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Anti-Thyroid Peroxidase and Anti-Thyroglobulin Antibodies in patients with Hypothyroidism

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Abstract

Background: *Autoimmune hypothyroidism is common and well-known in developed countries, the aim of this article is to determine theantithyroid peroxidase and antithyroglobulin antibodies in patients with primary hypothyroidism and comparing it with healthy subjects in Erbil governorate hospitals.*

Methods: *This case _control study was carried out in Hawler and Rizgary teaching hospitals. Which includes 140 subjects equally distributed in to 70 patients and 70 healthy person, All ages above 18 years were included. The study was carried out in the period between March and December 2015. It includes all patients who has/had hypothyroidism, either newly diagnosed or on treatment, or subclinical. Patients with history of thyroid operation, radioactive iodine treatment and secondary (central) hypothyroidism, were excluded in the study. Control subject was any one with normal thyroid function test and no any history of thyroid diseases, blood withdrawn and sent for assessment for Thyroid Stimulating Hormone (TSH), T4, T3, Thyroid Peroxidase and Anti-thyroglobulin antibodies.*

Results: *Total of 140 subjects was equally distributed in to 70 cases (patients) and 70 controls (healthy individuals). Their ages ranges between 18-76 years, with the mean age within the cases were 40.3 years and 40.9 years within the control group.*

From the total of 140 subjects, 112 were female and 28 were male. Gender distribution within the cases were 55 (78.57%) female and the remaining 15 (21.43%) were males. In the control side 57 (81.42%) were female and the remaining 13 were male with statistically no significant differences in sex distribution between cases and control.

Within the cases the goiter was detected clinically in 40 (57.1%) and no goiter detected in control group with highly significant differences between cases and control ($p<0.001$). Within the cases high titter of anti-thyroid peroxidase antibody was detected in the serum of 62 (88.6%) patients. While in control group Anti-Thyroid Peroxidase antibody was detected only in 8(11.4%) subjects, indicating highly significant difference between case and control group ($p<0.001$).

The ant- thyroglobulin antibody was detected in 52(74.3%) cases but in control grouponly in 12 (17.1%) indicating highly significant difference between the two groups (p<0.001)

Conclusion: *1.The majority of hypothyroid cases were having positive both anti-thyroid peroxidase and anti-thyroglobulin antibodies, and these antibodies were significantly higher in patients when compared with control group (healthy individual).*

2.The majority of hypothyroid patients were having goiter when compared with healthy individuals.

3. In this article the majority of cases with hypothyroidism were duo to autoimmune thyroid disease, depending on clinically detected goiter and positive both anti-thyroid peroxidase and anti-thyroglobulin antibodies.

Keywords: *autoimmune hypothyroidism, antithyroid peroxidase, antithyroglobulin.*

1 Introduction

Hypothyroidism is a clinical term characterized by Reduced production of thyroid hormone which is the central feature of the clinical state .[1,2] Permanent loss or destruction of the thyroid gland, through processes such as autoimmune destruction or irradiation injury, is described as primary hypothyroidism. Hypothyroidism due to transient or progressive impairment of hormone biosynthesis is typically associated with compensatory thyroid enlargement, Central or secondary hypothyroidism, caused by insufficient stimulation of a normal gland, is the result of hypothalamic or pituitary disease, or defects in the thyroid-stimulating hormone (TSH) molecule, primary hypothyroidism is the cause in approximately 99% of cases of hypothyroidism· estimates of the incidence of hypothyroidism vary depending on the population studied.[3] In the United States, 0.3% of the population have overt hypothyroidism, defined as an elevated serum TSH concentration and reduced free thyroxin concentration, and 4.3% have what has been described as subclinical or mild hypothyroidism, the incidence of hypothyroidism is higher among women, the elderly, and in some racial and ethnic groups.[4]

Among the causes of primary hypothyroidism the majority are duo to autoimmune processin iodine sufficient areas which is called Hashimoto's thyroiditis (HT) which is the most prevalent autoimmune thyroid disorder, where lymphocytic infiltration of the thyroid gland is often followed by a gradual destruction and fibrous replacement of the thyroid parenchymal tissue, Patients may or may not develop a goiter, The principal biochemical characteristic of the disease is the presence of thyroid autoantibodies in the patients' sera against two major thyroid antigens, thyroid peroxidase (TPO) and thyroglobulin (Tg). TPO antigen, located at the apical membrane of the thyrocyte, is essential for thyroid hormone synthesis, catalysis of iodine oxidation, iodination of tyrosine residues in Tg and coupling of the iodothyrosines into thyroxine (T_4) and triiodothyronine (T_3). The thyroid hormones are synthesized on Tg, a large glycoprotein within thyroid follicles, which also serves as the storage for thyroid hormones [5]. Small amount of Tg is secreted into the circulation where the estimated half-life is approximately 3 days [6].

Antibodies against TPO (TPOAbs) and Tg (TgAbs) are of immunoglobulin G class, both showing high affinity for their respective antigens. Unlike TgAbs, TPOAbs can activate complement and are able to cause damage to thyroid cells due to antibody dependent cell cytotoxicity [7]. Nevertheless, there is little evidence that both antibodies have a prime role in the pathogenesis of HT and it is far more likely that both T-cell mediated cytotoxicity and activation of apoptotic pathways influence the disease outcome. However, TAbs serve as a useful marker for the diagnosis of thyroid autoimmunity. In HT, TPO Abs are present in nearly all (>90 %) patients, while TgAbs can be detected in approximately 80% [5, 8].

The prevalence of HT confirmed by cytology was 13.4% in consecutive patients who underwent fine-needle aspiration biopsy of thyroid nodules [9].

According to large epidemiological surveys, HT is the most frequent cause of hypothyroidism recorded in 4% to 9.5% of the adult population ,the prevalence of HT is high which was also confirmed by the largest National Health and Nutrition Examination Survey (NHANES) III study(4). The results show that 18% of the population without previously known thyroid disease regardless age or gender presented with elevated TAbs; TPOAbs were positive in 11.3% and TgAbs in 10.4%. The prevalence of TAbs in females was twice as high as in males. It increased with age and was significantly higher in whites or Japanese than in blacks or Mexican Americans [4, 10]. Thus, approximately 20% of females older than 60 years were thyroid Abs positive [10].

Autoimmune (HT) arise due to complex interactions between environmental and genetic factors, and are characterized by reactivity to self-thyroid antigens which are expressed as distinctive inflammatory or anti receptor autoimmune diseases [11].Among the major Autoimmune thyroid diseases susceptibility genes that have been identified and characterized is the Human Leukocyte Antigen-DR(Death Recepter) gene locus, as well as non-Major Histocompatibility Complex genes including the Cytotoxic T-Lymphocyte Antigen-4, Cluster Differentiation (CD40), Protein tyrosine phosphatase nonreceptor-type-22(PTPN22), thyroglobulin, and TSH receptor genes [12]. The major environmental triggers of AITD include iodine, medications, infection, smoking, stress, and genetic predisposition to AITD which lead to novel putative mechanisms by which the genetic environmental interactions may lead to the development of thyroid autoimmunity [13].

The aim of the study: is to detect autoimmune hypothyroidism as a cause of the condition and to compare the posatitivity of auto antibodies with healthy subjects.

The objectives are:

1. Measurement of auto antibodies in serum of patients and healthy subjects.
2. Measure the prevalence of auto antibodies in hypothyroidism as an etiology

2. Materials and Methods:

2.1 Study design:

This case _control study was carried out in Hawler Teaching Hospitals (Rizgary and Hawler Teaching Hospitals), which include 140 subjects equally distributed in to 70 patients and 70 healthy subjects. All ages above 18 years were included.

The study was carried out in the period between march and December 2015.

2.2 Inclusion criteria:

It includes all patients who has/had hypothyroidism either newly diagnosed or on treatment or subclinical (defined by high TSH and normal T4 amd T3) [14] .

2.3 Exclusion criteria:

Patients with history of thyroid operation, radioactive iodine treatment and secondary (central) hypothyroidism were excluded in the study.

People with no history of thyroid diseases and normal thyroid function test were regarded as controls. and appropriate matching between case and control regarding approximation of age and gender were undertaken.

2.4 Data Collection:

Detailed history was obtained, physical examination was carried out and the patients and subjects were sent for assessment for auto antibodies in the form of antithyroid peroxidase antibody and antithyroglobulin antibody in the serum with the thyroid function test. And appropriately designed questionnaire filled by the researcher.

After withdrawing the blood from patients and subjects it was kept in special chemical container and appropriate temperature and then centrifuged and serum separated for measurement of thyroid auto antibodies and thyroid function test.

Throglobulin and Thyroid peroxidase antibodies were measured with a sensitive immunora-diometric quantitative assay, values greater than

115 U/mLand34 U/ml respectively were considered positive[15].

TSH was measured by immunoradiometric assay (IRMA), Normal value is considered 0.27 - 4.2 µIU/mL and Commercially available kits (Roche) was used to measure it[16].

Free T4 and T3 resin uptake measured by radioimmunoassay (RIA) on samples with abnormal TSH level (higher).

The normal (reference) ranges are free T3 (2.0 - 4.4) pg/mL and Free T4 0.93 - 1.7 ng/dL[17].

2.5 Ethical Consideration:

All the patients and subjects were informed about the aim and objective of the study, ethical consent obtained verballythen research protocol was evaluated and approved by Research Ethic Committee in Hawler Medical University.

2.6 Data Analysis:

The data analysis was performed with Statistical package of social sciences (SPSS) (version19.0). Appropriate chi-square test was used for comparison between the two groups. P values < 0.05 was considered statistically significant.

3.Results

From the total of 140 subjects which were equally distributed in to 70 cases (patients) and 70 control (healthy individuals) , There ages ranges between 18_76 years old with the mean age within the cases were 40.3 years and 40.9 years within the control group .

From the total of 140 subjects 112 were female and 28 male (figure1).

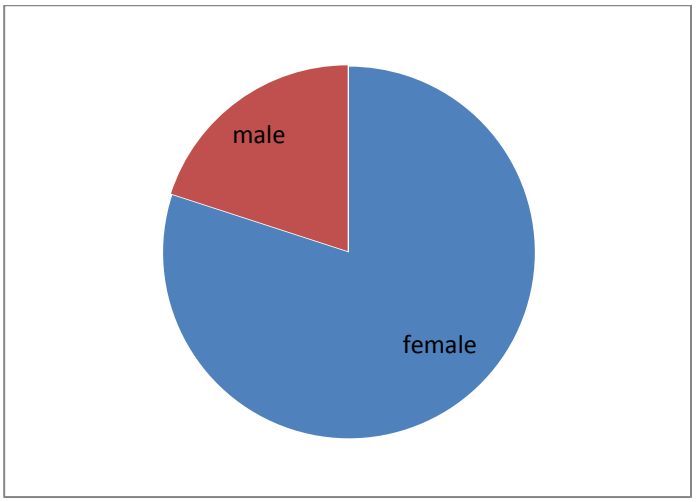

Figure 1: Total Sex Distribution.

Sex distribution within the cases were 55 (78.57%) female out of 70 and the remaining 15 (21.43%) were male, in the control side 57(81.42%) were female out of 70 and the remaining 13 were male with no significant differences in sex distribution between cases and control (figure2).

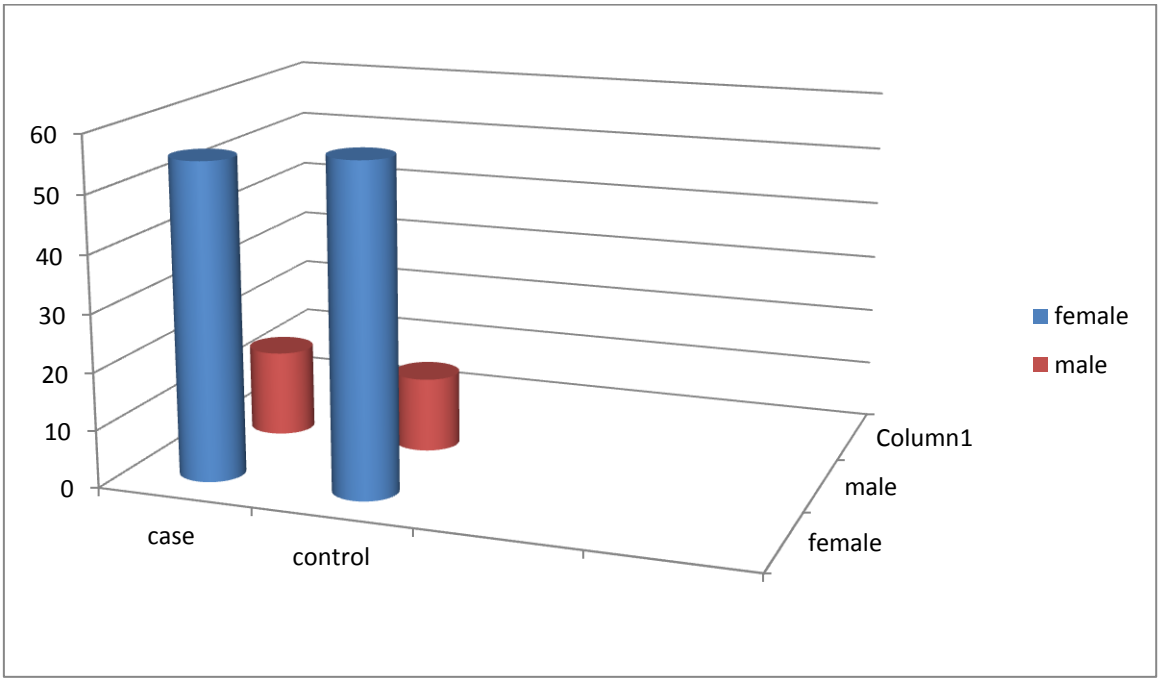

Figure 2 sex distribution in both cases and control.

Within the cases the goiter was detected clinically in 40 (57.1%) cases out of 70 and no goiter detected clinically in control group. With highly significant differences between cases and control ($p<0.001$) figure 3.

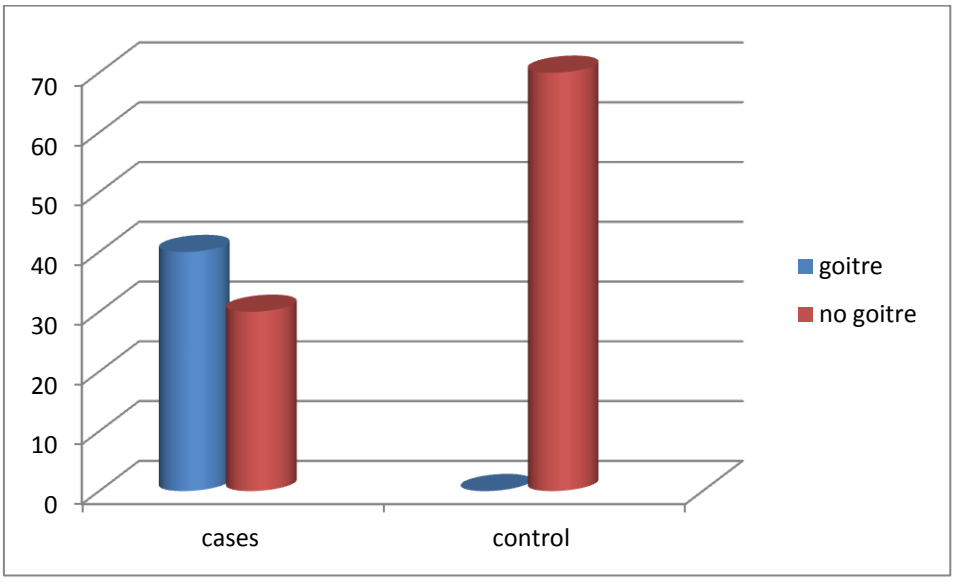

Figure 3: clinically detected goiter in both cases and control.

Within the cases high titter of antithyroid peroxidase antibody was detected in the serum of 62 (88.6%) out of 70 cases in opposite to that this antibody was detected only in 8(11.4%) in control group with highly significant differences between them ($p<0.001$).figure4

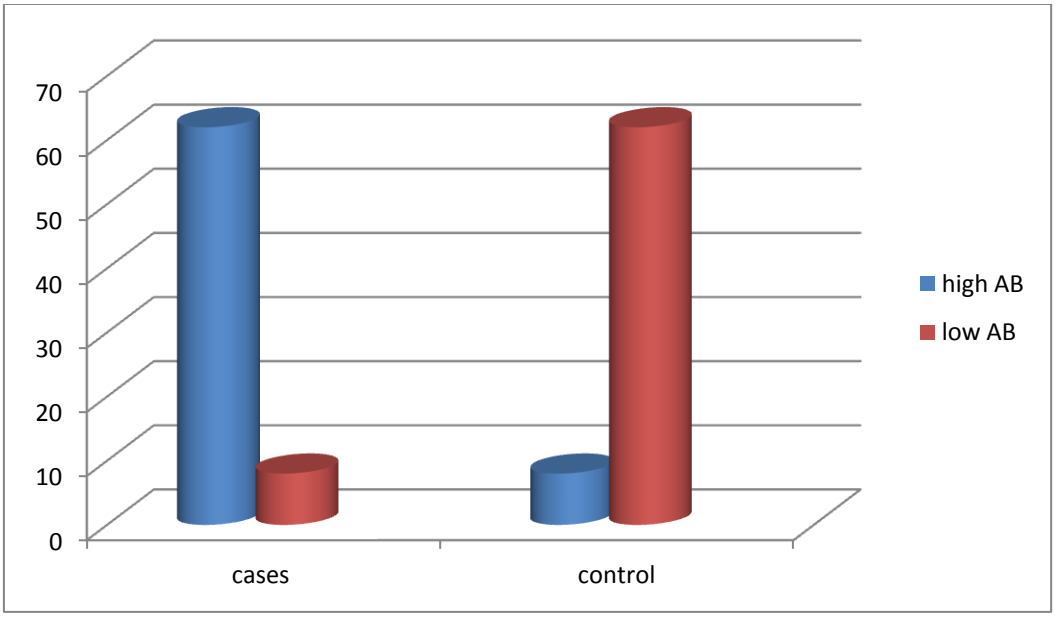

Figure 4: anti_thyroid peroxidase antibody detection in both cases and control group.

The antithyroglobulin antibody was detected in 52(74.3%) cases out of 70 but in opposite to that it was only detected in the serum of 12(17.1%) out of 70 in control group with statistically high significant differences between the two groups ($p<0.001$) figure 5.

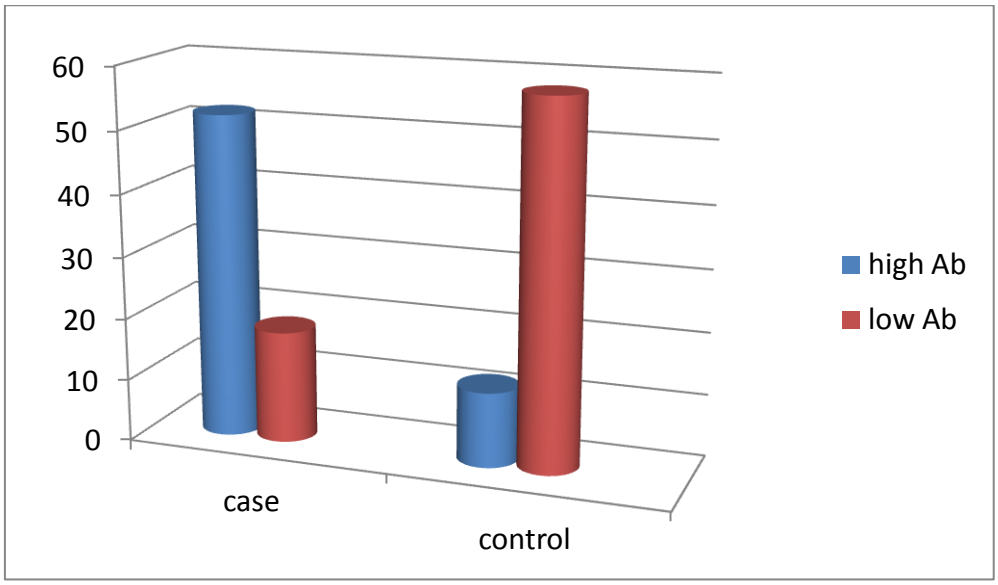

Figure 5: anti _thyroglobulin antibody detection in both cases and control group.

Within the cases 52(74.3%) were having overt hypothyroidism and the remaining 18(25.7%) were having subclinical hypothyroidism out of 70 cases figure 6.

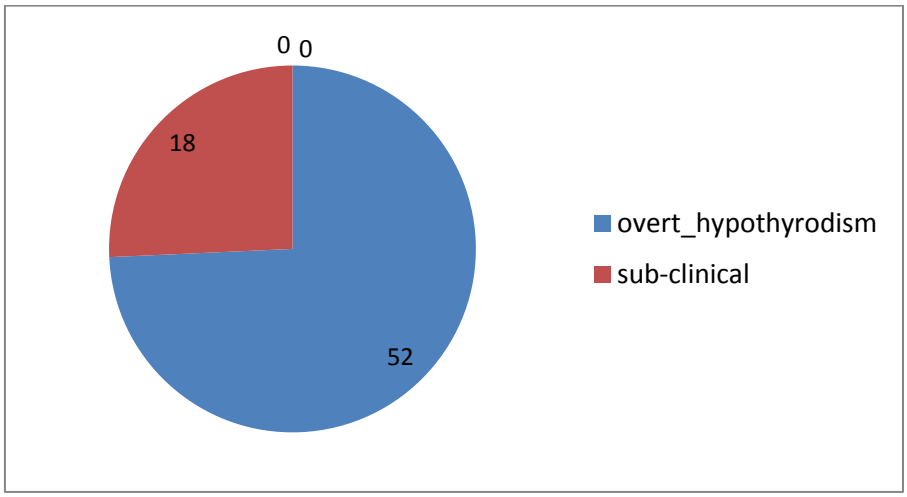

Figure 6 : shows the distribution of overt hypothyroidism and subclinical hypothyroidism within cases.

4. Discussion

Thyroid autoantibodies are the markers of autoimmunity in autoimmune thyroid diseases. Its prevalence in autoimmune and non-autoimmune thyroid disorders in the Erbil population is not known. This study outlines the prevalence of antithyroid peroxidase antibody and antithyroglobulin antibody among Erbil patients who were referred for investigations for suspected cases of autoimmune thyroid disorders. The results were compared with healthy persons without thyroid disorders. The prevalence and the value of each antibody was analyzed and correlated with gender and age in order to establish the relevance of measuring such antibodies in the diagnosis and prediction of disease progression.

The majority of patients with autoimmune thyroid diseases are between middle and old age with two peaks between 40-50 and 50-60 years[(18)]. In this article the mean age for both cases and control (normal population) were 40.3 years and 40.9 years respectively which they were near to each other which is important point for matching consideration.

In addition to age factor, the prevalence and incidence of thyroid disorders is influenced primarily by gender [19]. according to this article results the majority of participants were female, From the total of 140 subjects 112 were female and 28 male (figure1) , Sex distribution within the cases were (78.57%) female and the remaining (21.43%) were male, in the control side (81.42%) were female out of 70 and the remaining (18.58%) were male with no significant differences in sex distribution between cases and control (figure2) this another point which is important for matching consideration and points toward that majority of autoimmune thyroid diseases were females and this going with what was shown by Brixetal.[20]

In patients with primary hypothyroidism who had been participated in this study the anth- thyroid peroxidase antibody was detected in the serum of 88.6% but its only detected in 11.4% of normal population with highly significant differences between them p<0.001.

Regarding anti thyroglobulin antibody which was also shown to be significantly higher in patients with primary hypothyroidism 74.3% than in normal population 17.1% with p<0.001

The highest percentage of positive patients in this study, were in the hypothyroid groups, which may reflect the autoimmune destruction of thyroid glands in those patients. This ratio is relatively similar when compared with research carried out by Hasanat et al[21]. This data are in accord with the study carried out by Delemeretal [22]which shows that autoimmune process by antithyroid peroxidase and antithyroglobulin antibodies were the most common cause of primary hypothyroidism.

This point indicate that even in this region the majority of patients with primary hypothyroidism were duo to autoimmune process after exclusion of iatrogenic and secondary hypothyroidism these findings were consistent with what was found by NHALES III survey [4]

Determination of Anti-Thyroglobulin Antibody has been used in conjunction with antithyroid peroxidase antibody to maximize the probability of a positive result in patients with autoimmune thyroid disease, Several studies have suggested that Anti-Thyroglobulin Antibody is of less relevance than antithyroid peroxidase antibody in the detection of thyroid disease however detection of both increase the probability of autoimmune hypothyroidism as shown by Tomer et al[23]. Antithyroglobulin antibody appear in the circulation early before antithyroid peroxidase antibody and over hypothyroidism this point was studied by McLachlan et al[24] .

In other side in normal population this antibody was detected less and this result is variable from country to country as shown by cross sectional study of more than 17 000 US citizens from 1988 to 1994 (NHANES III) showed that 13% had antithyroid peroxidase antibody and 11.5% Anti-Thyroglobulin Antibody[4].

Within the cases the goiter was detected clinically in 40 (57.1%) cases and no goiter detected clinically in control group. With statically significant differences between them (p<0.001).

Goiter was common finding among cases this indicate that most patients with hypothyroidism were autoimmune and in autoimmune mostly were goitrous Hashimoto rather than to be atrophic autoimmune hypothyroidism based on clinically detected goiter ,highly positive antithyroid peroxidase and antithyroglobulin antibodies , The present finding of higher anti-thyroid antibody prevalence among patients with goiter than in the control, group, falls within the range of that described by Caturegli[25]. Wich evaluate patients with goiter and its correlation with antithyroid peroxidase Ab and antithuroglobulin Ab and he shown that these antibodies were more common in goitrous than non goitrous hypothyroidism.

5.Conclusuion & Recommendation

5.1. Conclusion

1. The majority of hypothyroidism were having positive both antithyroid peroxidase and antithyroglobulin antibodies and these antibodies

were significantly higher in patients when comparing with control group (healthy individual).

2. The majority of hypothyroid patients were having goiter when comparing with healthy individual.

3. Finally in this study the majority of primary hypothyroidism were duo to autoimmune depending on clinically detected goiter and positive both antithyroid peroxidase and atithyroglobulin antibodies.

5.2. Recommendation

Further studies are needed in the form of large survey to include large number of patients and all causes of hypothyroidism to determine exactly what the leading cause of hypothyroidism in Erbil specially and Kurdistan generally.

To determine and complete the definition of Hashimotos thyroiditis ultrasonography and histocytolog are required to roll out autoimmunity.

Follow study are required for healthy individual with positive antibodies to determine risk ratio for development of hypothyroidism in the future.

6. Acknowledgement

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7. Conflicts of interest:

The author reports no conflicts of interest.

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