care and central laboratory cardiac troponin assays in an emergency department. *PLoS One*, *12*(11), e0188706.

Yahya, M. Y. A. H., Putra, M. M. R., & Ummah, K. (2023). Thyroid Heart Disease Presenting Thyrotoxic Crisis with Jaundice. *Clinical and Research Journal in Internal Medicine*, *4*(1), 426-433.

Žarković, M. (2012). The role of oxidative stress on the pathogenesis of Graves' disease. *Journal of Thyroid Research*, *2012*.