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Original article

Correlation between Serum Prolactin Level and TSH Level in Newly Diagnosed Egyptian People with Subclinical Hypothyroidism

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Abstract:

Background: Hyperprolactinemia is present in a wide range of subclinical hypothyroidism (SCH) patients, from 0% to 40%. We aimed to find out the prevalence of hyperprolactinemia in newly diagnosed SCH subjects. Also, to estimate and correlate serum prolactin (PRL) levels in subjects with SCH. **Methods:** Three hundred participants, 200 SCH subjects, and 100 normal subjects aged 18 to 45 were classified into 3 groups according to TSH levels and compared. Group A includes: 100 subjects with TSH levels (4.5 to 7.49 uIU/L). Group B includes: 100 subjects with TSH levels (7.5 to 10 uIU/L). Group C includes: 100 subjects with normal TSH levels. Detailed clinical history was taken. Also, serum PRL, anti-thyroid peroxidase (anti-TPO), and anti-thyroglobulin (anti-TG) levels- were obtained. **Results:** The prevalence of hyperprolactinemia in SCH subjects was 22.5%. Hashimoto's thyroiditis represents 40% of SCH cases. There was a significant positive correlation between PRL level and the TSH (r=0.350), Anti-TPO (r=0.374), anti-TG (r=0.374), and BMI (r=0.381). Multivariate analysis demonstrates an increase in TSH level by one unit increases the risk of hyperprolactinemia by 1.79 times, the presence of Hashimoto's thyroiditis increases risk by 5.48, and an increase in BMI by one kg/m² increases risk by 1.38 times. TSH ≥7.22 uIU/L was the best-detected cut-off point, with 77.8% sensitivity and 52.9% specificity in detecting hyperprolactinemia. **Conclusion:** Hyperprolactinemia is prevalent in newly diagnosed SCH subjects. Thus, routine PRL estimation and consequent treatment are needed.

Keywords: Hyperprolactinemia; PRL; SCH; TSH.

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Introduction:

Hyperprolactinemia, a common endocrine disease of the hypothalamic-pituitary axis (HPA), occurs due to several causes such as drugs, hypothyroidism, and pituitary diseases. PRL production is suppressed by PRL inhibitor factor released from the hypothalamus, improved by dopamine antagonist and thyroid-releasing hormone (TRH) [(1)].

SCH refers to increased serum TSH levels with normal FT4 and FT3 values, accompanied by minimal or no manifestations of hypothyroidism. Its prevalence ranges from 3% to 15% [(2)]. A study by Vanderpump et al. [(3)] revealed that 4.3% of individuals with SCH develop clinically overt hypothyroidism in the presence of TPO antibodies (ABs), compared to 2.6% without these ABs. Notably, the incidence of SCH is higher in women and tends to increase with age.

Hyperprolactinemia and hypothyroidism are demonstrated to be closely interrelated. It has been found to be present in a wide range of SCH patients, from 0% to 40% [(4)]. TRH stimulates PRL and TSH release, as a result causing increased PRL values [(5)]. The higher prevalence of hyperprolactinemia in hypothyroidism is demonstrated in females than males as estrogen is needed for this action [(6)].

Low thyroid hormone (TH) level is accompanied by raised PRL levels. Both of them are involved in ovulatory dysfunction that can lead to infertility. Infertility accompanied by hyperprolactinemia is transient with treatment. Lowering serum PRL levels is crucial for good ovulation, and studies have shown that hyperprolactinemia accompanied by SCH reverses on thyroxine supplementation. So, the evaluation of serum PRL and TSH levels is essential for the assessment of the cause of infertility [(7)].

The current knowledge regarding the actual effects of hypothyroidism and accompanying hyperprolactinemia on fertility is based mainly on retrospective research. In addition, there are a limited number of studies that discussed hyperprolactinemia in SCH. In addition, these studies displayed inconsistent outcomes. As a result, the aim of this study is to detect the prevalence of hyperprolactinemia in recently diagnosed SCH cases. Also, to measure and correlate serum prolactin (PRL) values among individuals with SCH.

Patients and methods:

Patients:

This controlled cross-sectional study included 300 subjects, 200 subjects with SCH, and 100 normal subjects, aged 18 to 45 years who were recruited from the endocrinology outpatient clinic at Mansoura Specialized Medical Hospital, Mansoura University, Egypt over a period from June 2023 to June 2024. This study started after approval of the "Research Ethics Committee" of the Faculty of Medicine, Mansoura University (Code number R.20.07.961).

Inclusion Criteria:

1) Subjects between 18 and 45 years of age.
2) Subjects with normal TSH levels and levels between 4.5 to 10 mIU/L with normal free T3 and free T4 levels.

The following patients were excluded:

1) Pregnant and breastfeeding females.
2) Subjects after thyroid surgeries, irradiation, and supra-sellar surgeries.
3) Subjects with diabetes, heart failure, renal dysfunction, and post-myocardial infarction.
4) Subjects with prolactinoma, acromegaly, and pituitary disorders.
5) Subjects excluded if taking the following:
   - Antidepressants drugs.
   - Thyroid medications.
   - Oral Contraceptive Pills (OCP).

The studied cases were classified into three groups according to TSH levels and compared:

- **Group A:** included 100 Subjects with TSH levels between 4.5 to 7.49 uIU/L with normal FT3 and FT4 values.
- **Group B:** included 100 Subjects with TSH levels between 7.5 to 10 uIU/L with normal FT3 and FT4 values.
- **Group C:** included 100 Subjects with normal TSH, FT3 and FT4 values.

Methods:

All individuals were subjected to medical history with a special focus on menstrual irregularities, infertility, constipation, hair loss, puffiness around the eye, pedal edema, alopecia, fatigue & laziness; anthropometric measurements (weight, height, and BMI); and complete clinical examination.

Sampling:

After overnight fasting (8 h), 5 ml blood samples were withdrawn from all subjects through an appropriate venipuncture approach under aseptic conditions. Measurement of serum levels of TSH, FT3, FT4, PRL, anti-TPO, and anti-TG- was done by the Cobas E 411 analyzer (Germany) and the electrochemiluminescence technology approach.

Statistical analysis:

Data analysis was conducted by SPSS software, version 26 (PASW, Chicago: SPSS Inc.). Numbers and percentages were used to describe the qualitative data. Following a normality test using the Kolmogorov-Smirnov test, quantitative data were presented using the median regarding non-normally distributed data and mean ±SD for regularly distributed data. P-value of (0.05) level was used to assess the results' significance. When necessary, qualitative data was compared between groups using the chi-square test. Regarding non-normally distributed data, the Kruskal Wallis test was used to compare more than two examined groups, and the Mann Whitney U test- was used to compare two researched groups. For properly distributed data, two independent groups were compared using the student t-test. More than two independent groups were compared using the One-Way ANOVA test, and pairwise comparisons were detected using the Tukey test. Spearman's correlation was utilized to detect the strength and direction of a linear relationship between two non-normally distributed continuous variables. The ROC curve was utilized to calculate the validity of continuous variables with the calculation of the best cutoff point. Binary logistic regression was used to assess the effect of the combination of more than 2 independent variables on dichotomous outcomes using the Enter approach.

Results:

Demographic, clinical, and laboratory findings of the studied groups.

The present study was a controlled cross-sectional study that was conducted on 300 participants, 200 subclinical hypothyroid subjects, and 100 normal subjects and illustrates no significant difference between studied groups regarding age and sex of studied cases (p=0.905 and 0.075, respectively). The mean age of studied groups is 30.51±6.74, 30.26±6.21 and 30.68±7.12 years for groups A, B & C, respectively.

A significant higher mean TSH was detected among group B, followed by group A, and the lowest for group C, and. Lower mean free T3, T4 was detected for group B, followed by group A, and the highest for group C. Higher mean PRL was detected among group B, followed by group A, and the least for group C.

Incidence of hyperprolactinemia distributed as follows: 30% of cases in Group B, 15% in group A, and no cases were detected in Group C, as shown in **Figure (1)**. Among 200 cases with subclinical hypothyroidism, 80 cases (40%) have Hashimoto’s thyroiditis and are distributed as follows: 45 cases in group B (45%) and 35 cases in group A (35%). Also, a significant difference was detected between studied groups regarding the following parameters: positive anti-TPO, positive anti-TG, BMI, menstrual irregularities, infertility, hair loss, bowel

disturbance, puffiness around the eye, pedal edema, alopecia, fatigue & laziness as shown in **Table (1).**

Risk factors related to hyperprolactinemia among cases with subclinical hypothyroidism:

Among 200 cases with subclinical hypothyroidism, 45 cases (22.5%) have hyperprolactinemia, as shown in **Figure (2).** Among risk factors associated with hyperprolactinemia are higher mean TSH, lower free T4, presence of Hashimoto's thyroiditis, higher mean BMI, menstrual irregularities, infertility, hair loss, bowel disturbance, puffiness around the eye, pedal edema, alopecia, fatigue & laziness as shown in **Table (2).**

Table (1): Comparison of demographic, clinical, and laboratory findings among studied groups.

Variables	Group A (N=100)	Group B (N=100)	Group C (N=100)	Test of significance
Age/ years	30.51±6.74	30.26±6.21	30.68±7.12	F=0.099 P=0.905
Sex				
Male	10(10)	11(11)	20(20)	χ^2=5.14
Female	90(90)	89(89)	80(80)	P=0.076
TSH	5.84±0.87^{ab}	8.80±0.75^{ac}	2.07±1.04^{bc}	F=1412.47 P=0.001*
FreeT4	1.23±0.14^{a}	1.09±0.12^{ab}	1.27±0.17^{b}	F=39.92 P=0.001*
FreeT3	1.20±0.12^{ab}	1.14±0.12^{ac}	1.25±0.15^{bc}	F=18.41 P=0.001*
Prolactin	16.30±6.90^{ab}	20.09±8.71^{ac}	12.88±4.0^{bc}	F=27.95 P=0.001*
High prolactin	15(15.0)^{ab}	30(30.0)^{ac}	0^{bc}	χ^2=35.29 P<0.001*
Positive Anti-TPO	35(35)^{a}	45(45) ^{b}	15(15)^{ab}	χ^2=21.57 P<0.001*
ANTI-TPO	27.25(6-1300) ^{a}	31.5(5-1300) ^{b}	18(5-1300) ^{ab}	Kw=9.88 P=0.001*
Anti -thyroglobulin	17.5(5-630)^{a}	30.5(5-500)^{b}	11.35(5-334)^{ab}	Kw=12.33 P=0.001*
Positive anti -thyroglobulin	35(35)^{a}	45(45)^{b}	15(15)^{ab}	χ^2=21.57 P<0.001*
BMI	31.82±3.06^{ab}	33.07±3.58^{ac}	28.74±4.14^{bc}	F=37.91 P=0.001*
Menstrual irregularities	27(27)^{ab}	53(53)^{ac}	0^{bc}	χ^2=71.83 P<0.001*
Infertility	19(19)^{ab}	34(34)^{ac}	0^{bc}	χ^2=39.92 P<0.001*
Hair loss	39(39)^{a}	50(50)^{b}	14(14)^{ab}	χ^2=30.19 P<0.001*
Bowel disturbance	28(28)^{a}	34(34)^{b}	0^{ab}	χ^2=40.17 P<0.001*
Puffiness around eye	0^{a}	29(29)^{ab}	0^{b}	χ^2=64.21 P<0.001*
Pedal oedema	0^{a}	20(20)^{ab}	0^{b}	χ^2=42.86 P<0.001*
Alopecia	0^{a}	13(13)^{ab}	0^{b}	χ^2=27.18 P<0.001*
Fatigue & laziness	29(29)^{ab}	47(47)^{ac}	0^{bc}	χ^2=59.46 P<0.001*

^{abc} Similar superscripted letters denote a significant difference between groups within the same row

*Statistically significant difference, χ^2=Chi-Square test, KW: Kruskal Wallis test, F: One Way ANOVA test

data expressed as median (min-max), mean ±SD or number (percentage)

Group A: 100 Subjects with TSH levels between 4.5 to 7.49 uIU/L with normal FT3 and FT4 levels. **Group B:** 100 Subjects with TSH levels between 7.5 to 10 uIU/L with normal FT3 and FT4 levels. **Group C:** 100 Subjects with normal TSH, FT3 and FT4 levels.

Table (2): Risk factors related to hyperprolactinemia among cases with subclinical hypothyroidism.

	Hyperprolactinemia among cases with subclinical hypothyroidism		Test of significance
	-ve N=155(77.5%)	**+ve N=45(22.5%)**	
Age/ years	30.52±6.63	29.91±5.91	t=0.558 p=0.578
Sex			
Male	16(10.3)	5(11.1)	χ^2=0.023
Female	139(89.7)	40(88.9)	P=0.879
TSH	7.01±1.61	8.38±1.56	t=5.04 p<0.001*
FreeT4	1.18±0.15	1.10±0.13	t=2.69 p=0.008*
FreeT3	1.18±0.12	1.14±0.11	t=1.87 p=0.063
Positive Anti-TPO	48(31)	32(71.1)	χ^2=23.42 P=0.001*
ANTI-TPO	22(5-1300)	222(23-1300)	Z=6.08 P=0.001*
Anti -thyroglobulin	13(5-630)	125(11-500)	Z=5.62 P=0.001*
Positive anti -thyroglobulin	48(31)	32(71.1)	χ^2=23.42 P=0.001*
BMI	31.67±3.02	35.12±3.23	t=6.64 p=0.001*
Menstrual irregularities	40(25.8)	40(88.9)	χ^2=57.8 P=0.001*
Infertility	8(5.2)	45(100)	χ^2=161.05 P=0.001*
Hair loss	49(31.6)	40(88.9)	χ^2=46.32 P=0.001*
Bowel disturbance	27(17.4)	35(77.8)	χ^2=59.39 P=0.001*
Puffiness around eye	9(5.8)	20(44.4)	χ^2=41.99 P=0.001*
Pedal oedema	4(2.6)	16(35.6)	χ^2=42.14 P=0.001*
Alopecia	0	13(28.9)	χ^2=47.89 P=0.001*
fatigue & laziness	35(22.6)	41(91.1)	χ^2=69.52 P=0.001*

*Statistically significant difference, χ^2=Chi-Square test, t: Student t test, z: Mann Whitney U test
data expressed as median (min-max), mean ±SD, or number (percentage)

Predictors of hyperprolactinemia among cases with subclinical hypothyroidism:

Multivariate analysis done to assess Predictors of hyperprolactinemia among cases with SCH and demonstrates that an increase in TSH level by one unit increases the risk of hyperprolactinemia by 1.79 more times, the presence of Hashimoto's thyroiditis increases risk by 5.48, increase BMI by one kg/m2 increases risk by 1.38 more times also cases in group B have increased risk of hyperprolactinemia by 2.42 as shown in **Table (3).**

ROC curve and validity of thyroid profile in differentiating cases with

hyperprolactinemia among cases with subclinical hypothyroidism:

The Receiver Operating curve (ROC) assesses the validity of thyroid profile in differentiating cases with hyperprolactinemia among cases with SCH, demonstrating that the area under the curve was fair to good with the highest sensitivity and specificity detected for Anti-TPO and anti-TG followed by TSH, Free T4, and T3 as shown in **Figure (3)** and **Figure (4).** The best detected cut-off points from the curve were as follows: ≥7.22 for TSH, ≥25.5 for anti-TG, ≥29.5 for Anti-TPO, ≤1.20 for free T4 and ≤1.155 for free T3 as shown in **Table (4).**

Correlation between prolactin and laboratory findings among cases with subclinical hypothyroidism:

A significant positive relationship was detected between prolactin levels and the following: TSH (r=0.350), ANTI-TPO (r=0.374), anti-TG (r=0.374), and BMI (r=0.381), while a significant negative relationship was detected between prolactin level and Free T4 (r=-0.24) as shown in **Table (5).**

Linear regression for predictors of prolactin among cases with hypothyroidism:

Linear regression done to assess predictors of PRL level among studied cases and demonstrates that TSH, anti-TG, and BMI are statistically significant predictors of change in level of prolactin with the following prediction equation: Prolactin level =-14.30+0.950*TSH +0.014* Anti thyroglobulin+0.730*BMI with 25.2% of prolactin level- could predicted by the previous three detected predictors as shown in **Table (6).**

Table (3): Predictors of hyperprolactinemia among cases with subclinical hypothyroidism

	β	P value	Odds ratio (95%CI)
TSH	0.582	0.001*	1.79(1.32-2.42)
FreeT4	0.522	0.733	1.69(0.084-33.91)
Hashimoto's	1.70	<0.001*	5.48(2.65-11.37)
BMI	0.321	0.001*	1.38(1.23-1.55)
Group			
A (R)	0.887	0.012*	R
B			2.42(1.21-4.87)
Overall % predicted =77.5%			

β: regression coefficient, CI: Confidence interval, R: reference group

Table (4); Validity of thyroid profile in differentiating cases with hyperprolactinemia among cases with subclinical hypothyroidism:

	AUC (95%CI)	**P value**	**Cut off point**	**Sensitivity**	**Specificity**
TSH	0.745 (0.660-0.830)	0.001*	≥7.22	77.8%	52.9%
Anti-thyroglobulin	0.775 (0.711-0.839)	0.001*	≥25.5	86.7%	62.6%
Anti-TPO	0.797 (0.738-0.857)	0.001*	≥29.5	93.3%	62.6%
Free T4	0.624 (0.535-0.714)	0.01*	≤1.20	71.1%	41.3%
Free T3	0.588 (0.496-0.680)	0.073	≤1.155	62.2%	53.5%

AUC: Area under curve

Table (5): Relationship between prolactin and laboratory findings among cases with subclinical hypothyroidism

		Prolactin level
Age	*r*	.017
	P	.806
TSH	*r*	**.350**
	P	**.001***
Free T4	*r*	**-.240**
	P	**.001***
Free T3	*r*	-.096
	P	.174
ANTI-TPO	*r*	**.374**
	P	**.001***
Anti -thyroglobulin	*r*	**.374**
	P	**.001***
BMI	*r*	**.381**
	P	**.001***

r: Spearman correlation coefficient, *statistically significant

Table (6): linear regression for predictors of prolactin among cases with hypothyroidism

Model	**Unstandardized Coefficients**		**t**	**P value**	**95.0% Confidence Interval for β**	
	β	**Std. Error**			**Lower Bound**	**Upper Bound**
(Constant)	-14.309	8.409	-1.702	.090	-30.895	2.276
TSH	.950	.385	2.468	.014*	.191	1.709
Free T4	.714	4.091	.175	.862	-7.355	8.783
ANTI.TPO	-.001	.002	-.463	.644	-.005	.003
Anti thyroglobulin	.014	.006	2.251	.025*	.002	.026
BMI	.730	.171	4.263	.001*	.392	1.067
Prediction equation	Prolactin level =-14.30+0.950*TSH +0.014* Anti thyroglobulin+0.730*BMI					
R^2	**0.252**					

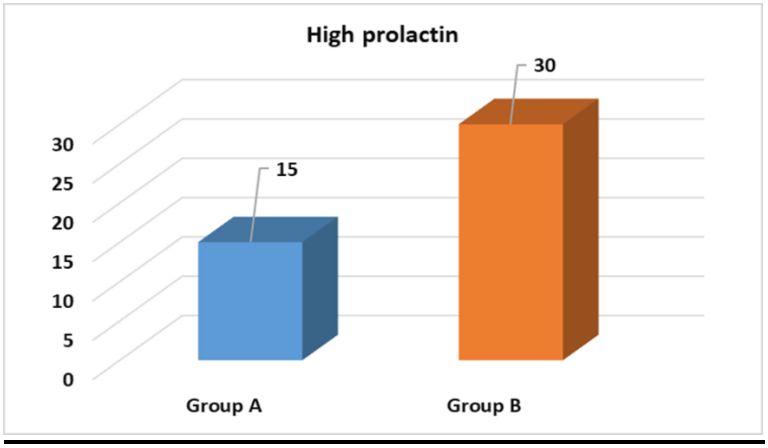

Figure (1): Incidence of hyperprolactinemia among studied groups.

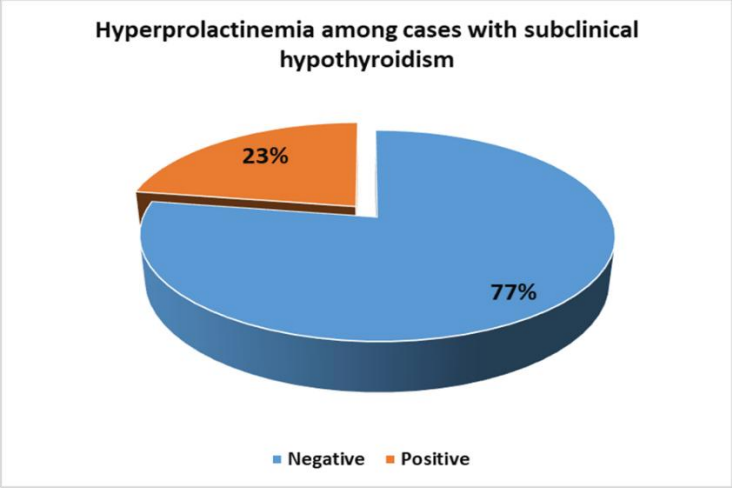

Figure (2): Prevalence of hyperprolactinemia among cases with subclinical hypothyroidism.

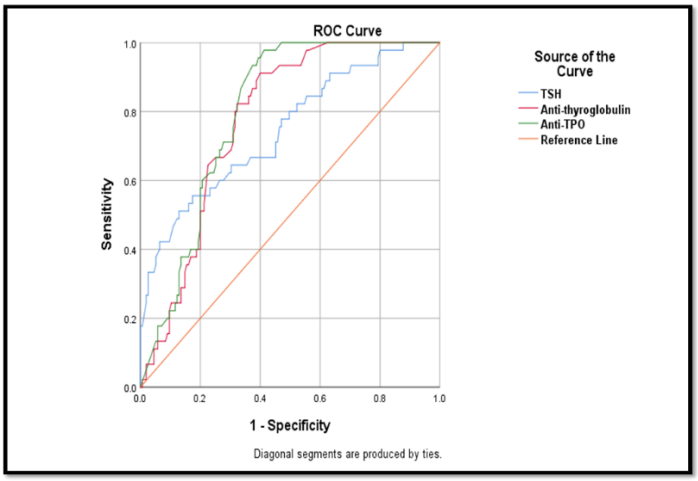

Figure (3): ROC curve of TSH, anti-thyroglobulin, and anti-TPO in differentiating cases with hyperprolactinemia among cases with subclinical hypothyroidism.

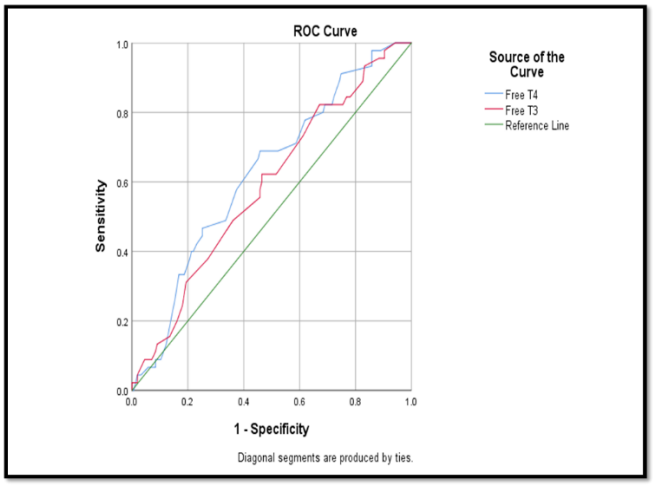

Figure (4): ROC curve of free T3, T4 in differentiating cases with hyperprolactinemia among cases with subclinical hypothyroidism.

Discussion:

Hyperprolactinemia and hypothyroidism seemed to be closely interrelated. Hyperprolactinemia is of variable magnitude and recorded in both overt and SCH. It has been demonstrated that its prevalence among females with overt hypothyroidism represents 39% to 57% [8], while it has been found to be present in a wide range of SCH patients, from 0% to 40% [4]. Research on SCH is limited and has different results.

SCH is a common endocrine disease characterized by increased serum TSH value but normal FT4 and FT3 levels. In the adults, SCH prevalence rose with age, reaching between 4 and 10% [9].

This current study showed that the prevalence of hyperprolactinemia in recently diagnosed SCH subjects was 22.5%. Among 200 cases with SCH (179 females and 21 males), 45 cases (22.5%) have hyperprolactinemia. The incidence of hyperprolactinemia was distributed as follows: 30% of cases in group B (30 cases), 15% of cases in group A (15 cases), and no cases were detected among group C.

Several studies showed similar results; Meir et al. [10] documented in a trial on 66 subjects with SCH that the prevalence of hyperprolactinemia was 19%. In addition, Hekimsoy et al. [11] reported in their study that the prevalence of hyperprolactinemia in overt and SCH was 23.3%.

Bahar et al. [12] displayed that the prevalence of hyperprolactinemia in males and females with SCH was 11% and 22%, correspondingly. Ninety-eight of 383 subjects (25.5%) had hyperprolactinemia (91 females and seven males). Also, Sirohi and Singh [13] reported that, of 150 subjects with SCH, 90% being females and 10% being male, with a mean of age 31.82 ± 6.18 years, the prevalence of hyperprolactinemia was 18% (27 subjects).

In the current study, a significant positive relationship was between PRL level and the following: TSH (r=0.350), Anti-TPO (r=0.374), anti-TG (r=0.374), and BMI (r=0.381). While, a significant negative relationship found between prolactin level and Free T4 (r=-0.24). This came in the same line with Hekimsoy et al. [11] and Sirohi and Singh [13] who demonstrated the same results.

In comparison, group B subjects with TSH levels in a greater range (7.5–10 uIU/L) were accompanied by a significant increase in the prevalence of hyperprolactinemia (30%) than group A subjects with TSH levels (4.5–7.49 uIU/L), who had a prevalence of 15%. That is because greater TRH values in subjects with more severe hypothyroidism (increased TSH values) lead to a higher TRH-mediated PRL production from lactotrophs [14]. Also, Shenenberger and Klachko [15] displayed that PRL secretion stimulated by TRH, epidermal growth factor, and dopamine receptor antagonists, wherein they reported that primary hypothyroidism with increased TRH values could be accompanied by hyperprolactinemia.

In the present study, 95 subjects (31.6%) of the 300 participants had positive anti-TPO antibodies. Hashimoto's thyroiditis represents 40% of SCH cases.

The current study was in agreement with Shrestha et al. [16] who recorded significant anti-TPO titers in 26.7% of subjects. Similarly, Somwaru et al. [17] displayed that the prevalence of positive anti-TPO ABs among SCH cases was 35% of participants. Also, Sharma et al. [18] recorded an elevation in the prevalence of anti-TPO ABs (58.3%) among SCH cases.

In a comparison of clinical symptoms among SCH subjects with normal PRL levels, we found that common clinical symptoms were hair loss (31.6%), menstrual irregularities (25.8%), fatigue & laziness (22.6%), bowel disturbance (17.4%), while among SCH subjects with hyperprolactinemia, the common clinical symptoms were, infertility (100%), fatigue & laziness (91.1%), menstrual irregularities (88.9%), hair loss (88.9%), bowel disturbance (77.8%), puffiness

around the eye (44.4%), pedal edema (35.6%), alopecia (28.9%).

Likewise, Raber et al. [4] displayed that menstrual disorders were detected in twenty six percent of subjects with hyperprolactinemia. Similarly, in Bahar et al. [12] 45.2% of the studied subjects had menstrual disorders, 23.5% in subjects with hyperprolactinemia, and 21.8% in subjects with normal PRL levels. Also, in Sirohi and Singh [13], the most frequent complaints in the studied subjects were menstrual abnormalities (16.7%) and infertility (16.7%).

A similar association between hyperprolactinemia and menstrual disorders in the background of SCH was noticed in another study performed by Binita et al. [19] as a result clarifying the causal role of hyperprolactinemia in infertility. A comparable record by Turankar et al. [20] noticed an increase in PRL values among infertile females compared to fertile ones.

On the contrary, in a study done by Meier et al. [10] conducted on 66 females with SCH, no cases of menstrual disorders and galactorrhea were reported.

Ovulatory dysfunction happens in hypothyroidism since TH has a direct effect on the granulosa cells and oocytes. In addition, hypothyroidism has been demonstrated to be accompanied by a drop in binding activities of sex hormone-binding globulin, elevated PRL values, and a delay in luteinizing hormone responses to gonadotropin-releasing hormone [21].

Similarly, Carlé et al. [22] in their study, recorded easy fatigability and alopecia in 81% and 4.15% of hypothyroid subjects, correspondingly. Also, Sirohi and Singh [13] showed similar findings in their study.

Among SCH subjects with hyperprolactinemia, alopecia was significantly higher (28.9%). Similarly, Hekimsoy et al. [11] and Sirohi and Singh [13] demonstrated the same results in their studies. Also, in the Bahar et al. [12] study, alopecia was significantly increased in females with hyperprolactinemia (14.4%) than in men (1.6%). Hypothyroidism and associated hyperprolactinemia have efficient roles in stimulating hair loss, as hyperprolactinemia triggers androgen formation from the adrenal gland, and the thyroxin hormone affects the free, total testosterone, and thyroid-binding globulin. As a result, the coexistence of both diseases could cause extensive loss of hair.

Multivariate analysis was done to assess Predictors of hyperprolactinemia among cases with SCH and demonstrates that an increase in TSH level by one-fold increases the risk of hyperprolactinemia by 1.79 times, the presence of Hashimoto's thyroiditis increases the risk by 5.48, and an increase in BMI by one kg/m2 increases the risk by 1.38 times. Also, cases in group B have increased the risk of hyperprolactinemia by 2.42.

The ROC was used to assess the validity of thyroid profile in differentiating cases with hyperprolactinemia among cases with SCH and demonstrates that the best-detected cutoff points from the curve with the highest sensitivity and specificity were as follows: ≥7.22 for TSH, ≥25.5 for anti-thyroglobulin, ≥29.5 for Anti-TPO, ≤1.20 for free T4 and ≤1.155 for free T3

In agreement with the current study, Sharma et al. [23] recorded that hyperprolactinemia and SCH coexist frequently and that when identifying hyperprolactinemia, a TSH result above eight mIU/L has a good specificity of almost 90%. They thought that much research was required to rule out confidence in the significant relationship between hyperprolactinemia and SCH.

Limitations of the work:

Several limitations should be acknowledged. First, the sample size of 300 participants could restrict the study power. Second, the single-center setting introduces selection bias and undermines the generalizability of the study. Third, since this was a cross-sectional study, the impacts of levothyroxine supplementation on PRL levels in SCH couldn't be assessed. Much research is needed to

prove or disprove the routine therapy of SCH in patients with hyperprolactinemia without increased levels of anti-TPO ABs.

Conclusion:

In the context of cases with SCH, particularly those with TSH ≥7.22 uIU/L and positive anti-TPO antibody, routine PRL measurement is required, and increased PRL levels might be one indication for treating asymptomatic SCH.

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