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Original Research Article

The Relation among Vitamin B12 and B9 in Hypothyroidism in Iraqi Patients

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Abstract: ***Background*****:** The thyroid gland constitutes an integral component of the endocrine system, exerting regulatory control over numerous vital physiological processes through the synthesis and release of specific hormones. Hypothyroidism is a disorder in which the thyroid gland fails to produce enough thyroid hormone to maintain normal physiological function. The prevalence of hypothyroidism varies substantially worldwide and is more common in populations with a relatively high iodine intake or severe iodine deficiency, Hashimoto's thyroiditis, inflammation of the thyroid, congenital hypothyroidism, hypothyroidism that is present from birth, iodine deficiency or excess, as well as diseases of the pituitary gland or hypothalamus, are the most frequent causes of hypothyroidism. ***Objective*****:** The study aims to investigate the relationship between some vitamins and hypothyroidism in Iraqi patients. ***Subjects and Methods*****:** This is a case-control study, manipulated from the first of March to the end May of 2023, 90 samples aged (18-70) years old, from Baghdad City, were selected and divided them into two groups. The first group consists of 60 people infected with hypothyroidism. The second group (control group) consists of 30 apparently healthy people. Blood samples were assessed for serum vitamin B12, and vitamin B9 using enzyme linked immunosorbent assay technique. ***Results*****:** The study showed that the level of vitamin B12 and folate B9 in hypothyroidism patients significantly lower compared to control group (p value < 0.001). ***Conclusion*****:** Patients with hypothyroidism had noticeably low levels of vitamin B12 and folate B9, indicating that this may be involved in the etiology of hypothyroidism.

Keywords: Hypothyroidism vitamin B12, folate B9.

1. INTRODUCTION

The thyroid gland is a vital butterfly-shaped endocrine gland situated in the lower part of the neck. It is present in the front and sides of the trachea, inferior to the larynx. It plays an essential role in regulating the basal metabolic rate (BMR) and stimulates somatic and psychic growth, besides having a vital role in calcium metabolism [1]. A condition known as hypothyroidism occurs when the thyroid gland is unable to produce enough thyroid hormone to maintain healthy physiological function. Low thyroid hormone levels make it challenging for body cells to obtain enough thyroid hormone, which causes a sluggish metabolism [2]. The area of the brain known as the hypothalamus is responsible for controlling bodily processes like digestion, blood pressure, heart rate, and body temperature [3]. Nearly every organ in the body is impacted by thyroid hormones because they regulate how the body uses energy, including how fast the heart beats. Many bodily activities slow down when there are insufficient thyroid hormones present [4]. The risk of developing hypothyroidism is substantially higher in women than in men. In addition, those above 60 are more likely to contract the condition [5].

Vitamin B12 The generation of red blood cells (RBCs), DNA synthesis, the health of the nervous system, and the preservation of chromosome structural integrity are only a few of the biological processes that are regulated by vitamin B12, an essential micronutrient [6]. The proteins Haptocorrin (R-binders), Intrinsic Factor (IF), and the Cell Surface receptor Cubilin are associated with each other, Cobalamin, a vital dietary component, is absorbed across the whole gastrointestinal tract (GIT) [7]. In the stomach, vitamin B12 from food binds to haptocorrin, and as the pH in the duodenum rises, the cobalamin-haptocorrin complex dissociates [8]. Salivary haptocorrin and stomach intrinsic factor (IF) are both necessary for the complex process of absorbing vitamin B12. A rare hereditary abnormality or, more frequently, a pernicious anemia-causing inflammatory condition can cause IF deficiency [9]. The cobalamin-IF receptor, made up of the two subunits cubilin (CUBN), encoded by CUBN, and amnion less (AMN), is responsible for absorbing the B12-IF complex in the terminal ileum. Mutations in CUBN or AMN lead to Imerslund-Grasbeck syndrome, an autosomal-recessive disease. Megaloblastic anemia in children is the outcome, and intramuscular vitamin B12 is effective [10]. As part of the autoimmune polyglandular endocrinopathy, hypothyroidism may be linked to pernicious anemia [11]. Malnutrition, malabsorption, autoimmune pernicious anemia, or medication use, such as metformin, proton-pump inhibitors, or H2 receptor antagonists, can result in vitamin B12 insufficiency [12]. Assays for intrinsic factor and antibodies to gastric parietal cells weren't accessible locally at the time of the study, Since B12 insufficiency is common in hypothyroid individuals, the underlying cause of this connection could not be identified [11]. Vitamin B12 exerts a substantial influence on the growth of red blood cells, the synthesis of DNA, and the proper functioning of the neurological system [13]. Additionally, it contributes to thyroid hormone metabolism however, there is little proof that a vitamin B12 shortage and hypothyroidism are causally related [14]. Having said that, hypothyroidism can interfere with the body's absorption of vitamin B12 [15]. It can result in atrophic gastritis, an inflammatory illness that causes the stomach lining to thin out [16]. This may lessen the levels of intrinsic factor and stomach acid, which are necessary for the absorption of vitamin B12. As a result, people with hypothyroidism may be at an increased risk of developing vitamin B12 deficiency [17]. Pernicious anemia and celiac disease have been identified as probable etiological factors contributing to the occurrence of B12 deficiency in individuals diagnosed with hypothyroidism [17].

Water-soluble vitamin folate, usually referred to as vitamin B9 or folic acid (the vitamin's synthetic version), is necessary for a variety of vital bodily processes [18]. In the form of folic acid, it is also added to foods and offered as a supplement; this form is actually more readily absorbed than that obtained from food sources—85% as opposed to 50% [19]. The methionine cycle converts 5-methyltetrahydrofolate (5-MTHF) and cobalamin (B12) into THF and methionine [20]. Reduced dihydrofolate (DHF) and tetrahydrofolate (THF) are required for the transfer of one-carbon groups, a process necessary for the production of amino acids, purines, pyrimidines, DNA, and ribonucleic acid (RNA) [21]. For the synthesis of purine and thymidine, which are both components of RNA and DNA, biochemically speaking, carbon fragments from glycine, serine, or histidine are physically allocated to THF lead to generate 5,10-Methylene THF (5,10-MTHF) [22]. The methyl group is transferred from 5,10-MTHF to Methionine via 5-MTHF, which then activates the formation of –SAM [23]. RNA, DNA, neurotransmitters, membrane lipids, proteins, and hormones are all bolstered by it [24]. Pregnancy and infancy, as times of rapid cell division and growth, highlight the vitamin folate's critical importance [25]. It's crucial for keeping anemia at bay and making sure people of all ages have plenty of healthy red blood cells. Fetal neural tube abnormalities are commonly the result of inadequate maternal nutrition [26]. Folic acid or folate B9 is also another vitamin with disrupted intestinal absorption that leads to macrocytic anemia in hypothyroidism [27]. Vitamin B12 helps to maintain normal folate metabolism and its deficiency may likely lead to the decrease in folate circulating levels. Methyl tetrahydrofolate remains unutilized by the cells and therefore MTHF will not be converted into THF and hence resulting in folic acid deficiency [28].

2. MATERIALS AND METHODS

This is a case-control study, manipulated from the first of March to the end May of 2023, 90 samples aged (18-70) years old, from Baghdad City, were selected and divided them into two groups and applied on the needed test to calculate important parameters that support our investigation.

- **First group**: 60 people (men and women) infected with hypothyroidism.
- **Second group (control group):** 30 healthy people (men and women).

2.1 Ethical Approval

A pre-tested questionnaire was created for each participant to get data. The protocol of this investigation was supported by the Scientific Committee in Tikrit University College of Medicine. All patients provided informed consent to participate in the study, data collection, and analysis for research purposes and were asked to answer a prepared questionnaire after their consent had been obtained by direct interview with them. On labor dates, height, weight, use of residency, medication, risk factors, and diseases.

2.2 Sample Collection

The blood samples were drawn from the vein. After cleaning the venipuncture site with iodine, five milliliters (5 ml) of the blood sample from each participant. After that, the blood sample is placed in the following method, as described below:

The blood specimen was set in the plane tube, left blood for (15-20) minutes until coagulating then the specimen was split by using a centrifuge for at least 10 minutes at 3000 rounds per minute (rpm) to assemble the serum.

3. RESULTS

3.1 Percentage of age in hypothyroidism patients

The present study involved 90 participants (60 hypothyroidism patients and 30 control group). The study showed that the peak age of hypothyroidism patients was between 36-50 years with a percentage of 43%, while the least age group was 20-35 years with a percentage of 22 %, see (Table 1).

Table 1: The age and percentage of hypothyroidism patients

Age group (years)	No.	%
20-35	13	22
36-50	26	43
51-65	21	35
Total	**60**	**100%**

The study revealed that the high rate of hypothyroidism disease 57 % in women compared with the low rate 43% in men, according to this value; women are more likely than men to have the condition, as presented in (Table 2).

Table 2: Relation the number of hypothyroidism patients with gender

Gender	No.	%
Men	26	43
Women	34	57
Total	**60**	**100%**

Multiple studies concur with this result and they reported that hypothyroidism is more prevalent in women and hypothyroidism with considerable gender differences is the most common organ-specific condition. This might be because women are more prone to autoimmune illnesses than men are. Numerous autoimmune diseases frequently afflict women at times of high stress, such as pregnancy, or times of significant hormonal change, as had recently been observed [29, 30].

3.2 A Comparative Analysis of Vitamin B12 Levels in Patients with Hypothyroidism and a Control Group

The study revealed that individuals with hypothyroidism exhibited the lowest average (mean ± standard deviation) levels of VIT-B12 in comparison to the control group (146.5 ± 44.1 versus 611.0 ± 58.5 ng/L). The difference is highly significant (p value < 0.001), as presented in (Table 3 and Figure 1.

Table 3: Comparison of serum level of VIT-B12 between hypothyroidism patients and control group

Study groups	No.	VIT-B12 (ng/L) Mean ± SD
Hypothyroidism patients	60	146.5 ± 44.1
Control group	30	611.0 ± 58.5
P value	-	0.0005

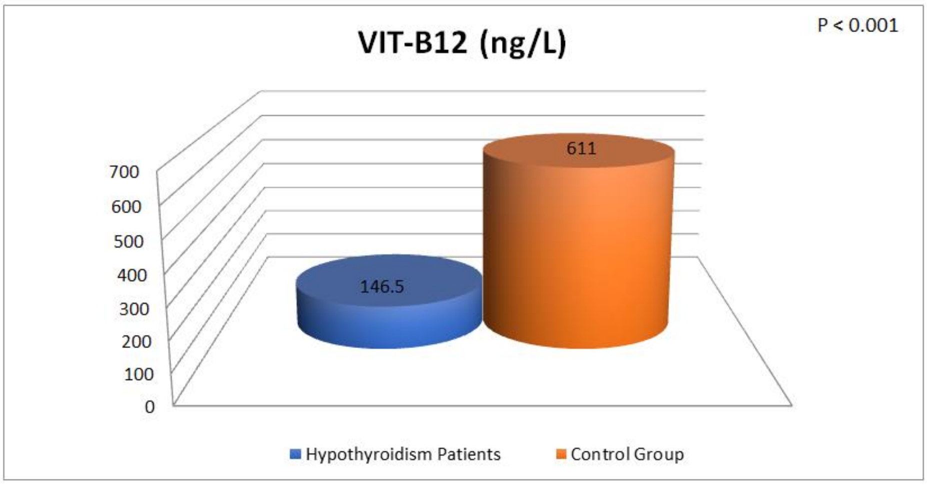

Figure 1: Mean of VIT-B12 (ng/L) between hypothyroidism patients and control group in the study

In agreement with this finding, a concurrent study found that serum vit-B12 was significantly decreased in hypothyroid patients as compared to normal individuals [28]. Patients with autoimmune thyroid disease typically experience vitamin B12 deficiency. This connection is most likely brought on by pernicious anemia linked to autoimmune thyroid illness and/or decreased vitamin B12 absorption caused by atrophic gastritis [31]. It was documented that atrophic gastritis is seen in 35–40% of autoimmune thyroid diseases and of them gastric parietal cells antibodies and pernicious anemia. Antibodies to intrinsic factor had also been seen in those patients [32].

The association between hypothyroidism and pernicious anemia is ascribed to the shared autoimmune origin of these conditions. Furthermore, individuals diagnosed with hypothyroidism may exhibit additional abnormalities that could potentially lead to a shortage in vitamin B12. These abnormalities may include factors such as increasing age, variations in dietary habits, or impaired intestinal absorption resulting from reduced gut motility and an overgrowth of bacteria.

On the other, another study found no significant difference in the prevalence of vitamin B12 insufficiency between individuals with primary hypothyroidism and the control group [17]. The variability in reported prevalence rates of vitamin B12 insufficiency in the previous study may be attributed to differences in methodology, nutritional status, and the laboratory cut points employed to identify vitamin B12 deficiency.

3.3 A Comparative Analysis of Folate B9 Levels in Individuals with Hypothyroidism and a Control Group

The study revealed that individuals with hypothyroidism exhibited the lowest levels of folate B9, as indicated by the mean ± standard deviation, in comparison to the control group (3.8 ± 1.29 versus 9.89 ± 3.28 ng/mL). The difference is highly significant (p value < 0.001), as observed in (Table 4) and Figure 2.

Table 4: Comparison of serum level of folate B9 between hypothyroidism patients and control group

Study groups	**No.**	**Folate B9 (ng/mL) Mean ± SD**
Hypothyroidism patients	60	3.81 ± 1.29
Control group	30	9.89 ± 3.28
P value	**-**	**0.0004**

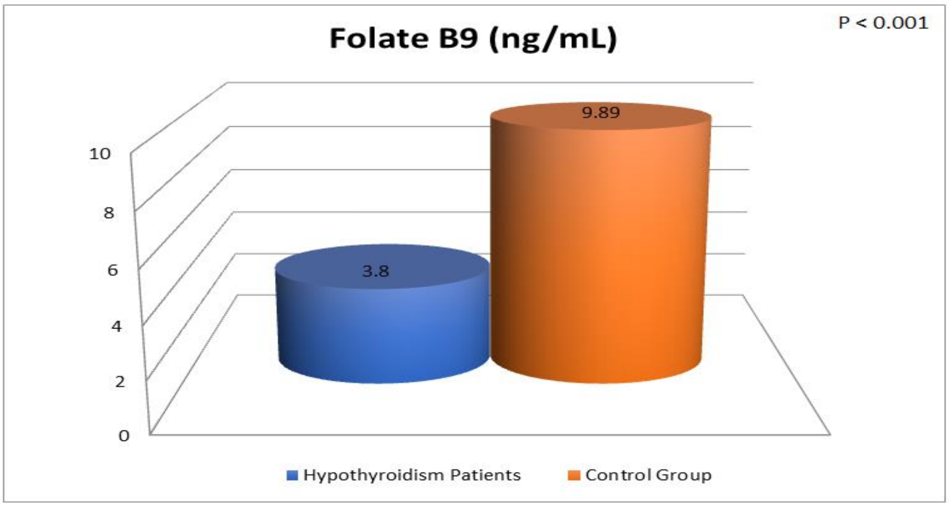

Figure 2: Mean of Folate B9 (ng/mL) between hypothyroidism patients and control group in the study

According to the similar study, hypothyroidism patients had low levels of folate compared to normal group [28]. VIT-B12 supports proper metabolism of folate. Its lack may also contribute to the drop in folate levels. Because free folate is trapped in 5-methyl tetrahydrofolate form and not consumed by cells, it cannot be converted into tetrahydrofolate and this result in functional folate shortage.

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