BMC Research Notes

RESEARCH NOTE

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Evaluation of the hematological parameters, inflammatory biomarkers, and thyroid hormones in hypothyroidism patients

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Abstract

Aim Hypothyroidism is created by disruption of thyroid hormone production, which can destroy the emotional, relational, social, and working life of patients if left untreated. Hypothyroidism has multiple etiologies. We evaluated the relationship of hematological parameters and inflammatory biomarkers with thyroid hormones to find the potential use of these items in patients screening and prognosis.

Methods This is a cross-sectional study, which was done on 88 individuals of both genders (32 male and 56 female), over 18 years old with a mean age of 45 years old. These patients were referred by physicians after examination to our laboratories of Qaem Medical Laboratory of Kuhchenar and Jahrom University of Medical Sciences, Fars, Iran. The patients had recent symptoms and signs of hypothyroidism with increased TSH above the normal range, and negative serum anti-TPO antibody. To determine ABO, Rh, and Lewis (Le) blood groups was used anti-A, anti-B, anti-D, anti-Lea, and anti-Leb monoclonal antibodies. Serum T3, T4, and TSH was measured by direct chemiluminescent immunoassay. Anti-TPO antibody was measured by ELISA. CRP was determined using an immunoturbidimetric assay. CBC count assessment was done via an automated cell counter.

Exclusion criteria were patients with acute or chronic inflammatory diseases. Herein, we evaluated the correlation of hematological parameters consisting ABO, Rh, and Le blood groups, RBC and WBC parameters, and platelet count as well as inflammatory biomarkers including ESR, CRP, IL-8, and NLR with T3, T4, and TSH in hypothyroid patients.

Results Our study showed a significant correlation between Lea blood group (non-secretor) in comparison with Leb blood group (secretor) with TSH ($P=0.01$). There was no correlation between Leb and Lea blood groups with T3 and T4. We did not observe the correlation between Rh and ABO blood groups with T3, T4, and TSH. We observed significant correlations between Hb, Hct, and MCH with T3 ($PHb=0.012$, $PHct=0.021$, and $PMCH=0.032$) and also, with T4 in hypothyroidism ($PHb=0.023$ and $PHct=0.026$). We revealed significant correlations between Hb, Hct, and MCH with TSH in hypothyroidism ($PHb=0.017$, $PHct=0.019$, and $PMCH=0.007$). The significant correlations between CRP and IL-8 with T3, T4, and TSH was not explored. The significant correlations between ESR with T3 and TSH was not detected. ESR showed a significant correlation with T4 ($PESR=0.020$). There were also no significant

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correlations between the counts of neutrophils, lymphocytes, monocytes, and eosinophils, as well as NLR with T4. There was only significant correlation between monocyte count with T3 (PMono = 0.029) and also lymphocyte count with TSH (PLymph = 0.041).

Conclusion In this investigation, we observed a significant relationship between Lea blood group in comparison with Leb blood group with TSH. We demonstrated significant correlations between Hb and Hct with T3, T4, and TSH, and also correlations between MCH with T3 and TSH. In conclusion, the assessment of Hb, Hct, MCH, and Le blood groups as hematological parameters can help physicians in the management of hypothyroidism.

Keywords Hypothyroidism, Hematological parameters, Inflammatory biomarkers

Introduction

Hypothyroidism is created by thyroid hormone deficiency that can destroy the emotional, relational, social, and working life of patients if left untreated [1]. Serum level of thyroid hormones is modulated by the hypothalamus-pituitary–thyroid axis. Thyrotropin-releasing hormone (TRH) production controls thyroid-stimulating hormone (TSH) levels. TSH affects the thyroxine (T4) and triiodothyronine (T3) secretion from the thyroid gland [2]. Hypothyroidism can be diagnosed by measuring TSH and the levels of free thyroxine (fT4), due to the free hormone hypothesis (the free hormone levels are better indicators of thyroid function than the total hormone levels because of the thyroid hormone-binding proteins (THBPs) alterations) [3]. Subclinical hypothyroidism is defined biochemically as serum TSH more the normal range and serum fT4 in normal range while overt hypothyroidism is determined as serum TSH over the normal range and serum fT4 level below the normal range [2]. Overt hypothyroidism affects 0.2–5.3% of the common population; In iodine-sufficient people of Tehran, the prevalence of subclinical and overt hypothyroidism was 7.62 and 2.0 per 1,000 persons, respectively [4, 5]. Central hypothyroidism is known by abnormal low TSH level, resulting in insufficient thyroid hormone production, which can be caused by hypothalamic or pituitary pathologies including pituitary adenoma, infiltrative disease, radiotherapy, surgery, pituitary apoplexy, and Sheehan's syndrome. In peripheral hypothyroidism the effectiveness of thyroid hormone on goal cells reduces.

Chronic autoimmune thyroiditis is the common primary hypothyroidisms, which may be due to genetic and environmental factors, micronutrients (mainly iodine and selenium), drugs, and immune system defects. Other hypothyroidism consist transient thyroiditis, postpartum thyroiditis, primary thyroid lymphoma, Reidel thyroiditis, and using some medications like lithium, amiodarone, and immune-checkpoint inhibitors have been reported [6]. Thyroid hormones are important in all body processes consisting metabolic pathways, growth, development, cognition, energy homeostasis, temperature regulation, and carcinogenesis, as well as thyroid function affects the emotional, relational, social, and working life of humans [1]. Indications of hypothyroidism are highly variable, and range from nonspecific symptoms such as fatigue, depression, weight enhancement, and menstrual irregularities to life-threatening diseases like cardiovascular, musculoskeletal, and neurological disease if left untreated [7]. TSH level shows an appropriate index of thyroid function because it can detect developing hypothyroidism and hyperthyroidism before fT4 abnormalities are visible in tests. Assessment of TSH is the best for screening thyroid dysfunction. There is worldwide agreement, which normal TSH concentrations are below 2.5 mIU/L and TSH levels above 10 mIU/L need treatment [8]. Levothyroxine (LT4) is a lifelong treatment for hypothyroidism and the physician's goal is resolution of hypothyroidism indication and improvement of quality of life utilizing of serum TSH normalization [9]. The endocrine system has a close correlation with the immune system and systemic inflammation can affect thyroid function so immune factors may help us differentiate patients with thyroid disorders from healthy ones. Interleukin (IL)−8 has a role in the pathogenesis of thyroid diseases. There are significant differences in IL-8 levels of thyroid disease patients and reference normal group [10]. Patients who developed hypothyroidism had higher C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels than the normal group [11, 12]. Neutrophils and lymphocytes counts, as well as neutrophil/lymphocyte ratio (NLR) is generally considered to predict an inflammatory condition[13] In Hashimoto's patients NLR is more than overt hypothyroidism in compared to subclinical hypothyroidism [14].

Human blood group antigens are glycoproteins expressed on red blood cells (RBCs). In addition, these blood groups are able to be presented on blood cells and tissues [15]. ABO blood types were associated with various infectious and noninfectious diseases in previous studies and ABO blood types and Rh may be different in benign thyroid diseases from the general populations [16]. Some studies have showed a higher rate of thyroid autoimmunity in non-secretors than in secretor groups. The secretor gene influences the Lewis (Le) expression

including Lea (non-secretors) and Leb (secretors) blood groups [17]. Thyroid hormones have an important effect on erythropoiesis through hyperproliferation of immature erythroid progenitors and increased secretion of erythropoietin [18]. Thyroid dysfunction is correlated with anemia in primary and subclinical hypothyroidism [19]. Examining these factors, along with thyroid hormones, is helpful in cases of hypothyroidism where the clinical diagnosis is suspicious or subclinical. Hence, in this investigation, we evaluated the relationship between hematological parameters and inflammatory biomarkers with T3, T4, and TSH in hypothyroidism.

Materials and methods

Study design and participants

This study performed based on the guidelines of the Medical Ethics Committee of the Jahrom University of Medical Sciences (IR.JUMS.REC.1400.093) on 88 individuals of both genders (32 male and 56 female), over 18 years old with a mean age of 45 years old. These patients were referred by physicians after examination to our laboratories of Qaem Medical Laboratory of Kuhchenar and Jahrom University of Medical Sciences, Fars, Iran since April 2022 until August 2022. Inclusion criteria: All the patients with recent signs of hypothyroidism who had increased TSH above the normal range, and negative serum anti-thyroid peroxidase (anti-TPO) antibody. Exclusion criteria were anti-TPO positive patients, and every acute or chronic inflammatory disease such as microbial infections, rheumatoid arthritis, renal disorders, and liver disorders.

Data collection

The study began after obtaining informed consent from all the participants by collecting 2 mL of blood in sodium citrated tube for measuring ESR, 2 mL of blood in K2-ethylenediaminetetraacetic acid (EDTA) containing tube for measuring complete blood cells (CBCs) count, white blood cells (WBC) differentiation, and ABO, Rh, and Le blood groups. 5 mL of blood in clotting tube for measuring anti-TPO, CRP, IL-8, and hormonal analysis (T3, T4, and TSH). CBC count (hemoglubin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW)), WBCs differentiation (the counts of neutrophils (Neut), lymphocytes (Lymph), monocytes (Mono), and eosinophils (Eosin)), platelet (PLT) count, and ABO, Rh, Lea, and Leb blood groups was determined for all the hypothyroid patients. We also evaluated ESR, CRP, IL-8, NLR, T3, T4, TSH, and anti-TPO for these patients.

Assessment of anti-TPO, T3, T4, and TSH

Measuring of serum anti-TPO, T3, T4, and TSH was performed by the sandwich enzyme-linked immunosorbent assay (ELISA) (Pishtazteb, Iran), and then ELISA results was confirmed by enzyme-linked fluorescent assay (ELFA) technology (VIDAS, USA). The coefficient of variation (CV) for anti-TPO antibodies at 26.5, 118.5, and 365.4 IU/mL were 6.8%, 4.5%, and 6.2% (limit detection = 0.92 IU/mL). The CV for T3 at 0.057, 1.66, and 5.65 ng/mL were 8.8%, 3.6%, and 4.9% (limit detection = 0.1 ng/mL). The CV for T4 at 3.8, 9.9, and 15.3 µg/dL were 5.5%, 7.7%, and 4.4% (limit detection = 0.4 µg / dL). Finally, the CV for TSH at 0.25, 4.4, and 12.1 mIU/L were 8%,7%, and 8.4% (limit detection = 0.1 mIU/mL). Our laboratory normal ranges were less than 39.2 IU/mL for anti-TPO antibody, 0.66–1.7 ng/mL for T3, 4.7–12.3 µg/dL for T4, and 0.4–5.1 mIU/L for TSH.

ABO, Rh, and Le blood groups assessment

ABO, Rh, and Le blood groups determination was performed using the hemagglutination cell type test. To determine ABO, Rh, and Le blood groups, all samples were washed three times with normal saline and 2 drops of 5% RBC suspension were prepared on 5 different tubes with the combination of 4 drops of anti-A, anti-B, anti-D (Cinnaclone, Iran), anti-Lea, and anti-Leb monoclonal antibodies (Lorne, UK).

Hemagglutination reaction with these antibodies was explored A, B, O, AB, Rh, Lea, and Leb antigens on RBCs. Confirmation of ABO blood groups cell type results were done through the back typing method by adding 2 drops of 5% known suspensions of A, B, and O cells to the 4 drops of serums of the hypothyroid patients on 3 different tubes.

CBC count and WBC differentiation assessment

CBC count assessment was done using an automated cell counter (Sysmex, Japan). RBC histogram is used for the determination of the RBC indices including RBC count, Hb, Hct, MCV, MCH, MCHC, and RDW. Determination of WBC count and consequently the counts of neutrophils, lymphocytes, monocytes, and eosinophils. NLR was done using a WBC count differentiation scattergram.

Inflammatory biomarkers assessment

CRP in the semi-quantitative method is determined using an immunoturbidimetric assay following manufacturer´s instructions (Bionic, Iran). The ESR evaluation is performed using the Westergren method following standard procedure.

IL-8 assessment

The serum concentration of IL-8 is determined using ELISA kits (eBioscience, USA). IL-8 concentration was measured at 450 nm wavelength and 630 nm as a reference wavelength.

Statistical analysis

Statistical Package for Social Science (SPSS) version 25 (IBM, USA) was applied for statistical analysis. All graphs are prepared using GraphPad version 8.4 (Prism, USA). The determination of correlation between quantitative variables is performed using the Spearman correlation test. P values less than 0.05 were considered as statistically significant and in the graphical representations, the data are presented here as mean ± standard deviation (SD) of three independent experiments.

Results

As a quality control assessment, there was a significant correlation between T4, T3, and TSH (PT3, PT4, and PTSH = 0.000), whereas there is no significant correlation between T3, T4, and TSH with anti-TPO concertation (PT3 = 0.908, PT4 = 0.204, and PTSH = 0.447). Herein, we evaluated the correlation of hematological parameters including blood groups (ABO, Rh, Lea, and Leb), RBC indices (Hb, Hct, MCV, MCH, MCHC, and RDW), platelet count, and also WBC parameters (the counts of WBCs, neutrophils, lymphocytes, monocytes, and eosinophils) with T3, T4, and TSH. Herein, we also evaluated the correlation of inflammatory cytokine consisting of ESR, CRP, IL-8, and NLR with T3, T4, and TSH. The correlation of hematological parameters and inflammatory biomarkers with T3, T4, and TSH is shown in Table 1. We found some significant correlation between hematological parameters and inflammatory biomarkers with T3, T4, and TSH in hypothyroidism.

The relationship between hematological parameters with thyroid hormones

The relationship between blood groups with thyroid hormones

The significant correlations between ABO, Rh, and Le blood groups with T3 (PABO = 0.142, PRh = 0.209, and PLe = 0.092), T4 (PABO = 0.305, PRh = 0.630, and PLe = 0.305), and TSH (PABO = 0.337 and PRh = 0.336) was not observed. Whereas, our study showed a significant relationship between Lea blood groups (non-secretor) compared to Leb blood groups (secretor) with TSH (PLe = 0.010), (Fig. 1).

Table 1 Summarizing significant and non-significant correlation between thyroid hormones including T3, T4, and TSH with hematological parameters [(blood groups, the counts of RBC and platelet, RBCs indices (Hb, Hct, MCV, MCH, MCHC, and RDW), and WBC parameters (the counts of WBCs, neutrophils, lymphocytes, monocytes, and eosinophils)] as well as inflammatory biomarkers (ESR, CRP, IL-8, and NLR)

Parameters/biomarkers	T3 (ng/mL) 1.04 ± 0. 39 (P-value)	T4 (µg /dL) 6.53 ± 2.16 (P-value)	TSH (mIU/mL) 23.38 ± 25.27 (P-value)
Hematological parameters			
Blood groups			
ABO (Mean ± SD)	0.142	0.305	0.337
A	1.05 ± 0.38	6.63 ± 2.22	20.2 ± 20.83
B	0.9 ± 0. 41	5.87 ± 2.20	24.53 ± 16.62
AB	0.72 ± 0.35	5.35 ± 1.46	43.53 ± 37.73
O	1.1 ± 0.39	6.75 ± 2.17	23.54 ± 28.38
Rh (Mean ± SD)	0.209	0.630	0.336
Rh +	1.02 ± 0.40	6.51 ± 2.22	23.75 ± 25.22
Rh −	1.18 ± 0.34	6.74 ± 1.67	20.15 ± 1.61
Lea/Leb (Mean ± SD)	0.092	0.305	0.010
Lea	0.94 ± 0.44	6.39 ± 2.52	35 ± 33.34
Leb	1.09 ± 0.35	6.66 ± 1.95	19.90 ± 16.50
RBCs indices (Mean ± SD)			
RBCs (cells/mm^3) 5.06 ± 0.63	0.878	0.525	0.938
Hb (g/dL) 14.49 ± 1.58	0.012	0.023	0.017
Hct (%) 42.94 ± 4.10	0.021	0.026	0.019
MCV (fL) 85.68 ± 7.61	0.060	0.183	0.144
MCH (pg/cell) 29.72 ± 2.61	0.032	0.051	0.007
RDW (%) 12.93 ± 1.10	0.318	0.452	0.109
MCHC (g/L) 31.51 ± 3.01	0.022	0.802	0.314
Platelet count (Mean ± SD)			
Platelets (cells/mm^3) 260.47 ± 70.53	0.746	0.709	0.831
WBCs parameters (Mean ± SD)			
WBCs (cells/mm^3) 7.98 ± 2.53	0.585	0.568	0.909
Neutrophils (cells/mm^3) 57.48 ± 10.03	0.064	0.095	0.070
Lymphocytes (cells/mm^3) 34.45 ± 9.14	0.087	0.082	0.041
Monocytes (cells/mm^3) 6.01 ± 2.35	0.029	0.336	0.445

Table 1 (continued)

Parameters/biomarkers	T3 (ng/mL) 1.04 ± 0. 39 (P-value)	T4 (µg /dL) 6.53 ± 2.16 (P-value)	TSH (mIU/mL) 23.38 ± 25.27 (P-value)
Eosinophils (cells/mm^3) 1.18 ± 0.84	0.925	0.517	0.675
Inflammatory biomarkers (Mean ± SD)			
ESR (mm/h) 14.25 ± 9.45	0.169	0.020	0.169
CRP (mg/L) 8.15 ± 18.02	0.987	0.481	0.707
IL-8 (pg/mL) 6.42 ± 8.65	0.217	0.349	0.294
NLR 1.93 ± 1.06	0.084	0.088	0.068
Anti-TPO (IU/mL) 5.64 ± 2.21	0.908	0.204	0.447

The relationship between RBC indices and platelets counts with thyroid hormones

According to our study, there were significant correlations between Hb, Hct, MCH, and MCHC with T3 in hypothyroidism. (PHb = 0.012, PHct = 0.021, PMCH = 0.032, and PMCHC = 0.022). We observed no significant correlations between RBC and platelet counts, MCV, and RDW with T3 in hypothyroidism (PRBC = 0.878, PPLT = 0.746, PMCV = 0.060, and PRDW = 0.318).

There were significant correlations between Hb and Hct with T4 (PHb = 0.023 and PHct = 0.026). We observed no significant correlations between RBC indices and platelets counts, as well as MCV, MCH, MCHC, and RDW with T4 (PRBC = 0.525, PPLT = 0.709, PMCV = 0.183, PMCH = 0.051, PMCHC = 0.802, and PRDW 0.452).

The significant correlations between Hb, Hct, and MCH with TSH was detected (PHb = 0.017, PHct = 0.019, and PMCH = 0.007). The significant correlations between ABO, Rh, the counts of WBCs, RBCs, and platelets, as well as MCV, MCHC, and RDW with TSH was not observed (PWBC = 0.909, PRBC = 0.938, PMCV = 0.144, PMCHC = 0.314, PPLT = 0.831, and PRDW = 0.109), (Fig. 2).

The relationship between WBC parameters with thyroid hormones

We found a significant relationship between monocyte count with T3 in hypothyroidism while the correlation between neutrophils, lymphocytes, monocytes, and eosinophils counts with T3 (PNeut = 0.064, PLymph = 0.087, PMono = 0.029, and PEosin = 0.925) was not observed.

We revealed no significant relationship between the counts of neutrophils, lymphocytes, monocytes, and eosinophils with T4 (PNeut = 0.095, PLymph = 0.082, PMono = 0.336, and PEosin = 0.517).

A significant correlation between lymphocyte count and TSH was found. There was no significant relationship between counts of neutrophils, monocytes, and eosinophils with TSH (PNeut = 0.070, PLymph = 0.04, PMono 0.445, and PEosin = 0.675), (Fig. 3).

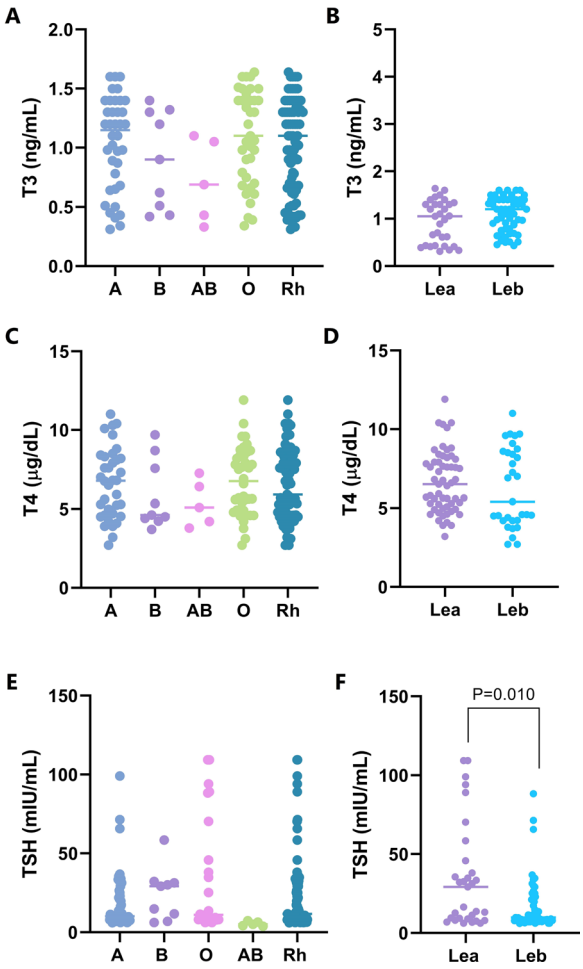


Fig. 1 The relationship between blood groups with thyroid hormones. ABO and Le blood groups had no significant correlations with T3 (**A** and **B**) and T4 (**C** and **D**) in hypothyroidism. TSH had no significant correlation with Rh and ABO blood groups. There was a significant correlation between Lea blood groups (non-secretor) in compared to Leb blood groups (secretor) with TSH (**E** and **F**)

The relationship between inflammatory biomarkers with thyroid hormones

The significant correlations between ESR, CRP, IL-8, and NLR with T3 in hypothyroidism was not observed. (PESR = 0.169, PCRP = 0.987, and PIL-8 = 0.217, and PNLR = 0.084).

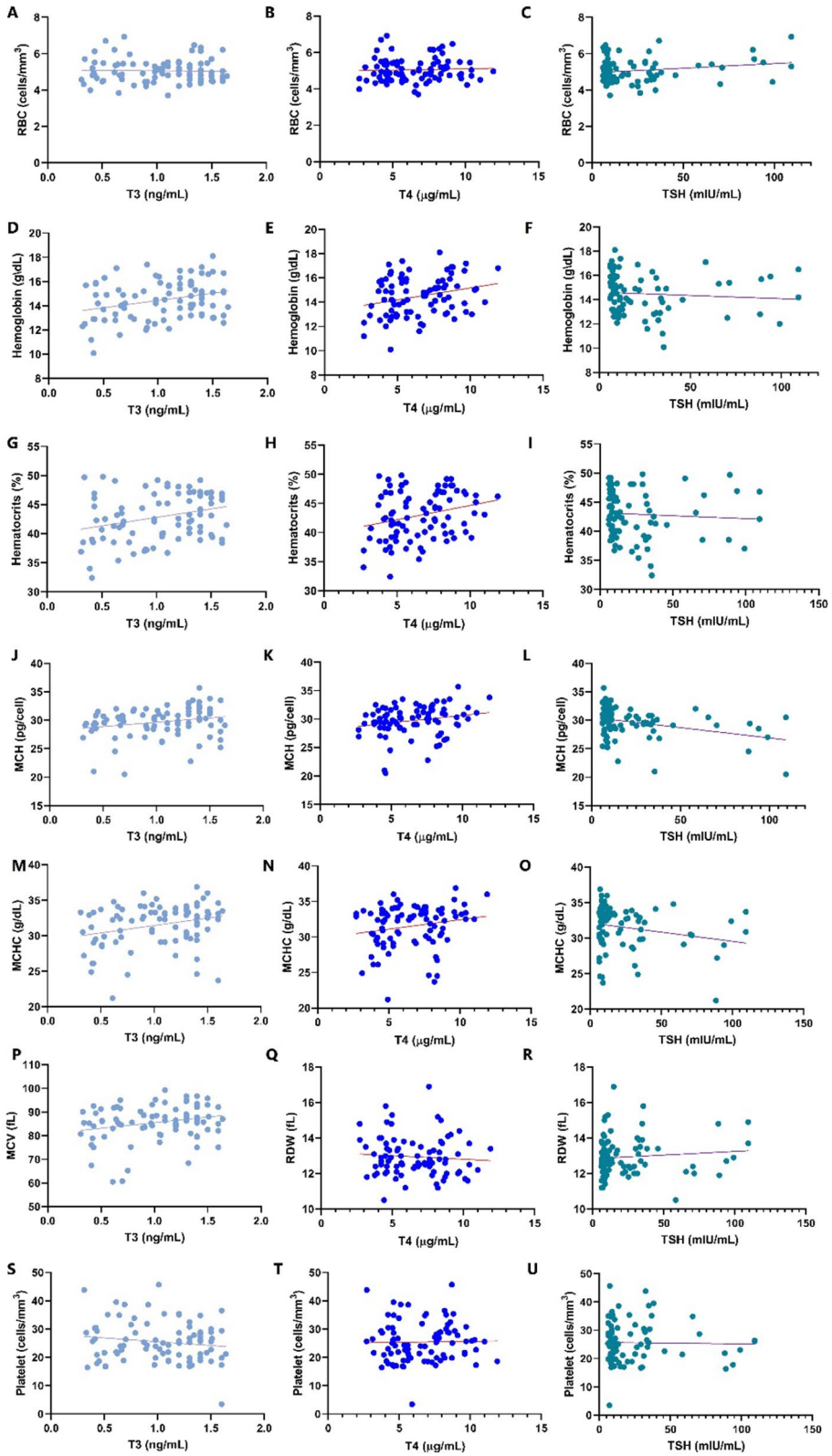
As well, there was also a significant correlation between ESR with T4 in hypothyroidism (PESR = 0.020). In addition, there were no significant correlations between CRP, IL-8, and NLR with T4 (PCRP = 0.481, PIL-8 = 0.349, and PNLR = 0.088). Herein, we didn't observe a significant correlation between ESR with TSH in hypothyroidism (PESR = 0.169). In addition, the significant correlations between CRP, IL-8, and NLR with TSH was not showed (PCRP = 0.707, PIL-8 = 0.294, and PNLR = 0.068), (Fig. 4).

Discussion

Hypothyroidism is created by disruption of thyroid hormone generation that can destroy the emotional, relational, social, and working lives of patients [1]. Our study showed hematological parameters consisting Hb, Hct, and MCH had a significant relationship with T3, T4, and TSH in hypothyroidism. The results of our study is in line with Bremner et al. showed a significant relationship between serum thyroid hormone concentrations and some indices in euthyroid subjects [20]. Thyroid hormones play main role in erythropoiesis. The suggested mechanisms, which hypothyroidism can induce anemia by depressed bone marrow stimulation, decreased erythropoietin production, and effects on iron metabolism [21]. Systemic inflammation may be involved in the deterioration of thyroid function [22]. The role of systemic inflammation in euthyroid sick syndrome has begun to be clarified [23, 24]. According to the National Health and Nutrition Examination Survey III presence of anti-TPO antibodies was significantly associated with thyroid failure. We observed the effect of systemic inflammation on thyroid function. Hence, we choose the negative anti-TPO patients. The relationship between CRP, and IL-8 with T3, T4, and TSH in hypothyroidism in the negative anti-TPO patients was not demonstrated. IL-8 is a chemokine that plays a vital role in neutrophil function and migration to the inflammation sites [25]. In line with the present study, Krassas et al. showed that IL-8 was not increased in some thyroid disorder including Hashimoto's thyroiditis, Graves' disease, and toxic nodular goiter [26]. In contrast, Kobawala et al. revealed that IL-8 was increased in thyroid cancer, goiter, and autoimmune diseases [27]. Gupta et al. reported the enhancement of ESR and CRP in subclinical hypothyroidism [22]. CRP is a sensitive, nonspecific marker of inflammation. CRP rises rapidly in various pathological conditions e.g. overt hypothyroidism and has a correlation with the severity, extent, and progression of the pathologies so CRP is not only a prognostic marker but also may have role in the pathogenesis of the disease [28, 29]. No significant relationship between ESR with T3 and TSH was shown, while ESR had a significant correlation with T4. ESR as an inflammatory biomarker is slow and insensitive to minor inflammation and can be affected by numerous physiologic and pathophysiologic conditions [30]. Ilera et al. showed the correlation between fT4 with ESR, which leads to systemic inflammation and reduces deiodinase activity. This results in decreased change of T4 to T3, leading to low fT3, low thyroxine-binding globulin, and increasing fT4 [31]. There was only significant correlation between monocyte count with T3 and also lymphocyte count with TSH. In confirm our result, Fang et al. showed the relationship between the lymphocyte count and TSH in hypothyroidism patients [32]. We explored no significant correlations between the counts of neutrophils, lymphocytes, monocytes, and eosinophils, as well as NLR with T4. The NLR is a cost-effective, accessible, and easily calculated index of systemic inflammation [33]. Kutluturk et al. revealed that the NLR was not statistically significant for subclinical and overt hypothyroidism in papillary thyroid carcinoma [34]. Onalan et al. demonstrated a higher NLR Hashimoto's thyroiditis compared to the control group [14]. According to the inflammation hypothesis, prophylactic interventions have not been adequately studied to protect the thyroid in systemic inflammation [35]. We explored a significant relationship between Lea blood group (non-secretor) in compared to Leb blood groups (secretor) with TSH, whereas there wasn't a correlation between ABO, Rh, and Le blood groups with T3,

(See figure on next page.)

Fig. 2 The relationship between RBC indices and platelet count with thyroid hormones. There were significant correlations between Hb, Hct, MCH, and MCHC with T3 in hypothyroidism. The significant correlations between RBC indices, platelet count, MCV, and RDW with T3 was not observed (**A**, **D**, **G**, **J**, **M**, **P** and **S**). There were significant correlations between Hb and Hct with T4, and also the significant correlations between the counts of RBCs and platelets, as well as MCH, MCHC, MCV, and RDW with T4 was not observed (**B**, **E**, **H**, **K**, **N**, **Q**, and **T**). We revealed significant correlations between Hb, Hct, MCH, and TSH. The significant correlations between RBC, MCV, MCHC, RDW, and platelet count with TSH was not observed (**C**, **F**, **I**, **L**, **O**, **R** and **U**)



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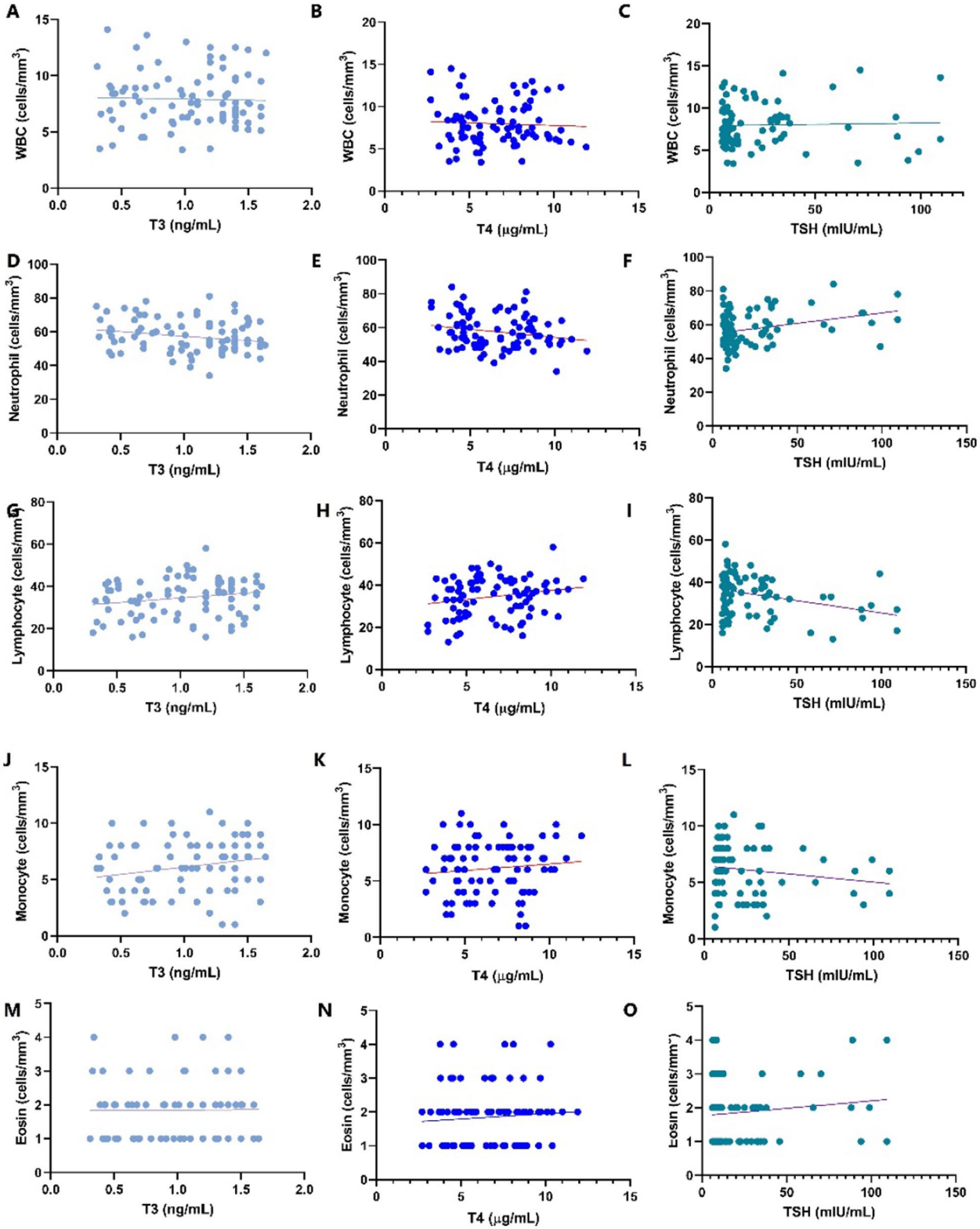

Fig. 3 The relationship between WBC parameters with thyroid hormones. There were significant correlations between monocyte count and T3. As well, the counts of WBCs, neutrophils, lymphocytes, and eosinophils had no significant correlation with T3 in hypothyroidism (**A**, **D**, **G**, **J**, and **M**). The between the counts of WBCs, neutrophils, lymphocytes, monocytes, and eosinophils with T4 was not detected (**B**, **E**, **H**, **K**, and **N**). The significant correlations between lymphocyte count with TSH was observed. The significant correlations between the counts of WBCs, neutrophils, monocytes, and eosinophils with TSH was not explored (**C**, **F**, **I**, **L** and **O**)

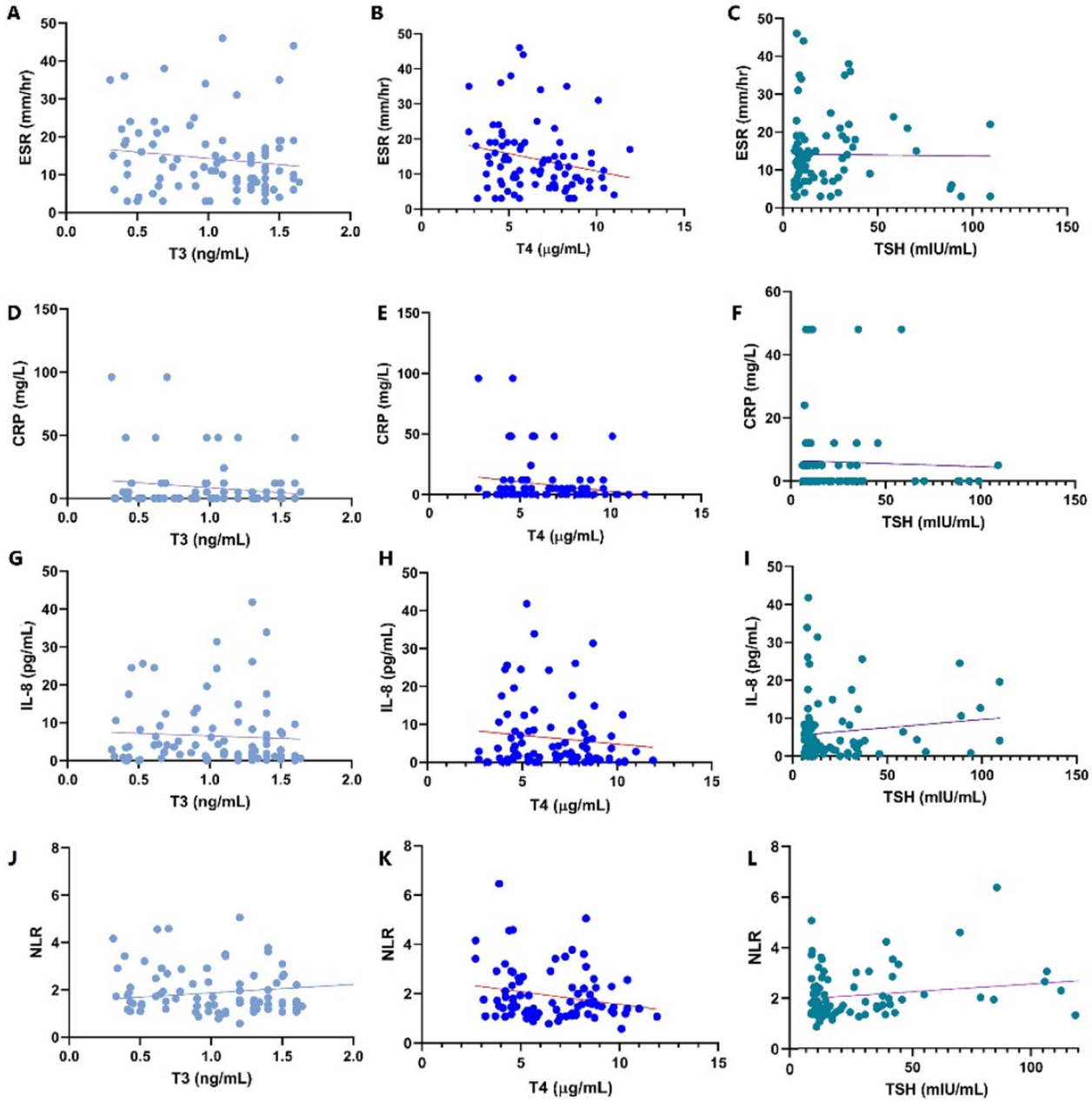

Fig. 4 The relationship between inflammatory biomarkers with thyroid hormones. The correlations between ESR, CRP, IL-8, and NLR with T3 in hypothyroidism (**A**, **D**, **G**, **J**) was not shown. In addition, there was a significant correlation between ESR with T4. Although, there were no significant correlations between CRP and IL-8, and NLR with T4 (**B**, **E**, **H** and **K**). The correlations between CRP, IL-8, and NLR with TSH was not observed. There was a significant correlation between ESR with TSH (**C**, **F**, **I**, and **L**)

T4, and TSH. In one study, Calapkulu et al. reported a relationship between O blood group with Hashimoto's thyroiditis and the AB blood group with Hashimoto's thyroiditis and Graves' disease [13]. Humans could be typed as Leb with A and/or B antigens and Lea without secreted A and/or B antigens in RBC surface and body fluids. A, B, Lea, and Leb antigens are related to blood transfusion reactions and organ rejection. As well, the occurrence and development of tumors [36].

Conclusion

There is a controversy about subclinical hypothyroidism therapy and millions of dollars have been spent on levothyroxine for subclinical hypothyroidism patients.

If some biomarkers help us to choose which subclinical individual should be treated [4, 5]. We revealed a significant relationship between Hb and Hct with T3, T4, and TSH. We explored a significant relationship between MCH with T3 and TSH. As well, we also showed a significant relationship between Lea (non-secretor) blood group with TSH. Thus, the assessment of Hb, Hct, MCH, and Lea and Leb blood groups as hematological parameters in hypothyroid patients can be used for the management of hypothyroidism.

Limitations

- Scares diversity of inflammatory and pro-inflammatory cytokines impose limitations in data interpretation.
- Scare sample amounts limit overall data interpretation.

Acknowledgements
This investigation was financially supported by Jahrom University of Medical Sciences and Qaem Medical Laboratory (Grant 400000165).

Author contributions
Kambiz Bagheri gathered and analyzed the data. Marzieh Haghbin, Fatemeh Razmjooei, Fatemeh Abbasi, Roxana Rouhie, Parisa Pourabbas, and Hamed Mir wrote the main manuscript text. Fatemeh Razmjooei and Mirza Ali Mofazzal Jahromi prepared figures and table. Mirza Ali Mofazzal Jahrom and Abazar Roustazadeh edited the article and checked its technical issues. Mirza Ali Mofazzal Jahromi and Kambiz Bagheri finally revised this article.

Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
The Research Ethics Committee at the Jahrom University of Medical Sciences gave ethical permission to this research. All authors confirm that all methods were performed according to the relevant guidelines and regulations. Experiments were performed based on the guidelines of the Medical Ethics Committee of the Jahrom University of Medical Sciences (IR.JUMS.REC.1400.093).

Consent for publication
Not applicable.

Competing interest
The authors declare no competing interests.

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Received: 19 May 2024 Accepted: 18 December 2024
Published online: 27 December 2024

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