

Serum inhibin b as a biomarker for ovarian reserve in Iraqi women with hypothyroidism

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Abstract

The condition known as hypothyroidism is common in women, even in those who are fertile. The quantity and caliber of follicles present in the ovary at any one moment are known as the ovarian reserve. Individuals who are susceptible to a decreased ovarian reserve ought to have an assessment of their ovarian reserve conducted. The purpose of this research is to assess the impact of hypothyroidism on Iraqi women's ovarian reserve using Inhibin B hormone and hormone tests FSH, LH. There was no discernible variation in the average (\pm SD) age from (20 to 40) years of the patient group compared to the control group (p-value 0.08). However the mean BMI of the patients were statistically significantly different from the controls (P- value 0.006). Women with positive and negative anti-TPO, those with overt and subclinical hypothyroidism, difference in mean values of studied parameters (Inhibin B, FSH and LH) in patients group according to regularity of menstrual cycle (regular vs. irregular), with significant decrease in mean value of Inhibin B in irregular menstruated patients when compared to regular ones (P -value 0.038). There was no significant difference in mean values of other measured parameters. A noteworthy inverse relationship was seen between BMI and inhibin B ($r = -0.34$, P- value 0.02). This study indicated that, regardless of the cause or state of thyroid function, women with established hypothyroidism should have their serum levels of Inhibin B measured.

Keywords: hypothyroidism, Ovarian reserve, BMI, Inhibin B

Introduction

Even among women who are of reproductive age, hypothyroidism is a frequent illness. Hypothyroidism is the result of low thyroid hormone levels, which can have a range of causes and symptoms. Untreated hypothyroidism increases morbidity and mortality. Although Hashimoto thyroiditis, an autoimmune thyroid disorder, is the most common cause of hypothyroidism in the world, a diet deficient in iodine is the main contributing factor. The patient may present with an asymptomatic disease or with myxedema coma. (Hasegawa Y., et al., 2022). Exogenous thyroid hormone can be used to treat hypothyroidism, which can be identified with straightforward blood testing. Primary hypothyroidism is the term used to describe a condition in which the thyroid gland is unable to produce enough thyroid hormone. Less frequently, secondary or central hypothyroidism is diagnosed when there is a pituitary or hypothalamic disease present with normal thyroid function. The most frequent cause of primary hypothyroidism in iodine-deficient areas of the world is iodine deficiency. (Taylor P. N., et al., 2018). Clinical signs of

hypothyroidism include constipation, irregular menstruation, weight gain, hair loss, easy fatigability, hoarseness or deepening of the voice, and increased sleeping (Samuels M. H., 2008). Beneath the beta-B subunit of Inhibin B is an alpha subunit connected to an alpha subunit; it is a member of the transforming growth factor-b superfamily. It is commonly known that the non-steroidal hormone, which is secreted by the granulosa cells of growing follicles, can prevent the production of follicle-stimulating hormone (FSH). When there's a rise in inhibin B in the blood, the pituitary gland experiences a direct negative feedback loop that lowers the FSH. Thus, one of the key elements in maintaining a low level of serum FSH is the increased amount of inhibin B in women of reproductive age. But as they become older, their ovarian follicles become fewer in number and quality, their serum inhibin B level steadily drops, and their FSH inhibitory action becomes less strong (Wen J., Huang K., Du X., et al 2021). The function of the ovarian reserve, which is frequently correlated with age and can indicate a woman's endocrine system and fertility, will gradually decline (Adamska, A., et al., 2021; Mansoor et al., 2025). Thyroid conditions are one of the variables influencing the ovary's functional

reserve. Subclinical and clinical hypothyroidism are prevalent in women of reproductive age (4–10%) and (0.1–2%), respectively. Thyroid abnormalities are among the most frequent endocrine disorders in women of reproductive age and can result in menstruation and ovulation difficulties, as well as infertility (Kabodmehri R., et al., 2021). Granulosa cells, which envelop oocytes, are constantly changing to provide essential support for oocytes. Follicle Stimulating Hormone (FSH) and TSH work in concert to encourage the growth of granulosa cells (Vissenberg R., et al., 2015). Follicle death is inhibited and FSH stimulation is regulated by thyroid hormones (Zhang C., et al., 2013; Abbas et al., 2025).

Subjects and Methods

This case-control study was carried out at the Endocrinology and Diabetes Consulting Clinic, Baghdad Hospital; the Department of Biochemistry, College of Medicine, University of Baghdad; and the National Center for Teaching Laboratories, Medical City, between November 2024 and March 2025. The study included 88 women between the ages of 20 and 40. 51 of them Group 1 had hypothyroidism, according to a consultant endocrinologist's diagnosis, which was based on a clinical examination and thyroid function tests, including blood TSH, T4, and T3. The thyroid status of these women was used to sub classify them: patients with overt hypothyroidism were those who had TSH levels above 10 μ IU/ml and T4 levels below the lower reference level of 60 nmol/ml, together with other symptoms and indicators of hypothyroidism (Chakera J. A. et al., 2011). To be able to distinguish between hypothyroidism patients with Hashimoto's disease, serum anti-thyroid peroxidase (anti-TPO) was used (Jantikar M. A. 2020). and hence, women with hypothyroidism were divided into those with positive and negative anti-TPO. 37 of the participating women were classified to Group 2 and were considered the control group because they

appeared to be in good health. Women in the age range of 20 to 40 years who had been diagnosed with overt or subclinical hypothyroidism were eligible. Women with a history of endometriosis, hyperprolactinemia, PCOS, pregnancy, hysterectomy or any other ovarian surgery, as well as those taking oral contraceptives, diabetic disorders, liver diseases, renal diseases, and smoking were excluded from consideration. Each of the included hypothyroidism women and the control group had five milliliters of peripheral venous blood drawn, allowed to clot for fifteen minutes, and then centrifuged for ten minutes at 2500 rpm to extract serum for T3, T4, and TSH measurements by Minividas. Inhibin B, FSH, and LH with cobase e411. anti-TPO and ELISA method. The following formula was used to assess and compute body mass index (BMI):

Weight (kg) / height (m²) = BMI (kg/m²).

Statistical analysis

Frequency, percentage, mean, and standard deviation were utilized to describe the data in all variables, an ANOVA is utilized to assess how the mean level of the numerical data differs. The correlation between numerical data was assessed using Pearson correlation regression coefficient (r). A significant threshold of $p < 0.05$ was selected. Statistical analyses using SPSS version 25.0 software. When comparing more than two.

Results

The demographic statistics, including the age and BMI of the patients and controls, are shown in Table 1. Patients and controls ranged in age from (20 to 40) years, with no significant difference in the mean (\pm SD) age of the patient group compared to the control group (p -value 0.08). However, the mean BMIs of the patients were statistically significantly different from the controls (p -value 0.006).

Table 1: Mean (\pm SD) values of age, BMI of patients and controls

Parameter	Hypothyroidism Patients mean (n=51)	Hypothyroidism Patients Std. Deviation (n=51)	Controls Mean (n=37)	Controls Std. Deviation (n=37)	p-value
Age (year)	31.75	6.28	29.41	6.20	0.08
BMI (kg/m ²)	26.27	5.01	23.05	5.55	0.006

According to Table 2, there were no appreciable variations in the measured parameters (inhibin B, FSH, and LH) between the female patients based on their thyroid status (clinical or sub-clinical hypothyroidism) (p-value 0.31, 0.27, 0.08 respectively).

Table 2: Mean (\pm SD) values of serum Inhibin B, FSH, and LH of clinical and subclinical hypothyroidism patients' group

Parameter	Clinical Hypothyroidism means (n=42)	Clinical Hypothyroidism Std. Deviation (n=42)	Subclinical hypothyroidism mean (n=9)	Subclinical hypothyroidism Std. Deviation (n=9)	P - value
Inhibin B (pg/ml)	46.2	11.88	41.78	11.5	0.31
FSH (mIU/ml)	9.162	5.43	7.09	3.343	0.27
LH (mIU/ml)	12.993	13.68	4.86	1.85	0.08

Table 3 shows the difference in mean values of studied parameters (Inhibin B, FSH and LH) in patients' group according to regularity of menstrual cycle (regular vs. irregular), with significant decrease in mean value of Inhibin B in irregular menstruated patients when compared to regular ones (P -value 0.038). There was no significant difference in mean values of other measured parameters.

Table 3: Mean (\pm SD) values of serum inhibin B, FSH, LH of hypothyroidism patients' group with regular and irregular menstrual cycle

Parameter	Regular cycle means (n=27)	Regular cycle Std. Deviation (n=27)	Irregular cycle means (n=24)	Irregular cycle Std. Deviation (n=24)	P - value
Inhibin B (pg/ml)	48.63	12.23	41.8	10.42	0.038
FSH (mIU/ml)	8.50	5.12	9.13	5.41	0.67
LH (mIU/ml)	11.4	14.3	11.74	11.19	0.92

Table 4 shows that there was no significant difference in the mean values of (inhibin B, FSH, and LH) between hypothyroidism women who had positive anti-TPO results and those who had negative anti-TPO results (P -value 0.30,0.34,0.82) respectively.

Table 4: Mean (\pm SD) values of serum inhibin B, FSH, LH of hypothyroidism patients' group with positive and negative anti-TPO

Parameter	Anti-TPO) positive)mean (n=22)	Anti-TPO) positive)Std. Deviation (n=22)	Anti-TPO (negative) mean (n=28)	Anti-TPO (negative) Std. Deviation (n=28)	P -value
Inhibin B (pg/ml)	43.50	10.32	47.04	13.02	0.30
FSH (mIU/ml)	9.50	6.31	8.09	4.07	0.34
LH (mIU/ml)	11.10	14.90	11.92	11.41	0.82

Figure 1 shows a strong inverse relationship ($r = -0.34$, P -value 0.02) between BMI and inhibitor B, which is regarded as a weak correlation.

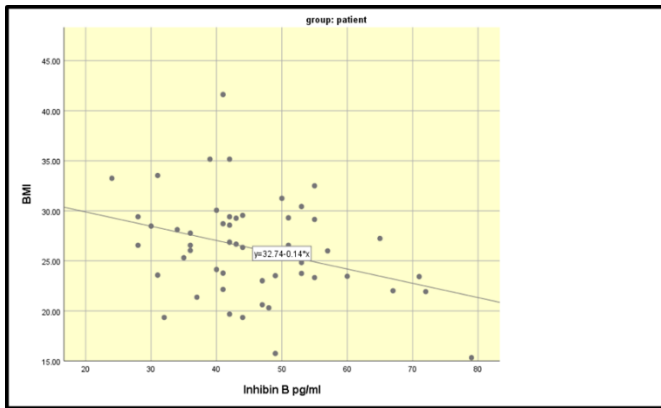


Figure 1: scattered dot diagram of correlation between Inhibin B and BMI

Discussion

The results of the investigation indicated that the mean (\pm SD) age values of the hypothyroidism patients and controls did not differ statistically significantly (table 1). According to Vedantham H. et al. Consistent with our findings, there was no noteworthy correlation seen between the age of women and thyroid impairment (Vedantham H. et al., 2020). That was chosen as part of the study design to reduce the impact of age on the outcomes. In addition, the research defines the age range of the patient women as between twenty and forty years old to avoid a physiological decline in serum inhibin B and a discernible rise in LH and FSH with aging. The study's findings indicate a significant distinction in the mean (\pm SD) BMI values between the sick women and the control group (table 1). This result was consistent with that published by Popławska-Kita A. et al. (2014), who discovered that patients with hypothyroidism had BMIs that were noticeably greater than those of healthy people. These authors came to the conclusion that patients with hypothyroidism receiving L-thyroxine for less than two years tended to have higher BMIs. The average (\pm SD) BMI of the hypothyroid women in this study was 26.27 kg/m², which was lower than the other group's BMI of 27.2 kg/m². The BMI category of the study's hypothyroidism-afflicted female participants shows an overweight class, which may be related to a recent diagnosis and inadequate thyroid gland function control, which results in a low basal metabolic rate. When there's a rise in inhibin B in the blood, the pituitary gland experiences a direct negative feedback loop that lowers the FSH.

Therefore, the higher level of inhibin B in women of reproductive age is one of the most important factors in maintaining a low level of serum FSH. One of the key causes of their serum FSH levels gradually rising is the weakening of the inhibitory impact on FSH (Wen J., et al 2021). Investigation Inhibin B was negatively correlated with both FSH ($R = -0.41$, $P < 0.001$) and LH ($R = -0.20$, $P < 0.001$). Which contradict our findings and show that there were no appreciable variations in the measured parameters (inhibin B, FSH, and LH) between the female patients based on the clinical and sub-clinical state of their thyroid.

(H. Vedantham et al., 2020) reported to be primarily caused by hypothyroidism's disruptive metab(Vedantham H., et al., 2020) reported to be primarily caused by hypothyroidism's disruptive metabolism. Hypothyroidism, or a smaller thyroid, is known to slow down metabolism, which makes patients heavier. According to N. Viceconti et al. (2003), inhibin B levels in postmenopausal women who were hyper- and hypothyroid stayed mostly at premenopausal levels. Thus far, there seems to be a considerable increase in serum inhibin B in both hypothyroid and hyperthyroid patients. FSH levels at reproductive age were unaffected by altered thyroid function. which support our research As per Table 3, which displays the variations in the mean (\pm SD) values of FSH, LH, and inhibin B in the patient group based on their regular and irregular cycles. When there was a significant statistical difference ($p=0.038$) between patients with regular cycles and those with irregular cycles, inhibin B levels were greater in the former group. However, there is no statistically significant difference in FSH and LH levels between patients with regular and irregular cycles (0.67 and 0.92, respectively).

The anti-TPO results, whether positive or negative, do not affect inhibin B, FSH, or LH, as seen in Table 4, which is consistent with prior research Osuka S. et al. state that there is no relationship between ovarian reserve negativity and anti-TPO positivity. In particular, according to Osuka S. et al. (2018), patients with hypothyroidism and anti-TPO positive did not have inferior ovarian reserves to those with isolated subclinical hypothyroidism. And contradicts another study: according to Magri F. et al. (2015), women with autoimmune thyroid illnesses typically responded poorly to managed ovarian

hyperstimulation. Figure 1 illustrates what is thought to be a weak association—a significant negative correlation ($r = -0.34$, $p = 0.02$) between BMI and inhibin B. According to Marsh E. E. et al., some research have found no correlation between BMI and inhibin B, while other investigations have found that there is an inverse relationship between the two. E. E. Marsh et al. (2016).

Conclusion

This study indicated that, regardless of the cause or state of thyroid function, women with established hypothyroidism should have their serum levels of Inhibin B measured.

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