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INVESTIGATION ROLE OF VITAMIN D3 AND IMMUNOLOGICAL MARKERS IN PATHOGENESIS OF HASHIMOTO THYROIDITIS

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Abstract:

Abstract
Background; The primary reason of hypothyroidism is Hashimoto's thyroiditis (HT), the most common autoimmune illness that causes thyroid cell damage due to lymphocyte invasion. Its distinctive features include an elevated amount of autoantibodies targeting thyroid peroxidase and thyroglobulin.
Objective IL-38, IL-15, vitamin D3, anti-TPO, and anti-TGA characteristics are being studied with the aim of determining their role in the etiology of Hashimoto's thyroid disorders (HT).
Materials and methods;
The present investigation was conducted in the Diyala province's Baquba educational hospitals between November 2022 and the end of January 2023. 60 specimens of blood were gathered from visitors to the Baquba Teaching Hospital as well as individuals who had Hashimoto Thyroiditis, which the specialist physician diagnosed in the advising units. Thirty specimens of blood from people in good health were taken and used as the control group. Sandwich ELISA was used to evaluate the serum quantities of IL-15, IL-38, Anti-TPO, and Anti-TGA antibody indicators in the samples. I-chroma vitamin D3 equipment was used to determine the level of total vitamin D in human serum using fluorescence immunoassay (FIA)
Results:
The results of this research showed patients who were female got higher percentages (76.7%) than those who were male (23.3%) and that patients in the age ranges of 21–30, 31–40, and 41–50 years scored higher percentages (36.7%, 28.3%, and 25.0%) than those in the 51–60 and >60 age groups. lowest percentage-scoring years (3.3% and 6.7%) with a significant difference of ($p<0.05$). levels of IL-15 was highest in patients (70.40±9.75) than healthy (37.03±7.90). In contrast, levels of IL-38 was lowest in patients (0.63±0.15) than healthy (1.53±0.33) with significant different ($p<0.05$). levels of Anti-TPO and AntiTGA antibodies were highest in patients (16.20±3.34 and 25.12±4.91) than healthy (6.47±1.11 and 13.47±2.30) with significant different ($p<0.05$). vitamin D3 was lowest in patients (16.02±2.54) than healthy (27.90±4.33) with significant different ($p<0.05$). Vitamin D3 is negative significant correlate with Anti-TPO ($r = -0.299^*$ and $p=0.020$). Finally, results study showed the IL_15, Anti-TPO, Anti-TGA, IL_38, and vitamin D3 parameters scored high sensitivity (93%, 100%, 100%, 96%, and 98%) and specificity (89%, 94%, 92%, 86%, and 80%) with significant different ($p<0.05$) in screening patients with hashimoto thyroiditis
Conclusions: According to a 3:1 ratio, girls are more likely than males to develop hashiomoto thyroid disease. IL-38, IL-15, and vitamin D3 characteristics may be useful in the identification of HT patients because of their high sensitivity and specificity.

Keywords: vitamin D3, IL-38, IL-15, and Hashimoto thyroiditis (HT)

INTRODUCTION

An essential aspect of autoimmunity thyroid disorders (AITD) is Hashimoto's thyroiditis (HT). HT is a

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significant contributor to hypothyroidism and is physiologically defined by fibrosis of lymphocytic infiltration, and widespread parenchymal atrophy (Ralli et al., 2020). Additionally, persons in HT are more likely to develop heart disease. The incidence of HT currently ranges from 0.3 to 1.5 instances per 1000 persons; the majority of those diagnosed are women, and the occurrence in males is 1/10 versus females (Li et al., 2018). Since there is currently no especially successful therapy for HT, oral Levo-Thyroxine3 is the major medication used to treat hypothyroidism.

Cellular and humoral immune systems are essential in the development of HT, although the reality that the exact reason is still not fully known. Research points to the importance of serum cytokines in the pathogenesis of HT, involving; IL-6, TNF-a, IL-17, IL-10, as well as IL-22 (Xu et al., 2022)

It is largely similar to IL-1 receptor anta-gonist (IL-1Ra) and IL-36Ra and functions as an anti-inflammatory mediators (Bensen et al., 2001). IL-38 is a member of the IL-1 group.

The placenta, heart, hepatic , thymus, spleen, and fetal tissues are the main organs where IL-38 is expressed. IL38 levels and autoimmune illnesses like rheumatoids arthritis (RA), systemics lupus erythematosus (SLE), as well as Behçet's syndrome have been shown to be significantly correlated (Xu et al., 2020).

IL-15 is a potentially harmful inflammatory cytokine that promotes the survival of CD8+ memory T cells, especially self-driven ones, and blocks self-tolerance mediated by Automatic Implantable Cardioverter Defibrillator (AICD). TNF- and IL-1 are also induced by IL-15.Disordered IL-15 expression has been seen in patients with a number of inflammatory autoimmune disorders in spite of a variety of regulations (Surcel et al., 2021).

Multiple autoimmune disorders, including rheumatoid arthritis, autoimmune DM, inflammatory bowel disease, celiac disorder, and psoriasis, are being linked by the pathophysiology of IL-15. Targeting IL-15 signaling in autoimmune disease has been demonstrated to have positive benefits in studies using pre-clinical models (Allard-Chamard et al., 2020)

Taking vitamin D supplements has been linked to positive benefits in human research investigations, such as a reduction in the severity of autoimmune disease (Altieri et al., 2017). However, the ideal serum levels of vitamin D are still up for debate.

vitamin D plays major role In maintaining phosphorus balance, regulating calcium, and enhancing the health of bones. Studies on both humans and animals have demonstrated that vitamin D is take part in the pathophysiology of a number of endocrine illnesses . Primary hyper-parathyroidism, type 1 DM (T1DM), type 2 DM (T2DM), autoimmune thyroiditis, illnesses of the adrenal glands, and polycystic ovarian syndromes (PCOS) are among these endocrine problems (Muscogiuri et al., 2014).

Some of the key conclusions is that vitamin D stoppage the creation of several mediators associated with inflammation, including the tumor necrosis factor-a (TNF-a), interleukin -1, IL-6, IL-8, and IL-12.

Major histocompatibility complex (MHC) class II proteins, co-stimulatory components, and IL-12 production are all downregulated, and sufficient quantities.

vitamin D inhibits the maturation and differentiation of such cells into dendritic cell types. (Szymczak-Pajor and Śliwińska, 2019). Another consideration is vitamin D's capacity to impact the activities of regulatory T cells, which decrease the influent of T-cell-dependent immunity in autoimmune conditions . T cells and B cells in particular react to thyroid antigens in individuals with a hereditary susceptibility, and this can cause hyperthyroidism to start. The manufacture of thyroid autoimmune such anti-thyroid peroxidase (TPOAb) and anti-thyro-globulin (TgAb) was found to be associated with serum levels of 1,25(OH)2-Vitamin D3 20 ng/mL (Galuşca et al., 2022).

We sought to examine serum amounts of IL-38, IL-15, and vitamin D3 in patients with AITD and their connection with matching autoantibodies in light of the aforementioned evidence about the involvement of these substances in autoimmune illnesses as well as the dearth of pertinent information in autoimmune disorders studies.

MATERIALS AND METHODS

Samples collection

The current investigation was carried out in the Diyala governorate's Baquba educational hospital between November 2022 and the end of January 2023. Following a checkup and assessment by the consultant physician at the advisory units/Baquba Education Hospital, Sixty specimens of blood were taken from individuals who arrived at the Baquba Teaching Hospital as well as people with Hashimoto Thyroiditis. Thirty samples of blood from people in good health were taken and used as the control group. The healthy volunteers and patients varied in range from 20 to 70.

METHODS

Five ml of human blood were spun for a period of five minutes at 3000 rpm to isolate the serum. Sandwich ELISA tests (a product of the CUSABIO firm) were used to determine the serum amounts of the markers IL-15, IL-38, Anti-TPO, and Anti-TGA antibodies in the samples. Fluorescence immunoassay (FIA) was utilized to measure the quantitative amount of total vitamin D in human serum using I-chroma vitamin D3 equipment. t was used to determine the quantitative level of total

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vitamin D in human serum using fluorescence immunoassay (FIA).

STATISTIC.ANALYSIS

Using the.Kolmogorov-Smirnov.and Shapiro-Wilk .tests. the mean value of the IL-15, IL-38, Anti-TPO, Anti-TGA, and vitamin D3 markers was first determined. The criteria that passed a normalcy tests (non significant different). were presented as Means SD, and the significance.of the differences was assessed.using the student t test.(comparison of the two groups.). Other factors, like gender.and age groups, were given.as percent of a number., and Pearson-Chi-square.analysis was applied to identify the frequency.of important variations .By using the Pearson.correlation, the type and degree.of the relationship.among the variables was.evaluated. AUC, sensitivity, and specificity of 6 parameters were calculated using.the receiver's operating.characteristic (ROC) curve. Significant was determined to be P0.05. Statistical analysis.was performed on.our information using SPSS 21.0.and Graph Pad Prism v.6.

RESULTS

1. Information..on respondents'.demographics.

The current.study'sfindings.revealed that.there.are.significant.variation ($p<0.05$) among.male vs female.sickers with hashimoto.thyroiditis in terms of.both gender.and age groups .Patients who were female rated.higher than male patients (23.3%).(76.7%)..In comparison.to age groups 51–60 and > 60, which scored lowest (3.3% and 6.7%), the age groupings 21–30, 31–40, and 41–50 years scored maximum .percentages (36.7%, 28.3%, and 25.0%) (table 1).

Table 1;.frequency and.percentage of gender.and age.groups of Hashimoto Thyroiditis.patients were.measured by Chi-square test.

		Count	Percent	P value
Gender	Males	14	23.3%	*P <0.001***
	Females	46	76.7%	
Age categories	21_30	22	36.7%	*P <0.001****
	31_40	17	28.3%	
	41_50	15	25.0%	
	51_60	2	3.3%	
	>60	4	6.7%	

2.Mean levels of interleukins (IL-15 and IL-38) of participants

The present study found a significant variance ($p>0.05$) in average levels of Interleukins (IL-15 and IL-38) across study groups. The average IL-15 levels was greater for patients (70.40+9.75) compared to healthy individuals (37.03+7.90). In contrast, the mean 7 levels of IL-38 in patients (0.630.15) were lower than in healthy (1.53+0.33) (table 2 and figure 1).

Table 2; comparative mean levels of interleukins (IL-15 and IL-38) between study groups were measured by *student t test* **.**

Groups		N	Mean	SD	P value
IL-15	Patients	60	70.40	9.75	*P <0.001****
	Healthy	30	37.03	7.90	
IL-38	Patients	60	0.63	0.15	*P <0.001****
	Healthy	30	1.53	0.33	

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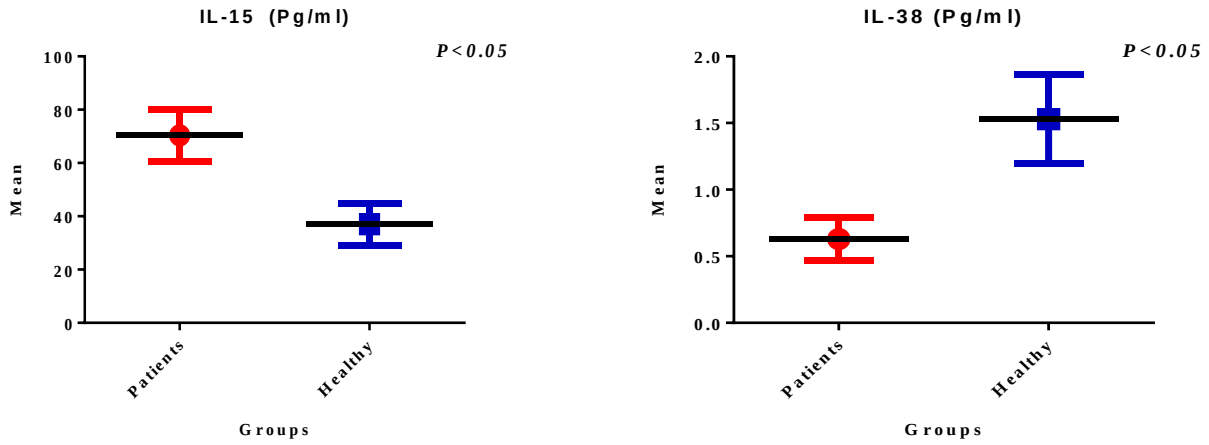

Figure 1; comparative mean levels of interleukins (IL-15 and IL-38) between study groups.

3. Mean levels.of Anti-TPO and .Anti-TGA .antibodies of participants.

The current investigation found a significant variance (p>0.05) among the levels of Anti-TPO and Anti-TGA antibodies between study groups. Patients had the highest mean levels of both anti-TPO and anti-TGA antibodies (16.20+3.34). and 25.12+4.91) than healthy (6.47+1.11 and 13.47+2.30) (table 3 and figure 2).

Table 3; comparative mean quantities of Anti-TPO and Anti-TGA antibodies between study groups were measured by *student t test* .

Groups		N	Mean	SD	P value
Anti-TPO	Patients	60	16.20	3.34	*P<0.001****
	Healthy	30	6.47	1.11	
Anti-TGA	Patients	60	25.12	4.91	*P<0.001****
	Healthy	30	13.47	2.30	

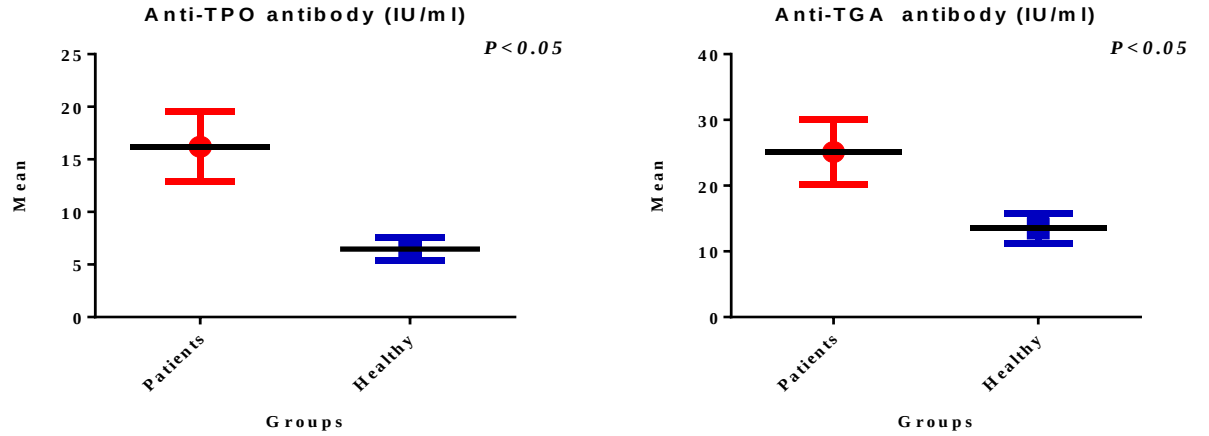

Figure 2; comparative mean levels of Anti-TPO and Anti-TGA antibodies between study groups .

4. Mean levels.of vitamin.D3 of participants

Results of present study showed there is significant (p<0.05) between mean levels of vitamin D3 and study groups. The mean levels of vitamin D3 was lowest in patients (16.02±2.54) than healthy (27.90±4.33) (table 4 and figure 3).

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Table 4; comparative mean levels of vitamin D3 between study groups were measured by *student t test*

Groups		N	Mean	SD	P value
Vitamin D3	Patients	60	16.02	2.54	p<0.001***
	Healthy	30	27.90	4.33	

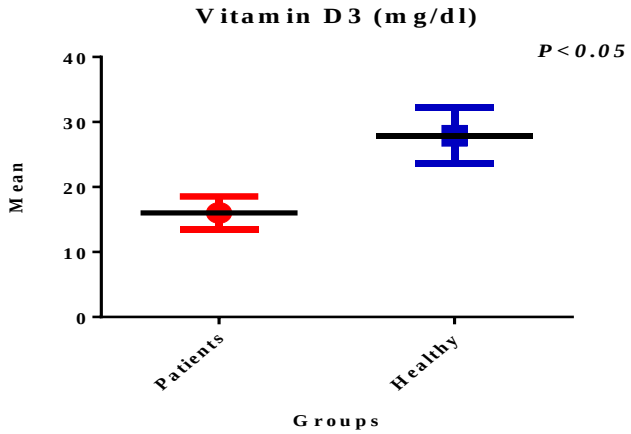

Figure 3; comparative mean levels of vitamin D3 between study groups

5. Correlation.relationship among.parameters .IL-15, IL-38, TPO,.TGA,

Vitamin D3.

The present research found both positive and negative associations between IL15, IL-38, TPO, TGA, and Vitamin D3 parameters. Notably, Vitamin D3 has a negative significant relationship with Anti-TPO (Pearson coefficient = -0.299* and Probability = 0.020) (table 5).

Table 5; Correlation relationship among parameters (IL-15, IL-38, TPO, TGA, Vitamin D3) were measured by *Pearson coefficient* .

		IL_15	Anti-TPO	Vitamin D3
IL_15	Pearson coefficient	1	0.176	-0.011
	Probability		0.178	0.936
IL_38	Pearson coefficient	-0.058	-0.198	0.069
	Probability	0.660	0.130	0.602
Anti-TGA	Pearson coefficient	0.094	0.244	-0.064
	Probability	0.474	0.061	0.627
Vitamin D3	Pearson coefficient	-0.011	-0.299*	1
	Probability	0.936	0.020	

6. Receiver.operator characteristic.(ROC) curve\

The IL_15, Anti-TPO Anti-TGA, IL_38, and vitamin D3 measures shown good sensitivity (93%, 100%, 100%, 96%, and 98%) and specificity (89%, 94%, 92%, 86%, and 80%) with significant differences (p<0.05) in screen individuals with hashimoto thyroid disease (figure 4)

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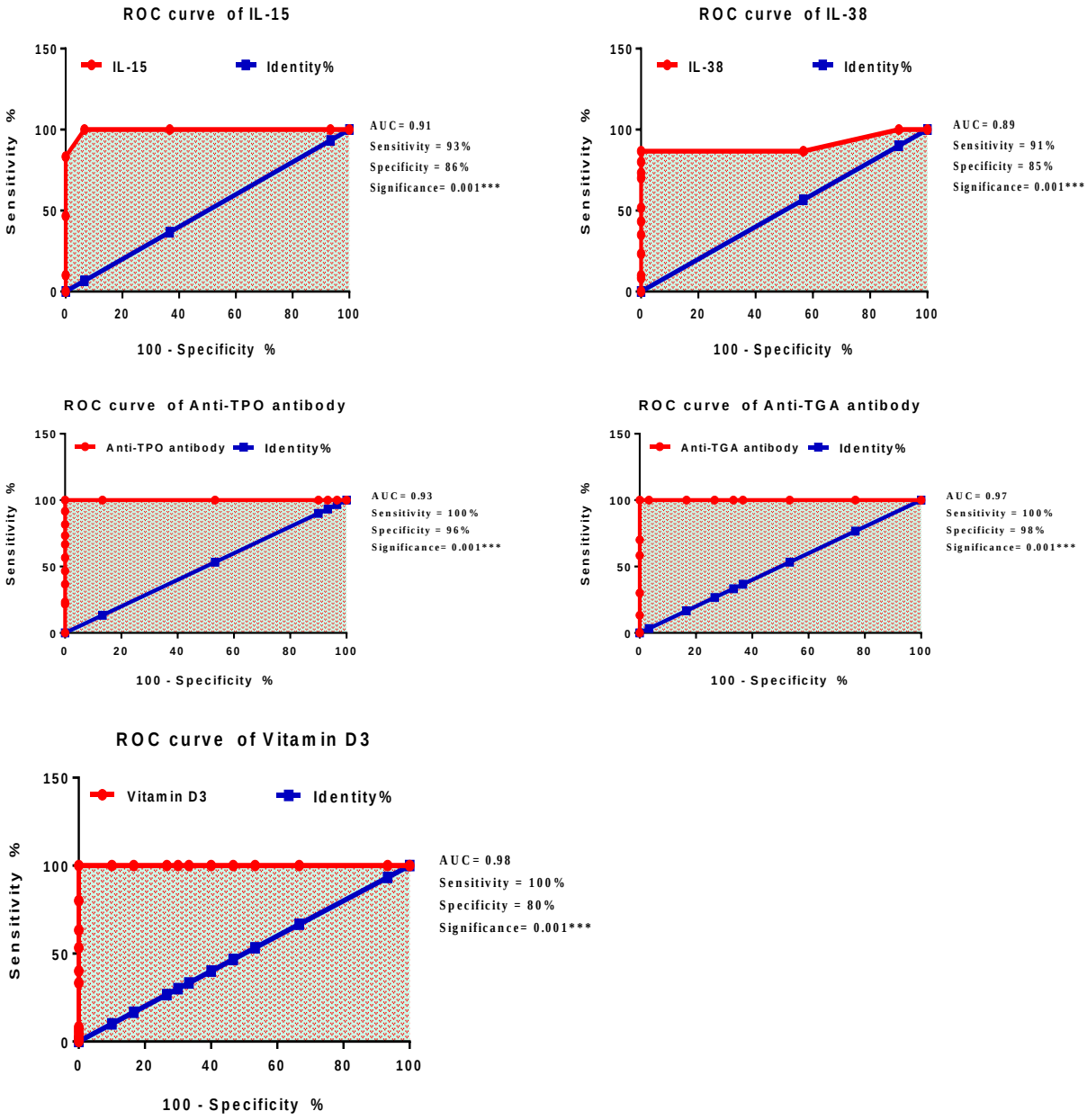

Figure 4; ROC curve, sensitivity and specificity of parameters

DISCUSSION

The condition.known as Hashimoto's thyroiditis.is an inflammatory illness.that produces systemic inflammation at the micro level in the body, resulting in hypothyroidsm.and the thyroid gland's hypertrophy Hashimoto's thyroidetis is a common cause of hypothyroidism and.goiter, particularly in areas.where iodine shortage is.not prevalent (Klubo-Gwiezdzinska.and Wartofsky, 2022). The pathogenesis of.Hashimoto's thyroidetis is.linked to T-cell activation, HLA,.DR3, DR4, DR5, and a.variety other hereditary variables However, its etiology may also be linked to iodine consumption,.additional viral infections, and various drugs..Several studies support this.(Weider et al., 2020).

The present.research found that females had a higher percentage.of hashimoto's thyroidetis than males between ages of 20 and 50, which is matched with the outcomes of Erge et al , (2023). Hashimoto's thyroidetis is more common in women The ratio of female/male is at least 10/1 Despite claims to the contrary from various sources, diagnoses happen more often most women are in their fifth decades of life.between those in the ages of 30 and 50 receive a diagnosis (Mikulska et al., 2022). Tang et al., (2021) discovered the average female-to-male ratio was just 1.7:1, which was much lower from the current stated

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ratio of 3-1. Additional examination of the data revealed that the male proportion was higher in patients under the age of two The female/male ratio in 2-3-year -old patients was 5.5/1,.which is according to recent findings (Admoni .et al., 2020). Females have a greater chance than males to get hashimoto's thyroidetis, which may be caused by hormonal and genetic Causes.

According to the most recent statistics, only 26% of children who were euthyroid at presentation developed hypothyroidsm, whereas over 50% of those with subclinical hypothyroidsm (SCH).required treatments 16% of individuals.who presented with overt hypothyroidsm recovered.gradually (Admoni et.al., 2020).

Another research study found that 70% of the children with hashimoto's thyroidetishad hypothyroidsm or subclinical hypothyroidsm during the time of the initial diagnosis kids with global.developmental delay require .on going assesment to identify if they have HT-induced hypothyroidsm, despite the fact their thyroid function is good after birth Thyroxine replacement could alleviate some of the clinical signs of hypothyroidsm, so early identification & therapy are critical for improving patient prognosis (Tang et al., 2021) .

The high.rate of hashimoto's thyroidetis in.children and adults, as well as boys and.females is due to hormonal, genetic, and immunological disorders. The present study.found that individuals had higher levels of anti-TPO and anti-TGA parameters.compared healthy people, which mirrored the findings of.Siriwardhane et al..(2019). Previous studies found that the presence of anti-TPO even in the absence.of thyroid hormone.disturbances indicated a·possibles risk of developing.thyroid dys-function (Siriwardhane et al., 2019)..Almost every one of Hashimoto's thyroidetis patients have high levels of anti-TPOAb. Thyroglobulin antibodes (Tg-Ab) .If the thyroid is injured, that can occur..After finishing.thyroid cancer treatment, these antibodies.are.frequently tested in to thyroglobulin testing (Tian et al., 2020). Previous.research.showed no.significant differences.comparing those who got.anti-Tg before the control*2 group This is to be expected, given that anti-Tg is a well-established marker in the detection of differentiated thyroid cancer (DTC) and is.regarded less specific diagnostic of thyroids illness than anti-TPO Jo and Lim (2018)

Because anti-TPO autoantibodies were dominants to anti-Tg antibodies.in all prior data, the scientists investigated if both of these markers could be employed.as standalone indicators The final collection.of study data on group patients and group controls revealed no significant variation when anti-TPO was done alone versus the binding of anti-TPO and anti-Tg evaluation As a result, the addition of an anti-Tg indicator to the anti-TPO performance had no significant effect, and it can thus be utilized as an independent marker .Those who were anti-Tg positive was tested separately and compared to the combined anti-TPO or anti-Tg screening , the combination group of anti-TPO or anti-Tg observed considerably higher results than anti-Tg alone As a result, it was clearly established that anti-Tg is not a virus.

The use of anti-TPO and anti-TGA tests, especially reveal the presence of autoimmune hashimoto thyroidtis, which is a decisive technique (Almsaid and Khalfa, 2020) A recent study found that anti TPO and anti TGA antibodies were significantly higher compared to control serological immunity parameters.(Redha and Khilfa, 2023), and these findings matched the current investigation.

In the past, studies found that the level of anti-TPO-Ab and anti-TG was dependent on age, showing higher levels in the first year of life and during puberty. When employed as diagnostic indications of autoimmune thyroid illness in a pediatric the population, higher "physiological" amounts of anti-TPO-Ab and anti-TG must be noted (Hirtz et al., 2020).

The current study demonstrated high sensitivity and specificity of anti-TPO (96% AND 100) and anti-TGA (100% and 96%) in examination patients with HT, which are consistent with the findings of Redha and Khilfa, (2023), who emphasize the vital role of anti-TPO and anti-TGA parameters in determining the diagnosis of patients with HT.

IL-38 is an original member of the IL-1 family that reduces inflammatory signaling to limit the release of mediators of inflammation. Probable IL-38 receptors include IL-1 receptor 1, IL-36 receptor, and IL-1 receptor 10, and IL-38 exerts anti-inflammatory impacts by binding to them A rising body of evidence suggests that IL-38 plays a critical role in autoimmune disorders (Mora et al., 2016).

Our research found.decreased serum IL-38 amounts.in HT compared to controls, which is agreed with IL-38's anti-inflammatory characteristics However, this observation contradicts previous reports of elevated IL-38 cytokine expression in inflammatory conditions involving ; RA and SLE (Xu et al., 2020)..Maryam et al. (2019) discovered.lower serum IL-38 levels in.Behçet's illness patients variances in IL-38 concentrations in AITD and another auto-immune illnesses may be ascribed to variances in disease pathophysiology. AITD is characterized by lymphocytic infiltration, autoimmune antibody creation , and thyroid-related hormone dysregulation (Xu et al., 2022).

The researchers discovered that anti-TPO and anti-TgA concentrations were increased in patients than in controls Shi et al., (2021) discovered that IL-38 levels in the blood.and orbital connective tissue were

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decreased in TPO patients.when compared to controls In vitro, IL-38 inhibits the creation of inflammatory mediators by reducing IL-23R and IL-17A amounts in peripheral blood mononuclear cells from TPO patients (Pan et al., 2021).

Because the function of IL-38 in common inflammatory auto-immune disorders has been well established, it was suggested that IL-38 could be used as abiomarker for the development of other inflammatory.autoimmune diseases (Xu. et al., 2022). Previous study has shown that IL-38, especially plays significant roles in autoimmune illnesses, can increase in serological and lesion samples (Redha and Khilfa, 2023). However, it was shown to decrease in the same study, which may explain its role as a regulatory immune cytokine, and because of its broad.anti-inflammatory properties, it is lowered in hashimoto thyroidites patients to boost other pro-inflammatory cytokines such as IL-17 (Redha and Khilfa, 2023).

Previous study shows that, although the use of positive serological diagnostic tests to properly confirm the presence of Hashimoto thyroidites, there are complex immunological cascades that drive the pathological courses of hashimoto thyroidites Interleukin 17 is extensively understood and studied in·connection with hashimoto thyroidites, although there is little evidence that interleukin 38 is active in hashimoto thyroidites (Pan et al., 2021).

Jin et al , (2022) found that the IL-38 id plays an essentialpart in screening patients with HT due to its high sensitivity and specificity, and these outcomes were compatibles with present research.

The current investigation found that individuals had higher levels of IL-15 than controls, which is consistent with the findings of Arakawa et al., (2017). Interleukin-15 (IL-15) is a cytokine in the IL-2 family that signals through receptor complexes containing the common gamma (c) chain IL-15 is involved in the development of various immunological disorders and has critical roles in innate and adaptive immune responses.

IL-15 is widely expressed by hematopoietic and non-hematopoietic the cells, impacts several components of the innate as well as adaptive immune systems, and is implicated in the pathophysiology of several autoimmune illnesses If not adequately managed, IL-15 can be a dangerous cytokine, limiting self-tolerance mediated by an Automatic Implantable Cardioverter Defibrillator (AICD) (Allard-Chamard et al., 2020).

Despite not thoroughly explored, IL-15, whose is important in T-helper 17 cell development, is believed to be linked to autoimmune thyroid disorders (AITD) such as Graves disease and Hashimoto thyroidites Serum IL-15 concentrations were higher in Hashimoto thyroidites patients than in euthyroid persons (Figueroa-Vega et al., 2010) Furthermore, Pappa et al. (1997) discovered IL-15 in 33% of thyroid-associated ophthalmopathy extraocular muscle biopsies Additional results show that cytokine patterns in the several diseases.studied are heterogeneous; that thyroid cells can showed IL-12, IL-13,.and IL-15 mRNA in culture, particularly after TSH, IL-1, or IFN-gamma.production ; and that IL-15 is observed in the majority of tissue samples studied.(Ajjan et al., 1997).

Previous research has shown that the IL-15.genetic polymorphism connects with the severity of HT, most likely via boosting Th17 cells, which encourage the release of proinflammatory cytokines, which increase inflammation (Arakawa et al., 2017).

Ajjan et al. (1997) discovered that the IL-15 id plays a crucial role in screening patients with HT due to its high sensitivity and specificity, and these findings were consistent with the current investigation.

According to the findings of the research, those who had hypothyroidsm had hypovitaminosis D with hypocalcaemia, which is highly related to the level and severity of the hypothyroidsm. This supports the use of vitamin D supplementation and suggests screening for vitamin D deficiency and serum calcium.levels in all individuals with hypothyroidism.(Mackawy et al., 2013).Vitamin D deficiency is prevalent in Hashimoto's thyroidites, and treating sufferers with this disorder with vitamin D may halt the development of hypo-thyroidism and reduce heart risks in these people. Vitamin D testing and replenishment could be crucial in these patients.(Ucan et al., 2016). Vitamin D deficiency is one of the causes of HT, and the larger the vitamin D deficiency, higher the chance of HT (Salem et al., 2021). Vitamin D insufficiency was common in endocrine disorders, and treatment restored levels that are normal. Low creation of vitamin D appears to be connected to a greater titer of anti-TPO antibodies and.thyroid volume in Hashimoto's disease, and supplementation was associated with a reduction of antibodies in several trials. Supplementations appeared to lower TSH levels in other studies. Given all of this evidence of vitamin D supplementation's beneficial impact, previous idea is that determining vitamin D blood concentrations.and correcting insufficiency are worthwhile additions to conditional therapies (Galuşca et al., 2022).

Hashimoto's thyroidetis (HD) is an auto-immune thyroid condition.which manifests histologically as chronically lymphocytic thyroidetis Its pathogenesis is.uncertain; however, recent researches have revealed that among the most critical pathogenic variables.are Th1/Th2 im-balance and elevated Th1 cell activity. Vitamin D, which acts as an.immunosuppressive drug, could decrease the.immune response in HD (Krysiak et al., 2017).

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In patients with HT, vitamin D levels have a positive.correlation with serum TNF-, IL-5, and IL-17,.cytokine that mediated the cellular immunity towards inflammation.and are released by Th1 cells (Botelho et al., 2018) Because cellular immunity is the primary pathogenesis factor in HT individuals , the link between vitamin D and these cytokines shows that vitamin D plays a role in HT pathophysiology (Cayres et al.2021)

The biological important of active vitamin D result from the stimulation of some essential signals by the interactions of vitamin D with receptors 1,25(OH)2-vitamin D3 forms a heterodimeric molecule with the VDR on target cells, ensuring protein-dependent transport (Bouillon et al., 2022).

Vitamin D deficiencies was much greater in AITD patients than control group (72% vs. 30.6%; p 0.001),.and it was also greater in HD patients comparing to non-AITDs (79% vs. 52%; p <0.05) Significantly decreased vitamin D amounts have also been associated to the identification of anti-thyroid antibodies (p =0.01) and aberrant thyroid function markers (p = 0.059), implying a role in AITD pathogenesis and emphasizing the importance of supplement (Khozam et al., 2022).

In 218 individuals with hyper-thyroidism and normal thyroid function, Mazokopakis et al discovered a negative connection between serum 25(OH)-vitamin D amounts and anti-TPO synthesis of antibodies Anti-TPO antibody levels were substantially greater in vitamin D deficient patients than in non-deficient ones In.186 individuals who.received oral vitamin D3 supplementations (1200-4000 IU/day) for four months, blood anti-TPO levels decreased significantly (20.3%) (Chen et al., 2022).

The current investigation discovered that vitamin D3 has a high sensitivity (100%) and specificity (80%) in screening individuals with HT, which is agreed with findings of Botelho et al., (2018).

CONCLUSIONS

We concluded that.girl are three times.more likely than.males to develop hashimoto thyroidetis. Because of their.high sensitivity and.specificity, IL-38, IL-15, and vitamin D3.characteristics plays an.important part in the identification.of HT patients.

REFERENCES

1. Admoni, O., Rath, S., Almagor, T., Elias-Assad, G., & Tenenbaum-Rakover, Y. (2020). Long-term follow-up and outcomes of autoimmune thyroiditis in childhood. *Frontiers in endocrinology*, *11*, 309.
2. Admoni, O., Rath, S., Almagor, T., Elias-Assad, G., & Tenenbaum-Rakover, Y. (2020). Long-term follow-up and outcomes of autoimmune thyroiditis in childhood. *Frontiers in endocrinology*, *11*, 309.
3. Ajjan, R. A., & Weetman, A. P. (2015). The pathogenesis of Hashimoto's thyroiditis: further developments in our understanding. *Hormone and Metabolic Research*, *47*(10), 702-710.
4. Ajjan, R. A., Watson, P. F., & Weetman, A. P. (1997). Detection of IL-12, IL-13, and IL-15 messenger ribonucleic acid in the thyroid of patients with autoimmune thyroid disease. *The Journal of Clinical Endocrinology & Metabolism*, *82*(2), 666-669.
5. Allard-Chamard, H., Mishra, H. K., Nandi, M., Mayhue, M., Menendez, A., Ilangumaran, S., & Ramanathan, S. (2020). Interleukin-15 in autoimmunity. *Cytokine*, *136*, 155258.
6. Almsaid, H., & Khalfa, H. M. (2020). The effect of Ketogenic diet on vitamin D3 and testosterone hormone in patients with diabetes mellitus type 2. *Current Issues in Pharmacy and Medical Sciences*, *33*(4), 202-205.
7. Altieri, B., Muscogiuri, G., Barrea, L., Mathieu, C., Vallone, C. V., Mascitelli, L., ... & Della Casa, S. (2017). Does vitamin D play a role in autoimmune endocrine disorders? A proof of concept. *Reviews in Endocrine and Metabolic Disorders*, *18*, 335-346.
8. Arakawa, Y., Watanabe, M., Takemura, K., Inoue, N., Hidaka, Y., & Iwatani, Y. (2017). The IL 15+ 96522 A> T functional polymorphism is related to the differentiation of Th17 cells and the severity of Hashimoto's disease. *International Journal of Immunogenetics*, *44*(2), 41-50.
9. Bensen, J. T., Dawson, P. A., Mychaleckyj, J. C., & Bowden, D. W. (2001). Identification of a novel human cytokine gene in the interleukin gene cluster on chromosome 2q12-14. *Journal of Interferon & Cytokine Research*, *21*(11), 899-904.
10. Botelho, I. M. B., Neto, A. M., Silva, C. A., Tambascia, M. A., Alegre, S. M., & Zantut-Wittmann, D. E. (2018). Vitamin D in Hashimoto's thyroiditis and its relationship with thyroid function and inflammatory status. *Endocrine journal*, *65*(10), 1029-1037.
11. Bouillon, R., Manousaki, D., Rosen, C., Trajanoska, K., Rivadeneira, F., & Richards, J. B. (2022). The health effects of vitamin D supplementation: Evidence from human studies. *Nature Reviews Endocrinology*, *18*(2), 96-110.
12. Cayres, L. C. D. F., de Salis, L. V. V., Rodrigues, G. S. P., Lengert, A. V. H., Biondi, A. P. C., Sargentini, L. D. B., ... & de Oliveira, G. L. V. (2021). Detection of alterations in the gut

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

microbiota and intestinal permeability in patients with Hashimoto thyroiditis. *Frontiers in immunology*, *12*, 579140.

13. Chen, Y., Han, B., Zhu, C., Li, Q., Chen, C., Zhai, H., ... & Lu, Y. (2022). Bidirectional mendelian randomization analysis for vitamin D and thyroid peroxidase antibody. *International Journal of Endocrinology*, *2022*.
14. Erge, E., Kiziltunc, C., Balci, S. B., Atak Tel, B. M., Bilgin, S., Duman, T. T., & Aktas, G. (2023). A Novel Inflammatory Marker for the Diagnosis of Hashimoto's Thyroiditis: Platelet-Count-to-Lymphocyte-Count Ratio. *Diseases*, *11*(1), 15.
15. Figueroa-Vega, N., Alfonso-Perez, M., Benedicto, I., Sanchez-Madrid, F., Gonzalez-Amaro, R., & Marazuela, M. (2010). Increased circulating pro-inflammatory cytokines and Th17 lymphocytes in Hashimoto's thyroiditis. *The Journal of Clinical Endocrinology & Metabolism*, *95*(2), 953-962.
16. Galușca, D., Popoviciu, M. S., Babeș, E. E., Vidican, M., Zaha, A. A., Babeș, V. V., ... & Bodog, F. (2022). Vitamin D implications and effect of supplementation in endocrine disorders: autoimmune thyroid disorders (Hashimoto's disease and Grave's disease), diabetes mellitus and obesity. *Medicina*, *58*(2), 194.
17. Galușca, D., Popoviciu, M. S., Babeș, E. E., Vidican, M., Zaha, A. A., Babeș, V. V., ... & Bodog, F. (2022). Vitamin D implications and effect of supplementation in endocrine disorders: autoimmune thyroid disorders (Hashimoto's disease and Grave's disease), diabetes mellitus and obesity. *Medicina*, *58*(2), 194.
18. Hirtz, R., Keesen, A., Hölling, H., Hauffa, B. P., Hinney, A., & Grasemann, C. (2020). No effect of thyroid dysfunction and autoimmunity on health-related quality of life and mental health in children and adolescents: Results from a nationwide cross-sectional study. *Frontiers in Endocrinology*, *11*, 454.
19. Jin, B., Wang, S., & Fan, Z. (2022). Pathogenesis Markers of Hashimoto's Disease—A Mini Review. *Frontiers in Bioscience-Landmark*, *27*(10), 297.
20. Jo, K., & Lim, D. J. (2018). Clinical implications of anti-thyroglobulin antibody measurement before surgery in thyroid cancer. *The Korean journal of internal medicine*, *33*(6), 1050.
21. Khozam, S. A., Sumaili, A. M., Alflan, M. A., & Shawabkeh, R. A. A. S. (2022). Association between vitamin D deficiency and autoimmune thyroid disorder: A systematic review. *Cureus*, *14*(6).
22. Klubo-Gwiezdzinska, J., & Wartofsky, L. (2022). Hashimoto thyroiditis: an evidence-based guide to etiology, diagnosis and treatment. *Pol. Arch. Intern. Med*, *132*, 16222.
23. Krysiak, R., Szkróbka, W., & Okopień, B. (2017). The effect of vitamin D on thyroid autoimmunity in levothyroxine-treated women with Hashimoto's thyroiditis and normal vitamin D status. *Experimental and Clinical Endocrinology & Diabetes*, *125*(04), 229-233.
24. Li, J., Sun, X., Yao, D., & Xia, J. (2018). Elevated serum IL-17 expression at cessation associated with Graves' disease relapse. *International journal of endocrinology*, *2018*.
25. Mackawy, A. M. H., Al-Ayed, B. M., & Al-Rashidi, B. M. (2013). Vitamin D deficiency and its association with thyroid disease. *International journal of health sciences*, *7*(3), 267.
26. Mikulska, A. A., Karaźniewicz-Łada, M., Filipowicz, D., Ruchała, M., & Główka, F. K. (2022). Metabolic Characteristics of Hashimoto's Thyroiditis Patients and the Role of Microelements and Diet in the Disease Management—An Overview. *International Journal of Molecular Sciences*, *23*(12), 6580.
27. Mora, J., Schlemmer, A., Wittig, I., Richter, F., Putyrski, M., Frank, A. C., ... & Brüne, B. (2016). Interleukin-38 is released from apoptotic cells to limit inflammatory macrophage responses. *Journal of molecular cell biology*, *8*(5), 426-438.
28. Muscogiuri, G., Mitri, J., Mathieu, C., Badenhoop, K., Tamer, G., Orio, F., ... & Pittas, A. (2014). Mechanisms in endocrinology: vitamin D as a potential contributor in endocrine health and disease. *European journal of endocrinology*, *171*(3), R101-R110.
29. Pan, Y., Wang, M., Chen, X., Chen, Y., Ai, S., Wang, M., ... & Liang, D. (2021). Elevated IL-38 inhibits IL-23R expression and IL-17A production in thyroid-associated ophthalmopathy. *International immunopharmacology*, *91*, 107300.
30. Pappa, A., Calder, V., Ajjan, R., Fells, P., Ludgate, M., Weetman, A. P., & Lightman, S. (1997). Analysis of extraocular muscle-infiltrating T cells in thyroid-associated ophthalmopathy (TAO). *Clinical & Experimental Immunology*, *109*(2), 362-369.
31. Ralli, M., Angeletti, D., Fiore, M., D'Aguanno, V., Lambiase, A., Artico, M., ... & Greco, A. (2020). Hashimoto's thyroiditis: An update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. *Autoimmunity Reviews*, *19*(10), 102649.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

32. Redha, H. M., & Khilfa, H. M. (2023). Hashimoto thyroiditis serological examination of interleukin-17 and 38.
33. Salem, T. M., Abdelmonem, E., & Fayad, A. (2021). Hashimoto's thyroiditis, iron, and vitamin D deficiency among Egyptian female patients: associations and possible causalities. *Hormones*, *20*(4), 833-836.
34. Shi, L., Ye, H., Huang, J., Li, Y., Wang, X., Xu, Z., ... & Yang, H. (2021). IL-38 exerts anti-inflammatory and antifibrotic effects in thyroid-associated ophthalmopathy. *The Journal of Clinical Endocrinology & Metabolism*, *106*(8), e3125-e3142.
35. Siriwardhane, T., Krishna, K., Ranganathan, V., Jayaraman, V., Wang, T., Bei, K., ... & Krishnamurthy, H. (2019). Significance of anti-TPO as an early predictive marker in thyroid disease. *Autoimmune diseases*, *2019*.
36. Surcel, M., Munteanu, A. N., Bratu, O. G., Ionita-Radu, F., Neagu, M. T., & Chiritoiu-Butnaru, M. (2021). Therapeutic potential of interleukin-15 in cancer. *Experimental and Therapeutic Medicine*, *22*(1).
37. Szymczak-Pajor, I., & Śliwińska, A. (2019). Analysis of association between vitamin D deficiency and insulin resistance. *Nutrients*, *11*(4), 794.
38. Tang, S., Yang, M., Zhang, D., Tong, Y. J., & Xin, Y. (2021). Clinical Characteristics and Follow-Up of 19 Children With Hashimoto's Thyroiditis Aged Below 3 Years: A Single-Center Retrospective Analysis. *Frontiers in Endocrinology*, *12*, 737527.
39. Tian, X., Li, N., Su, R., Dai, C., & Zhang, R. (2020). Selenium supplementation may decrease thyroid peroxidase antibody titer via reducing oxidative stress in euthyroid patients with autoimmune thyroiditis. *International Journal of Endocrinology*, *2020*.
40. Ucan, B., Sahin, M., Sayki Arslan, M., Colak Bozkurt, N., Kizilgul, M., Güngünes, A., ... & Ozbek, M. (2016). Vitamin D treatment in patients with Hashimoto's thyroiditis may decrease the development of hypothyroidism. *Int J Vitam Nutr Res*, *86*(1), 9-17.
41. Weider, T., Richardson, S. J., Morgan, N. G., Paulsen, T. H., Dahl-Jørgensen, K., & Hammerstad, S. S. (2020). Upregulation of HLA class I and antiviral tissue responses in Hashimoto's thyroiditis. *Thyroid*, *30*(3), 432-442.
42. Xu, J., Huang, G., Weng, L., Gong, L., Mao, Y., Li, Y., & Li, M. (2022). Low serum interleukin-38 levels in patients with Graves' disease and Hashimoto's thyroiditis. *Journal of Clinical Laboratory Analysis*, *36*(1), e24101.
43. Xu, J., Huang, G., Weng, L., Gong, L., Mao, Y., Li, Y., & Li, M. (2022). Low serum interleukin-38 levels in patients with Graves' disease and Hashimoto's thyroiditis. *Journal of Clinical Laboratory Analysis*, *36*(1), e24101.
44. Xu, W. D., Su, L. C., Liu, X. Y., Wang, J. M., Yuan, Z. C., Qin, Z., ... & Huang, A. F. (2020). IL-38: A novel cytokine in systemic lupus erythematosus pathogenesis. *Journal of Cellular and Molecular Medicine*, *24*(21), 12379-12389.
45. Xu, W. D., Su, L. C., Liu, X. Y., Wang, J. M., Yuan, Z. C., Qin, Z., ... & Huang, A. F. (2020). IL-38: A novel cytokine in systemic lupus erythematosus pathogenesis. *Journal of Cellular and Molecular Medicine*, *24*(21), 12379-12389.
46. Zarrabi, M., Gholijani, N., Shenavandeh, S., Aflaki, E., & Amirghofran, Z. (2019). IL-38 serum levels in patients with Behcet's disease and the relationship with clinical features. *European Cytokine Network*, *30*, 82-87.