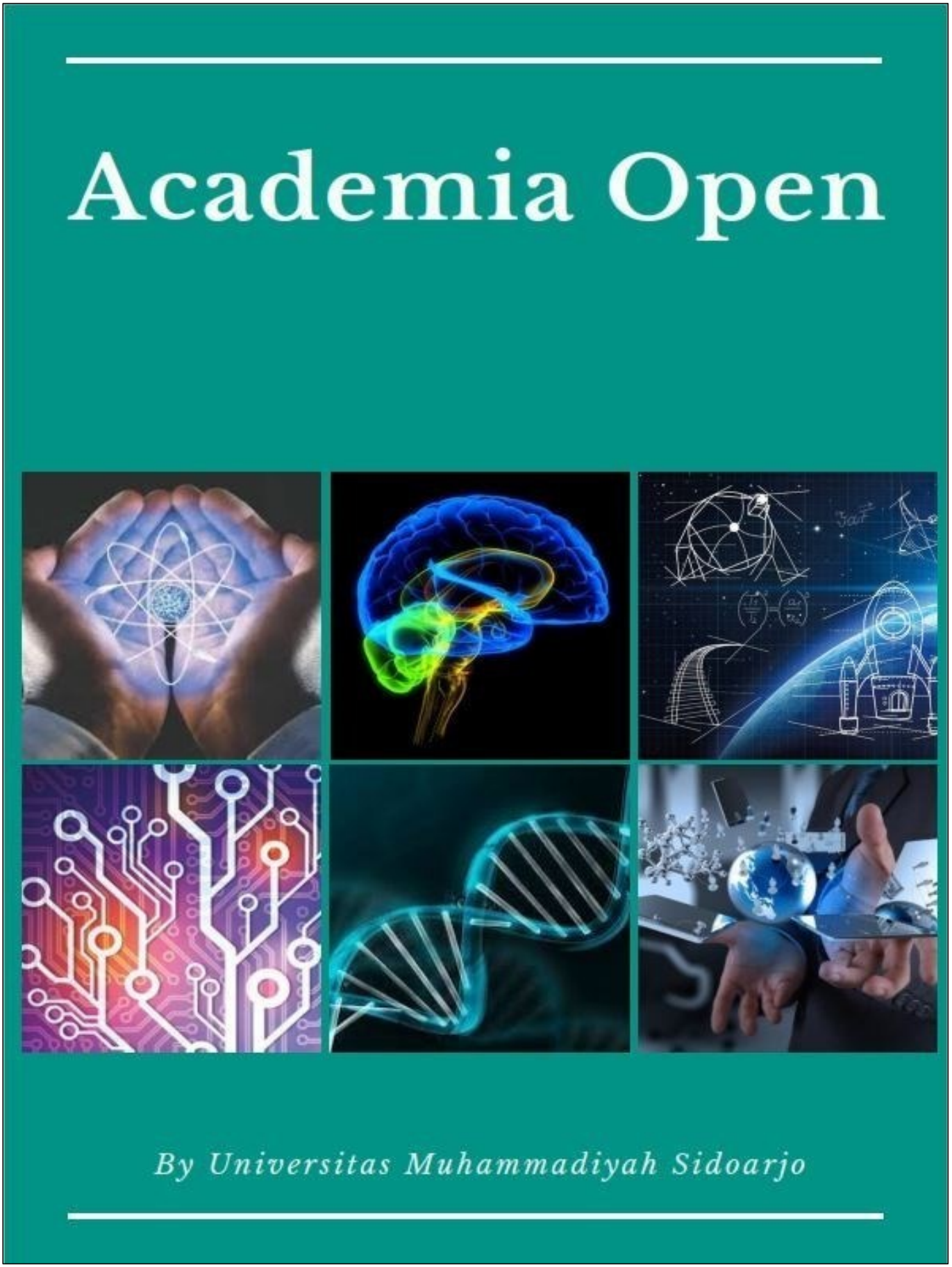
Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809



ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Table Of Contents

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Originality Statement

The author[s] declare that this article is their own work and to the best of their knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the published of any other published materials, except where due acknowledgement is made in the article. Any contribution made to the research by others, with whom author[s] have work, is explicitly acknowledged in the article.

Conflict of Interest Statement

The author[s] declare that this article was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright Statement

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

EDITORIAL TEAM

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Article information

Check this article update (crossmark)

Check this article impact (*)

Save this article to Mendeley

(*) Time for indexing process is various, depends on indexing database platform

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Interleukins and Some Physiological Parameters in Patients with Autoimmune Thyroid Disorders

Thikra Majid Muhammed, thikra.m.m@uoanbar.edu.iq, (1)

Dept. of Biology, College of Education for pure sciences, University of Anbar, Al-Anbar, Iraq

Qabas Huussein Allawi, thikra.m.m@uoanbar.edu.iq, (2)

Basic Science Branch, College of Dentistry, University of Anbar, Al-Anbar, Iraq.

Hala Mahdi Hamad, thikra.m.m@uoanbar.edu.iq, (3)

Dept. of Biology, College of sciences, University of Anbar, Al-Anbar, Iraq

(1) Corresponding author

Abstract

General Background: Autoimmune thyroid diseases (ATDs), such as Graves' disease and chronic autoimmune thyroiditis, are among the most prevalent endocrine disorders characterized by immune-mediated thyroid dysfunction. Specific Background: Cytokines and immune markers play pivotal roles in the pathogenesis of ATDs, yet their association with hematological indices and ovarian reserve markers, such as Anti-Müllerian Hormone (AMH), remains underexplored. Knowledge Gap: Despite the known role of interleukins in autoimmune conditions, limited data exist linking IL-10, IL-17, and IL-18 levels with hematological and reproductive parameters in ATD patients. Aims: This study aimed to assess immunological (IL-10, IL-17, IL-18, AMH) and hematological (Hb, WBC, PLT) parameters in ATD patients compared to healthy individuals. Results: Findings revealed significantly higher serum IL-10, IL-17, and IL-18 levels in ATD patients, while AMH and hemoglobin were markedly reduced. White blood cell and platelet counts were significantly elevated, suggesting immune-driven hematopoietic alterations. Novelty: This study provides integrated evidence linking cytokine dysregulation with hematological and ovarian reserve disturbances in ATD, highlighting potential biomarkers for disease activity. Implications: The results underscore the need for cytokine profiling in ATD management and suggest that IL-10 and IL-18 may serve as predictive indicators for immune and reproductive dysfunction in affected individuals.

Highlight :

- The study found significant increases in IL-10, IL-17, and IL-18 levels among patients with autoimmune thyroid disorders.
- Patients showed lower AMH and hemoglobin levels, with higher WBC and platelet counts compared to controls.
- These results emphasize the role of cytokines in immune and hematological alterations associated with autoimmune thyroid disease.

Keywords : Autoimmune Thyroid Dysfunction, IL-18, IL-17, AMH, IL-10

Published date: 2025-10-22

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Introduction

The clinical picture of ATD is characterized by hyperthyroidism in Graves' disease (GD) and hypothyroidism in chronic autoimmune thyroiditis (cAIT). Both of such diseases have antibodies against thyroid antigens, however they have distinct functional antibodies because of differences in their specific epitopes [1]. Loss of the immune tolerance to the autoantigens and thyroid reactivity causes AITD development. T and B cells then infiltrate the gland and result in the production of anti-bodies that are specific to clinical signs of hypothyroidism (cAIT) and hyperthyroidism (GD), respectively [2]. Regulatory T cells CD4+CD25+ (Treg) are responsible for the existence of immunologically competent cell component with suppressive activities, leading to the prevention of possibly damaging autoimmune responses [3]. Arthritis, thyroiditis, multiple sclerosis, gastritis, ovarian inflammation, and other systemic autoimmune illnesses are brought on by a lack of T regulatory cells in human beings [4]. Th-1 cells generate pro-inflammatory cytokines IFN-g, IL2, TNF, and IL-1b that trigger the macrophage activation and have cytotoxic effects [5]. Th-2 cells generate IL5, IL4, IL10, IL6, and IL13, which could suppress Th1 cytokine production however, mainly activate anti-apoptotic molecules and B cells to make antibodies [6], [7]. Then. Under physiological conditions, proapoptotic death ligands and receptors, including TNF, FasL, and TRAIL, which are found on thyroid cells, are dormant [8], [9]. Nevertheless, thyroid cell apoptosis is triggered through the expression regarding Fas/FasL, which is triggered as a response to the pro-inflammatory Th-1 cytokines through the infiltration of TNF, IFNg, and IL-1b [10]. According to Nagayama (2007), the GD stimulates a Th2 humoral response mostly by the generation of antibodies by B cells, which raises the levels of immunoglobulin G (IgG) and Th2 cell-produced cytokines. The schematic in Figure 1 depicts the pathogenesis of AITD. The pathogenesis of GD might possibly entail a new subtype of Th17 response [12,13]. The purpose of the presented work was to estimate the serum levels of IL-18, IL-17, AMH, and IL-10, also a few other hematological parameters in patients with thyroid autoimmune disorder and comparing those levels to those of healthy controls [11].

Methodology

A. Population of Study

Eighty people participated in this study: thirty healthy people served as the control group, and fifty thyroid disorders sufferers, ages 16 to 50, who visited the General Teaching Hospital in Fallugah General Hospital between November 1, 2024, and January 1, 2025.

B. Blood Samples Collection

An appropriate vein yielded ten milliliters of venous blood. The blood sample (2.5 ml) was promptly moved to a dry, clean EDTA tube. The remaining blood sample was after that placed in a glass tube without anticoagulant and left to coagulate for serum separation for 5 mins in a 4000 rpm centrifuge after being gently shaken and used directly for the blood count blood test. The separated serum has been gathered and kept in clean and sterile white tubes at a temperature of -20 °C for use in serological research.

C. Kits used in the study

The current research employed commercially available kits of enzyme linked immunosorbent assay (ElISA) (Biosource InC, USA) as well as chemical reagents to quantitatively determine IL-17, IL-18, AMH, and IL-10 serum levels. The complete blood count (CBC) test was used in duplicate by Coulter HMX Inc. to determine the WBC, Hb, and PLT parameters.

D. Statistical Analysis

Utilizing T-test, a statistical analysis tool, collected data were analyzed. Results have been displayed in the form of mean ± standard deviation (SD) and were viewed as statistically significant in the case where p value<0.050.

Result

A. Correlation Between Hematological and Immunological Biomarkers

Correlation analysis results showed that platelet count showed a statistically significant positive correlation with IL-18 level (r=0.438, p=0.028), indicating a statistically significant positive relationship, while no significant relationships were recorded with the other variables [12]. A significant positive correlation was also found between white blood cell (WBC) count and hemoglobin level (r=0.534, p=0.0059), while its relationship with the other indicators was insignificant [13]. The cytokine IL-18 was statistically significantly positively correlated with platelets but did not show significant relationships with IL-17, IL-10, AMH, or Hb. On the other hand, the cytokines IL-17 and IL-10 did not record any strong significant correlations with the other variables. AMH showed weak and insignificant correlations with all indicators, while hemoglobin was positively correlated with white blood cells only [14]. These results reflect the heterogeneity in the nature of the relationships between the studied hematological and immune indices, and indicate the distinct role of each in hematological and immune changes [15] (Table 1).

Table 1: Spearman's Correlation Coefficients and p-Values Among Platelet Count, WBC, Cytokines, AMH, and Hemoglobin

Variable	Ratelet	WBC	IL-18	IL-17	IL-10	AMH	Hb

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Ratelet	**1.0000**	0.08703	0.4380	0.1721	0.1978	-0.07514	-0.06385
p-value	—	0.6791	**0.02853**	0.4108	0.3434	0.7211	0.7617
WBC	0.08703	**1.0000**	0.1207	0.1024	0.3328	-0.07689	**0.5344**
p-value	0.6791	—	0.5656	0.6261	0.1041	0.7149	**0.005920**
IL-18	**0.4380**	0.1207	**1.0000**	-0.1616	0.04087	-0.1843	0.1779
p-value	**0.02853**	0.5656	—	0.4403	0.8462	0.3779	0.3949
IL-17	0.1721	0.1024	-0.1616	**1.0000**	-0.1338	0.2671	0.01475
p-value	0.4108	0.6261	0.4403	—	0.5236	0.1968	0.9442
IL-10	0.1978	0.3328	0.04087	-0.1338	**1.0000**	-0.1524	0.2818
p-value	0.3434	0.1041	0.8462	0.5236	—	0.4670	0.1723
AMH	-0.07514	-0.07689	-0.1843	0.2671	-0.1524	**1.0000**	0.07501
p-value	0.7211	0.7149	0.3779	0.1968	0.4670	—	0.7216
Hb	-0.06385	**0.5344**	0.1779	0.01475	0.2818	0.07501	**1.0000**
p-value	0.7617	**0.005920**	0.3949	0.9442	0.1723	0.7216	—

B. Correlation Analysis Between Hematological and Immunological Biomarkers

Correlation analysis results showed that platelet count showed a significant positive correlation with IL-10 levels (r=0.509, p=0.0094), while all other correlations with WBC, IL-18, IL-17, AMH, and hemoglobin were statistically insignificant. White blood cell (WBC) counts did not show any significant relationships with the other indices, although there was a weak, non-statistically significant positive correlation with IL-17 (r=0.334, p>0.05). As for cytokines, IL-18 and IL-17 did not show any significant correlations with the other variables, while IL-10 showed a weak, non-statistically significant positive correlation with AMH (r=0.279, p>0.05). AMH and hemoglobin recorded weak, non-significant correlations with all indices [16]. These results reflect the heterogeneity in the relationships between hematological and immune markers, and point to the specific role of each variable in hematological and immune changes, with IL-10 being important as a potential marker of platelet-associated immune activity (Table 2).

Table 2: Spearman's Correlation Coefficients and p-Values Among Platelet Count, WBC, Cytokines, AMH, and Hemoglobin

Variable	Platelet	WBC	IL-18	IL-17	IL-10	AMH	Hb
Platelet	1.0000	-0.1015	0.04199	-0.1130	**0.5087**	0.2031	-0.2030
p-value	—	0.6292	0.8420	0.5908	**0.0094**	0.3303	0.3305
WBC	-0.1015	1.0000	-0.04220	0.3344	0.1260	-0.1449	0.1851
p-value	0.6292	—	0.8413	0.1023	0.5485	0.4894	0.3756
IL-18	0.04199	-0.04220	1.0000	-0.2490	-0.01229	0.01727	-0.07353
p-value	0.8420	0.8413	—	0.2300	0.9535	0.9347	0.7269
IL-17	-0.1130	0.3344	-0.2490	1.0000	-0.2674	0.007450	-0.008406
p-value	0.5908	0.1023	0.2300	—	0.1963	0.9718	0.9682
IL-10	**0.5087**	0.1260	-0.01229	-0.2674	1.0000	0.2791	-0.1923
p-value	**0.0094**	0.5485	0.9535	0.1963	—	0.1766	0.3572

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

AMH	0.2031	-0.1449	0.01727	0.007450	0.2791	1.0000	0.008171
p-value	0.3303	0.4894	0.9347	0.9718	0.1766	—	0.9691
Hb	-0.2030	0.1851	-0.07353	-0.008406	-0.1923	0.008171	1.0000
p-value	0.3305	0.3756	0.7269	0.9682	0.3572	0.9691	—

C. Immunological Data Analysis:

Levels of AMH:

As illustrated in figure 1, this study demonstrated a considerable difference in the AMH levels between patients (i.e., cases) and normal people (i.e., the control) with a p-value (<0.05). average AMH levels in cases were lower when compared to those in controls, with respective mean values of 19.56 pg/ml and 81.60 pg/ml [17].

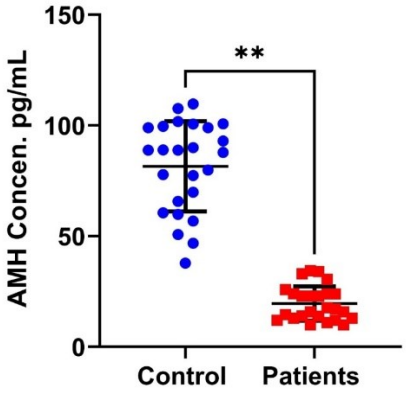


Fig 1: Average levels of AMH (pg/ml) in controls and patients.

levels of IL-17:

According to fig (2), this study had demonstrated a considerable increase in IL-17 levels in the cases in comparison with normal people (controls) with a p-value (<0.05). The average IL-17 levels in the patients have been greater when compared to those in the controls, with respective mean values of 86.80 pg/ml and 25.08 pg/ml [18].

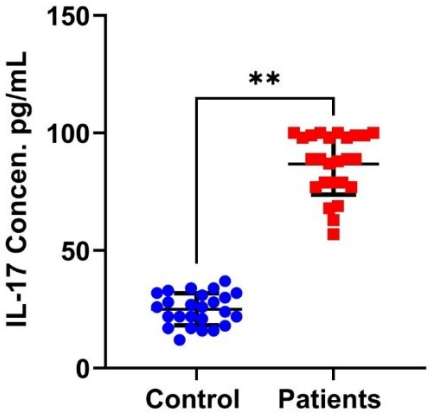


Fig 2: Average levels of IL-17 (pg/ml) in the controls as well as the patients.

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open
Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Levels of IL-10:

As illustrated in fig (3), this paper demonstrated a considerable increase in IL-10 levels in the cases in comparison to normal individuals with a p-value (<0.05). The average IL-10 levels in the cases were greater when compared to those in the controls, with respective mean values of 95.84 pg/ml and 23.51 pg/ml [19].

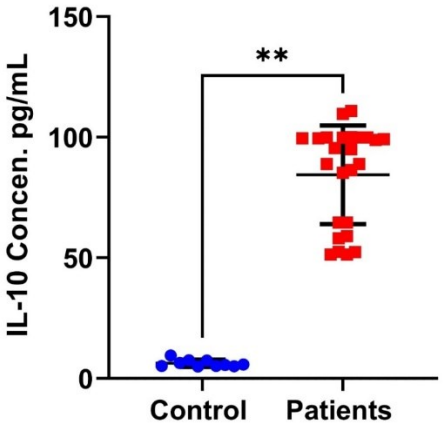


Fig 3: Average levels of IL10 (pg/ml) in the controls as well as the patients.

Levels of IL-18:

According to fig (4), this paper had demonstrated a considerable rise in IL-18 levels in the patients (i.e., the cases) compared with the normal people (i.e., the controls) with a p-value (<0.050). The average IL18 levels in the patients were greater when compared to those in control, with the respective mean values for their groups being 106.1 pg\ml and 33.07 pg\ml [20].

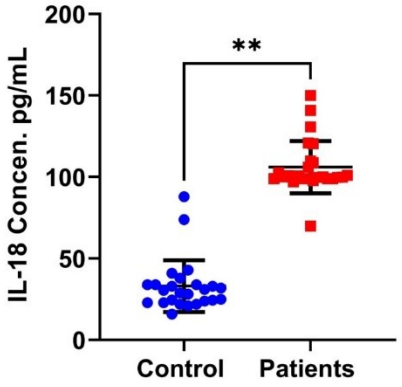


Fig 4: Average levels of IL18 (pg/ml) in the controls as well as the patients.

Hematological Data Analysis:

Concentration of Hemoglobin (Hb):

As seen in fig (5), the current study demonstrated a significant difference in Hb concentration between the controls and the cases, with a p-value of less than 0.05. The means regarding Hb for the two groups were 9.240 g/dl and 13.55 g/dl, respectively [21].

Academia Open
Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

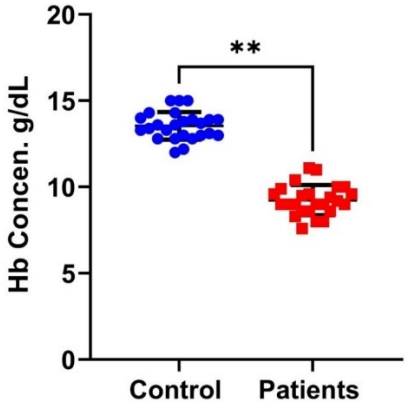


Fig 5: Mean levels of HB in control and patients.

Total Number of WBC:

With a p-value of < 0.050, the current work had demonstrated a significant difference between number of WBCs in the controls and the cases. As seen in fig (6), the WBC means for the two groups were 6.828X 10^3 c/ mm^3 and 16.86X 10^3 c/ mm^3, respectively [22].

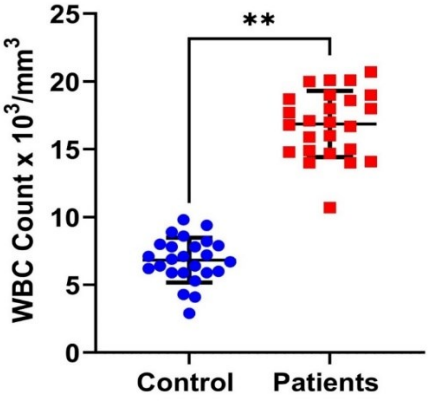


Fig 6: Mean levels of WBCX 10^3 c/mm^3in patients and control.

Total Number of PLT:

With a p-value of < 0.050, the current paper had demonstrated a significant difference in the numbers of PLT between the controls and the cases. As seen in fig (7), the PLT means for the two groups were, respectively, 207.6X 10^3 c/ mm^3 and 746.1X 10^3 c/ mm^3.

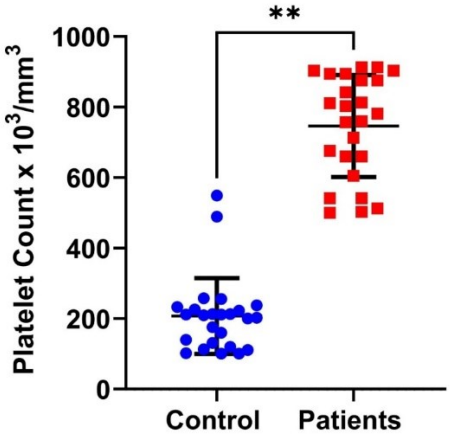


Fig 7: Mean levels of PLTX 10^3 c/mm^3in patients and control**.**

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open
Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

The correlation between parameters in patients and control:

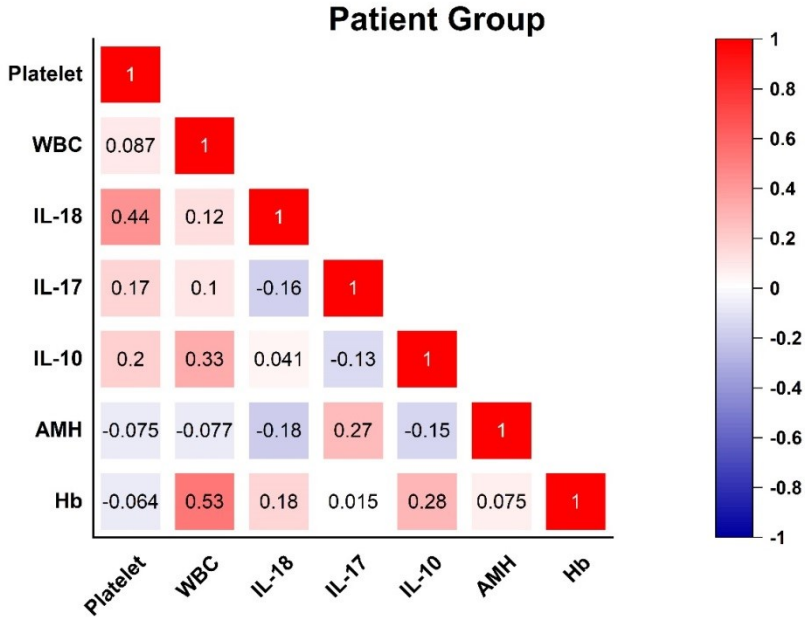


Fig 8: The correlation between parameters in patients

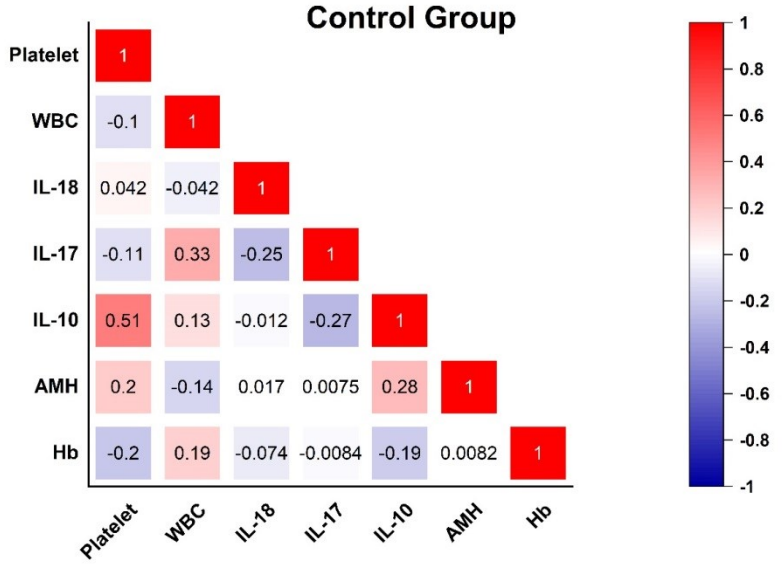


Fig 9: The correlation between parameters in control

Discussion

Working The present study demonstrated that serum levels of IL-17, IL-18, and IL-10 were significantly elevated in patients with autoimmune thyroid disease (ATD) compared with the control group [23]. Cytokines are low-molecular-weight proteins secreted by a variety of cells, including fibroblasts, macrophages, dendritic cells, and lymphocytes [24]. These proteins exert intrinsic and adjunctive effects on multiple tissues, such as the nervous and immune systems, through interactions with specific receptors [25]. Acting as mediators of immune and inflammatory responses, cytokines play a crucial role in the pathogenesis of autoimmune diseases, a link recognized since 1983 when their association with enhanced antigen presentation and autoimmunity was first reported.

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12809

Numerous studies have confirmed that cytokine expression increases with disease progression through the generation of inhibitory and anti-inflammatory mediators such as TGF-β receptor 1 antagonists, TNF-α, and IL-1 receptor antagonists (IL-1Ra) [26]. Thyroid disorders, similar to many other immune-related diseases, may evade immune regulation [27]. High IL-10 levels have been particularly associated with autoimmune diseases, indicating that this cytokine is central to disease pathogenesis [28]. Twin and family studies have shown that heritable genetic factors contribute to interindividual variability in IL-10 production, with genome-wide analyses linking the chromosomal region containing the IL10 locus to autoimmune susceptibility [29]. IL-10 polymorphisms in promoter regions can alter cytokine expression, influencing immune regulation. Its effects on B cells—particularly stimulation and survival of autoreactive B cells suggest IL-10 plays a vital role in autoimmunity [30].

Pro-inflammatory cytokines such as interferons (e.g., IFN-γ), interleukins (IL-1, IL-6, IL-8, IL-12, IL-18), and tumor necrosis factors (TNF-α) are key mediators in autoimmune responses. IL-18, a member of the IL-1 family, exerts potent pro-inflammatory effects and regulates both innate and adaptive immune responses [31]. It promotes IFN-γ production by T and NK cells, contributing to T helper cell activation. Dysregulated IL-18 expression has been linked to several immunologically mediated diseases, including ATD [32]. Al-Bassam et al. reported that both autoimmune and non-autoimmune hyperthyroidism are characterized by elevated cytokine levels, possibly due to prolonged exposure to high thyroid hormone concentrations. These findings align with those of Fallahi et al., who also observed significantly increased IL-18 levels in ATD patients [33]. Similarly, De Ciuces et al. found elevated serum IL-18 in autoimmune thyroid disease, suggesting thyrotropin (TSH) may regulate IL-18 production in thyrocytes [34]. TSH has been shown to enhance cytokine production from hematopoietic cells, increase NK cell cytotoxicity, and stimulate T-cell proliferation.

Cytokines are thus potential candidate genes for ATD pathogenesis, as they are involved in both the induction and effector phases of immune and inflammatory responses. Several cytokines, including IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-13, IL-14, TNF-α, and IFN-γ, are produced by thyroid follicular and intrathyroidal inflammatory cells [35]. The cytokine network is highly complex, with overlapping regulatory functions that may enhance or inhibit the activity of other cytokines. Depending on the immune context, cytokine secretion profiles are classified as Th1 (cell-mediated, IL-2, IFN-γ) or Th2 (humoral, IL-4, IL-5, IL-6, IL-10, IL-13) responses [36].

Autoimmune thyroid disease represents one of the most common endocrine disorders, affecting 5–15% of the reproductive-age population [37]. Women with ATD are at increased risk of ovarian insufficiency due to age-related decline in ovarian reserve. Anti-Müllerian Hormone (AMH), a biomarker of ovarian function, has been shown to decrease in women with ATD. The current findings agree with Busnelli et al. [38] and Krassas et al. [39], who reported significantly lower AMH levels in ATD patients compared to controls, whereas Stang [40] reported opposite results. Reduced AMH may contribute to infertility, as shown by studies demonstrating significantly lower AMH levels in ATD patients (2.60 ± 2.0 ng/ml) versus controls (4.49 ± 2.0 ng/ml, $p < 0.001$) [41]. Despite varying reports, thyroid dysfunction and autoimmune thyroiditis are recognized as risk factors for impaired fertility [42].

Kuroda et al. [43] observed that hypothyroidism is associated with menstrual irregularities and infertility due to impaired gonadotropin-releasing hormone secretion, hyperprolactinemia, and altered estrogen metabolism. AMH is a reliable marker of ovarian aging, and thyroid dysfunction may adversely affect ovarian physiology [44]. Moreover, thyroid hormones interact with estrogen and progesterone to maintain endometrial health and promote oocyte maturation [45].

In the current study, hematological profiles—hemoglobin (Hb), white blood cell (WBC), and platelet (PLT) counts—were also assessed. ATD patients exhibited lower Hb levels and higher WBC and PLT counts, consistent with the hypothesis that thyroid hormones influence bone marrow hematopoiesis. Decreased RBC and WBC counts suggest bone marrow suppression, as thyroid hormones, particularly triiodothyronine (T3), regulate pro-B-cell proliferation and normal hematopoiesis [46]. Low Hb indicates anemia, often macrocytic hypochromic in nature, which may arise from hypothyroidism-related bone marrow suppression. The elevated PLT counts likely represent a compensatory response to hematopoietic imbalance [47].

Thyroid hormones play a central role in hematopoiesis by stimulating erythropoietin and hematopoietic factor synthesis in non-erythroid cells [48]. Conversely, hypothyroidism can result in macrocytic hypochromic anemia or proliferation of immature erythroid progenitors [49]. Patients with hypothyroidism may present with neutropenia, thrombocytopenia, or mild leukopenia, whereas hyperthyroidism can cause pancytopenia, anemia, lymphopenia, or thrombocytopenia [50]. Furthermore, thyroid dysfunction influences hepatic and endothelial protein synthesis, predisposing individuals to bleeding (hypothyroidism) or thrombosis (hyperthyroidism) [51]. Erythrocyte sedimentation rate (ESR) remains a valuable clinical marker of inflammation and therapeutic response. Elevated ESR levels have been observed in anemic patients and those with subacute thyroiditis, reflecting systemic inflammatory activation.

Conclusion

The current study's findings led us to the conclusion that, in comparison to healthy individuals, patients who have ATD had much higher IL-10, IL-17, and IL-18 levels. ATD patients have significantly more WBC and platelets than normal people, and their AMH and Hb levels are significantly lower than those of normal people.

Recommendations

The authors would like to express thanks to volunteers who have taken part in completing this research. Also they would like to thank Al-Anbar University, Anbar, Iraq for its support in the present study.

Authors' Declaration

• Conflicts of Interest: None.

• We hereby confirm that all the Tables in the manuscript are ours.

• No animal studies are present in the manuscript.

• Authors sign on ethical consideration's approval.

• Ethical Clearance: The project was approved by the local ethical committee at Anbar University.

Authors' Contribution Statement

The authors contributed equally to this research. The first researcher T. M. M. collected the samples, and then, in collaboration with Q. H. A. and H. M. H. developed the methods. Q. H. A. performed the statistical analysis. H. M. H. wrote the manuscript and searched for reputable journals for publication

References

1. E. Tywanek, A. Michalak, J. Swirska, and A. Zwolak, "Autoimmunity, New Potential Biomarkers and the Thyroid Gland—The Perspective of Hashimoto's Thyroiditis and Its Treatment," International Journal of Molecular Sciences, vol. 25, no. 9, p. 4703, Apr. 2024, doi: 10.3390/ijms25094703.

2. A. I. Arhire, M. C. Coman, A. M. Mihalache, and C. A. Mitu, "Association of HLA Haplotypes with Autoimmune Pathogenesis in Newly Diagnosed Type 1 Romanian Diabetic Children: A Pilot, Single-Center Cross-Sectional Study," Life (Basel), vol. 14, no. 6, p. 78, 2024, doi: 10.3390/life14060781.

3. C. LeGuern and J. F. Markmann, "Regulatory CD4+ T Cells: Permanent or Temporary Suppressors of Immunity," Frontiers in Immunology, vol. 15, Art. no. 1293892, 2024, doi: 10.3389/fimmu.2024.1293892.

4. P. Pandiyan, L. Zheng, S. Ishihara, J. Reed, and M. J. Lenardo, "CD4+CD25+Foxp3+ Regulatory T Cells Induce Cytokine Deprivation-Mediated Apoptosis of Effector CD4+ T Cells," Nature Immunology, vol. 8, no. 12, pp. 1353–1362, 2007, doi: 10.1038/ni1536.

5. M. J. Butcher and J. Zhu, "Recent Advances in Understanding the Th1/Th2 Effector Choice," Faculty Reviews, vol. 10, p. 30, 2021, doi: 10.12703/r/10-30.

6. P. Bretscher, "On Analyzing How the Th1/Th2 Phenotype of an Immune Response Is Determined: Classical Observations Must Not Be Ignored," Frontiers in Immunology, vol. 10, p. 1234, 2019, doi: 10.3389/fimmu.2019.01234.

7. Y. Zeng, L. Wang, H. Zhou, and Y. Qi, "A Meta-Analysis of Th1 and Th2 Cytokine Profiles Differentiating Tuberculous from Malignant Pleural Effusion," Scientific Reports, vol. 12, no. 1, p. 2743, Feb. 2022, doi: 10.1038/s41598-022-06685-8.

8. P. F. D. S. Teixeira, P. B. Dos Santos, and C. C. Pazos-Moura, "The Role of Thyroid Hormone in Metabolism and Metabolic Syndrome," Therapeutic Advances in Endocrinology and Metabolism, vol. 11, p. 2042018820917869, 2020, doi: 10.1177/2042018820917869.

9. A. Guerrache and O. Micheau, "TNF-Related Apoptosis-Inducing Ligand: Non-Apoptotic Signalling," Cells, vol. 13, no. 6, p. 521, 2024, doi: 10.3390/cells13060521.

10. A. Smith, J. Eccles-Smith, M. D'Emden, and K. Lust, "Thyroid Disorders in Pregnancy and Postpartum," Australian Prescriber, vol. 40, no. 6, pp. 214–219, 2017, doi: 10.18773/austprescr.2017.075.

11. A. Fulton, N. Mittal, and A. Deb, "Postpartum Psychosis as a Consequence of Thyroiditis versus Relapse: A Diagnostic Dilemma," Cureus, vol. 16, no. 1, p. e52357, 2024, doi: 10.7759/cureus.52357.

12. Y. Nagayama, "Graves' Animal Models of Graves' Hyperthyroidism," Thyroid, vol. 17, no. 10, pp. 981–988, 2007, doi: 10.1089/thy.2007.0161.

13. J. Bernal, "Thyroid Hormones in Brain Development and Function," in Endotext [Internet], K. R. Feingold et al., eds. South Dartmouth (MA): MDText.com, Inc., 2000–, updated Jan. 14, 2022. Available: https://www.ncbi.nlm.nih.gov/books/NBK285549/

14. World Health Organization, WHO Guidelines on Drawing Blood: Best Practices in Phlebotomy, Geneva: WHO, 2010. Available: https://www.ncbi.nlm.nih.gov/books/NBK138650/

15. P. Zhou, T. Zheng, and B. Zhao, "Cytokine-Mediated Immunomodulation of Osteoclastogenesis," Bone, vol. 164, p. 116540, 2022, doi: 10.1016/j.bone.2022.116540.

16. H. M. Hamad, Z. A. Shabeeb, and M. M. Awad, "Expressions of CD274 (PD-L1) and CD47 Receptors on the Surface of Blast Cells in AML Patients," Iraqi Journal of Science, vol. 63, no. 6, pp. 2373–2387, 2022, doi: 10.24996/ijs.2022.63.6.6.

17. X. Wang, K. Wong, W. Ouyang, and S. Rutz, "Targeting IL-10 Family Cytokines for the Treatment of Human Diseases," Cold Spring Harbor Perspectives in Biology, vol. 11, no. 2, p. a028548, 2019, doi: 10.1101/cshperspect.a028548.

18. T. Kuwabara, F. Ishikawa, M. Kondo, and T. Kakiuchi, "The Role of IL-17 and Related Cytokines in Inflammatory Autoimmune Diseases," Mediators of Inflammation, vol. 2017, p. 3908061, 2017, doi: 10.1155/2017/3908061.

19. C. K. Wong, C. W. Ho, E. K. Ko, C. W. Lam, P. C. Ho, and C. W. Lee, "Proinflammatory Cytokines (IL-17, IL-6, IL-18, and IL-12) and Th Cytokines (IFN-γ, IL-4, IL-10, and IL-13) in Patients with Allergic Asthma," Clinical and Experimental Immunology, vol. 125, no. 2, pp. 177–183, 2001, doi: 10.1046/j.1365-2249.2001.01602.x.

20. S. A. Ihim, M. A. Suleiman, R. E. Chinedu, and O. O. Ilesanmi, "Interleukin-18 Cytokine in Immunity, Inflammation, and Autoimmunity: Biological Role in Induction, Regulation, and Treatment," Frontiers in Immunology, vol. 13, p. 919973, 2022, doi: 10.3389/fimmu.2022.919973.

21. A. Winikajtis-Burzynska, M. Brzosko, and H. Przepiera-Bedzak, "Increased Serum Interleukin 10 Levels Are Associated with Increased Disease Activity and Increased Risk of Anti-SS-A/Ro Antibody Positivity in Patients with Systemic Lupus Erythematosus," Biomolecules, vol. 13, no. 6, p. 974, 2023, doi: 10.3390/biom13060974.

22. K. D. Sekiyama, M. Yoshiba, and A. W. Thomson, "Circulating Proinflammatory Cytokines (IL-1β, TNF-α, and IL-6) and IL-1 Receptor Antagonist (IL-1Ra) in Fulminant Hepatic Failure and Acute Hepatitis," Clinical and Experimental Immunology, vol. 98, no. 1, pp. 71–77, 1994, doi: 10.1111/j.1365-2249.1994.tb06609.x.

23. J. Mai, H. Wang, and X. F. Yang, "Th17 Cells Interplay with Foxp3+ Tregs in Regulation of Inflammation and Autoimmunity," Frontiers in Bioscience (Landmark Edition), vol. 15, no. 3, pp. 986–1006, 2010, doi: 10.2741/3657.

24. F. Zador, P. Nagy-Grócz, Z. Kántor, and B. Tuka, "Pro-Inflammatory Cytokines: Potential Links Between the Endocannabinoid System and the Kynurenine Pathway in Depression," International Journal of Molecular Sciences, vol. 22, no. 11, p. 5903, 2021, doi: 10.3390/ijms22115903.

25. K. Nakanishi, "Unique Action of Interleukin-18 on T Cells and Other Immune Cells," Frontiers in Immunology, vol. 9, p. 763, 2018, doi: 10.3389/fimmu.2018.00763.

26. W. Al-Bassam, A. Ad'hiah, and K. Mayouf, "Biomarker Significance of Interleukin-18 in Juvenile Idiopathic Arthritis," Iraqi Journal of Science, vol. 61, no. 12, pp. 3200–3207, 2020, doi: 10.24996/ijs.2020.61.12.7.

27. P. Fallahi, A. Ferrari, C. Ruffilli, and A. Antonelli, "Cytokines as Targets of Novel Therapies for Graves' Ophthalmopathy," Frontiers in Endocrinology (Lausanne), vol. 12, p. 654473, 2021, doi: 10.3389/fendo.2021.654473.

28. C. De Ciuceis, A. Pilu, E. Rizzoni, and F. Agabiti-Rosei, "Decreased Number of Circulating Endothelial Progenitor Cells in Patients with Graves' Hyperthyroidism," Journal of Endocrinological Investigation, vol. 34, no. 5, pp. 335–339, 2011, doi: 10.1007/BF03347455.

29. L. Weng, S. Zhang, and F. Xu, "Low Levels of Serum IL-39 Are Associated with Autoimmune Thyroid Disease," Journal of Clinical Laboratory Analysis, vol. 36, no. 4, p. e24284, 2022, doi: 10.1002/jcla.24284.

30. A. A. Justiz Vaillant and A. Qurie, "Interleukin," in StatPearls, Treasure Island (FL): StatPearls Publishing, 2025. Available: https://www.ncbi.nlm.nih.gov/books/NBK499840/

31. F. Foroozanfard, A. Soleimani, E. Arbab, M. Samimi, and M. R. Tamadon, "Relationship Between IL-17 Serum Level and Ambulatory Blood Pressure in Women with Polycystic Ovary Syndrome," Journal of Nephropathology, vol. 6, no. 1, pp. 15–24, 2017, doi: 10.15171/jnp.2017.04.

32. G. E. Krassas, K. Poppe, and D. Glinoer, "Thyroid Function and Human Reproductive Health," Endocrine Reviews, vol. 31, no. 5, pp. 702–755, 2010, doi: 10.1210/er.2009-0041.

33. R. Mazzilli, M. Cimino, G. Oliviero, and F. Cipolla, "The Role of Thyroid Function in Female and Male Infertility: A Narrative Review," Journal of Endocrinological Investigation, vol. 46, no. 1, pp. 15–26, 2023, doi: 10.1007/s40618-022-01883-7.

34. C. C. Repelaer van Driel-Delprat, P. R. Boon, and J. H. Evers, "Thyroid Function and IVF Outcome for Different Indications of Subfertility," Reproduction and Fertility, vol. 2, no. 4, pp. 280–291, 2021, doi: 10.1530/RAF-20-0065.

35. J. S. Younis and H. S. Taylor, "The Impact of Ovarian Endometrioma and Endometriotic Cystectomy on Anti-Müllerian Hormone and Antral Follicle Count: A Contemporary Critical Appraisal of Systematic Reviews," Frontiers in Endocrinology (Lausanne), vol. 15, p. 1397279, 2024, doi: 10.3389/fendo.2024.1397279.

36. A. Busnelli, F. Paffoni, L. Serafini, and E. Candiani, "Levothyroxine Dose Adjustment in Hypothyroid Women Achieving Pregnancy Through IVF," European Journal of Endocrinology, vol. 173, no. 4, pp. 417–424, 2015, doi: 10.1530/EJE-15-0151.

37. A. Stang, "Critical Evaluation of the Newcastle-Ottawa Scale for the Assessment of the Quality of Nonrandomized Studies in Meta-Analyses," European Journal of Epidemiology, vol. 25, no. 9, pp. 603–605, 2010, doi: 10.1007/s10654-010-9491-z.

38. M. Kuroda, M. Kato, T. Horie, and Y. Ohta, "Histological Assessment of Impact of Ovarian Endometrioma and Laparoscopic Cystectomy on Ovarian Reserve," Journal of Obstetrics and Gynaecology Research, vol. 38, no. 9, pp. 1187–1193, 2012, doi: 10.1111/j.1447-0756.2012.01845.x.

39. T. M. Muhammed, H. M. Saleem, H. R. A. K. Al-Hetty, and D. A. Salman, "The Relation Between Some Parasitological Parameters and Inflammatory Bowel Disease Infection," International Journal of Health Sciences, vol. 6, suppl. 4, pp. 9687–9697, 2022, doi: 10.53730/ijhs.v6nS4.12046.

40. K. R. Hansen, G. M. Hodnett, N. Knowlton, and L. B. Craig, "Correlation of Ovarian Reserve Tests with Histologically Determined Primordial Follicle Number," Fertility and Sterility, vol. 95, no. 1, pp. 170–175, 2011, doi: 10.1016/j.fertnstert.2010.04.006.

41. J. W. Wang, X. X. Liao, and T. Li, "Thyroid Autoimmunity in Adverse Fertility and Pregnancy Outcomes: Timing of Assisted Reproductive Technology in AITD Women," Journal of Translational Internal Medicine, vol. 9, no. 2, pp. 76–83, 2021, doi: 10.2478/jtim-2021-0001.

42. Q. M. Reshi, I. Ahmed, K. M. Al-Anazi, and M. A. Farah, "Indexing Hematological and Serum Biochemical Reference Intervals of Himalayan Snow Trout, Schizothorax esocinus, to Instrument in Health Assessment," Frontiers in Physiology, vol. 14, p. 989442, 2023, doi: 10.3389/fphys.2023.989442.

43. C. S. Lima, F. R. Cury, and L. C. Moraes, "Pancytopenia in Untreated Patients with Graves' Disease," Thyroid, vol. 16, no. 4, pp. 403–409, 2006, doi: 10.1089/thy.2006.16.403.

44. S. Chandra, A. K. Tripathi, S. Mishra, M. Amzarul, and A. K. Vaish, "Physiological Changes in Hematological Parameters During Pregnancy," Indian Journal of Hematology and Blood Transfusion, vol. 28, no. 3, pp. 144–146, 2012, doi: 10.1007/s12288-012-0175-6.

45. D. Liu, V. Saikam, K. A. Skrada, D. Merlin, and S. S. Iyer, "Inflammatory Bowel Disease Biomarkers," Medicinal Research Reviews, vol. 42, no. 5, pp. 1856–1887, 2022, doi: 10.1002/med.21893.

46. M. Rashied, M. I. Salman, H. S. H. Hamad, and H. M. Hamad, "Effect of Coenzyme Q10 Against Alloxan-Induced Diabetes and Liver Toxicity in Male Rats," Biochemistry and Cellular Archives, vol. 20, no. 2, pp. 4925–4930, 2020. Available: https://connectjournals.com/pages/articledetails/toc032343.

47. C. Leberbauer, R. Boulmé, M. Unfried, W. Huber, and E. G. Beug, "Different Steroids Co-Regulate Long-Term Expansion Versus Terminal Differentiation in Primary Human Erythroid Progenitors," Blood, vol. 105, no. 1, pp. 85–94, 2005, doi: 10.1182/blood-2004-03-1002.

48. M. A. Iddah, B. N. Macharia, A. G. Ng'wena, A. Keter, and A. V. Ofulla, "Thyroid Hormones and Hematological Indices Levels in Thyroid Disorders Patients at Moi Teaching and Referral Hospital, Western Kenya," ISRN Endocrinology, vol. 2013, p. 385940, 2013, doi: 10.1155/2013/385940.

49. S. S. Ahmed and A. A. Mohammed, "Effects of Thyroid Dysfunction on Hematological Parameters: Case Controlled Study," Annals of Medicine and Surgery (London), vol. 57, pp. 52–55, 2020, doi: 10.1016/j.amsu.2020.07.008.

50. C. Erem, "Thyroid Disorders and Hypercoagulability," Seminars in Thrombosis and Hemostasis, vol. 37, no. 1, pp. 17–26, 2011, doi: 10.1055/s-0030-1270067.

51. M. P. Baruah and B. Bhattacharya, "Significant Role of Serum CRP in Differentiating Inflammatory from Non-Inflammatory Causes of Thyrotoxicosis," Indian Journal of Endocrinology and Metabolism, vol. 16, no. 6, pp. 976–981, 2012, doi: 10.4103/2230-8210.103002.