A Study of serum Thyroid stimulating hormone levels in patients with menorrhagia

Biochemistry

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ABSTRACT

Aims & Objectives: 1) To study the serum thyroid stimulating hormone (TSH) levels in 100 females regular menstrual cycle control group & 100 females patients with menorrhagia. 2) To compare the serum TSH levels in 100 regular menstrual cycle control group & 100 patients with menorrhagia. Materials & Methods: The present study is a cross-sectional observational study with comparison group & has been carried out in Dept. of Biochemistry, GMC, Nagpur from Feb. 2015 to Nov. 2016. A total of 100 patients with menorrhagia aged between 20 – 45 years were selected from the Obs. & Gyn. OPD of GMC, Nagpur & 100 normal healthy females of same age group 20 – 45 years were selected as controls after satisfying all inclusion & exclusion criteria, ethical committee approval & willingness to give consent. Serum TSH levels was estimated by one step non competitive immunoenzymatic sandwich ELISA assay for ERBA thyrotik TSH kit. The samples were analyzed by Robonik readwell touch Elisa plate analyzer & Robonik Washwell plate ELISA washer. Results: The results presented in the table indicates that mean TSH levels were significantly raised (>3.45 μIU/ml) in 23 patients as compared to 11 controls. Discussion: Prevalence of thyroid dysfunction was higher in females patients with menorrhagia as compared to the normal menstrual cycle females control group & we found that the commonest type of uterine bleeding pattern seen in overt & subclinical hypothyroidism cases was menorrhagia.

KEYWORDS:

TSH, ELISA.

INTRODUCTION

The reproductive period is the most important period in the life span of women which extends from menarche to menopause1. Abnormal uterine bleeding in excess amount can lead to anemia, affecting her daily routine activities & health & is a common clinical presentation. Thyroid dysfunction is one of the important etiological factor which disturbs normal hypothalamo-pituitary-ovarian (H-P-O) axis of a woman & hence affects normal menstrual cycle, reproduction & fertility2. Thus, hypothalamo-pituitary-thyroid (H-P-T) axis interacts with H-P-O axis making a direct connection between thyroid & reproductive system. As H-P-O axis regulates normal menstrual cycle any abnormality in serum thyroxin levels will affect H-P-T axis which in turn disturbs normal H-P-O axis leading to irregular menstrual cycle & abnormal bleeding from the uterus.

Wiksten A M et al3 established links between menstruation & thyroid diseases. Ely et al4 states that any irregular bleeding in nonpregnant patients with menorrhagia, TSH should be evaluated. Four types of thyroid dysfunctions are known to affect menstrual cycle, these are i) Overt hypothyroidism (Increased TSH, decreased T & T3), ii) Subclinical hypothyroidism (Increased TSH with normal T & T3), iii) Overt hyperthyroidism (Decreased TSH, increased T & T3), iv) Subclinical hyperthyroidism (Decreased TSH, normal T & T3).

There is evidence support association between hypothyroidism & menorrhagia5. According to some old studies menorrhagia & oligomenorrhea were most common in patients with hypothyroidism5. Studies done afterwards found that patients of hypothyroidism presented with menorrhagia, PolyMenorrhagia, metropathia & menometrorrhagia6. After going through all studies, it has been found that any type of menstrual abnormality should be considered as a possible presenting symptom of thyroid dysfunction & it may indicate clinical or subclinical abnormality5,6,7.

The studies conducted by Wilansky D L et al8, Blum et al9, Menon et al10 & Doifode CD et al11 gave encouraging results regarding normalization of menstrual cycle after Levo- thyroxin supplementation in overt hypothyroidism15,16,17. Hence the present study was conducted.

MATERIALS AND METHODS

The present study was carried out in GMCH, Nagpur during the period of February 2015 to November 2016. All the subjects were examined & investigated according to predesigned proforma. The study protocol was approved by the ethical committee of GMCH, Nagpur.
colour is directly proportional within the working range of the assay, to the concentration of the TSH in the sample. The concentration of the TSH in a patient's sample or controls is then determined by interpolation on the calibration curve.

Normal range of TSH in μIU/ml is 0.39-3.45 (Euthyroid) while in hypothyroidism it is >3.4 & in hyperthyroidism is <0.39.

Statistical analysis: Continuous variables (Age, BMI, TSH, T4 & T3 levels) were presented as Mean ± SD (mean ± standard deviation). Categorical variables (Type of uterine bleeding, Thyroid status) were expressed in actual number. Age, BMI, TSH, T4 & T3 levels were compared between cases & controls by unpaired t-test. Categorical variables were compared by performing chi-square test. One way ANOVA test was applied to compare Mean BMI in euthyroid, overtly hypothyroid, subclinical hypothyroid & hyperthyroid cases. p<0.05 was taken as significant (S), p<0.001 was taken as highly significant (HS) & p>0.05 was taken as non-significant (NS). Statistical software STATA version 10.0 was used for statistical analysis.

OBSERVATIONS & RESULTS

Table 1: Age wise distribution of cases & controls

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Cases (n = 100)</th>
<th>Controls (n = 100)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30</td>
<td>20</td>
<td>19</td>
<td>0.798 (NS)</td>
</tr>
<tr>
<td>31-40</td>
<td>53</td>
<td>60</td>
<td>0.153 (NS)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>27</td>
<td>21</td>
<td>0.14 (NS)</td>
</tr>
<tr>
<td>Mean age ± SD</td>
<td>34.83 ± 7.09</td>
<td>34.15 ± 5.72</td>
<td></td>
</tr>
<tr>
<td>Median (Range)</td>
<td>36 (20-45)</td>
<td>30 (21-45)</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.456 (NS)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The difference between mean age of cases & controls was found to be statistically non significant (p-value 0.4563).

Table 2: Distribution of cases in relation to uterine bleeding pattern

<table>
<thead>
<tr>
<th>Uterine bleeding pattern</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menorrhagia</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Polymenorrhagia</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Oligomenorrhagia</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Metorrhagia</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Hypomenorrhagia</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Acyclic bleeding</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

The commonest uterine bleeding pattern in all cases was menorrhagia (51%).

Table 3: Comparison of BMI status in cases & controls

<table>
<thead>
<tr>
<th>BMI (Kg/m2)</th>
<th>Cases</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5 (underweight)</td>
<td>3</td>
<td>74</td>
<td>0.786 NS</td>
</tr>
<tr>
<td>18.5-24.99 (Normal weight)</td>
<td>85</td>
<td>23</td>
<td>0.002, S</td>
</tr>
<tr>
<td>25-29.99(overweight)</td>
<td>11</td>
<td>5</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>≥ 30 (Obese)</td>
<td>1</td>
<td>3</td>
<td>0.04, S</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Mean TSH levels were highly significantly raised (>3.45 μIU/ml) in 23 cases as compared to 11 controls.

DISCUSSION

Normal ovulation requires communication between the hypothalamus, pituitary & ovary. H-P-T axis and the H-P-O axis are physiologically related and act together as a unified system in a number of pathological conditions including infertility, menstrual disturbances and recurrent miscarriages. The suggestion that specific thyroid hormone receptors at the ovarian level might regulate reproductive function, as well as the suggested influence of estrogens at the higher levels of HPT axis, seems to integrate the reciprocal relationship of these two major endocrine axes. Both hypo and hyperthyroidism interfere with HPO axis by altering steroid hormone metabolism, by acting on thyroid hormone receptors (present on oocyte, pituitary, endometrium) and TSH receptors (present on endometrium), alteration in gonadotrophin levels. Cross-talk between estrogen & thyroid receptors provides multiple and flexible opportunities for relations between two major hormonal systems important for neuroendocrine feedbacks & reproductive behaviours.

Hypothyroidism is commonly associated with ovulatory dysfunction due to numerous interactions of thyroid hormones with the female reproductive system. Both hyperprolactinemia due to increased TSH production, & altered GnRH pulsatile secretion, leads to a delay in LH response & inadequate corpus luteum formation leading to anovulation. This anovulation leads to no progesterone secretion. Unopposed estrogen allows the endometrium to proliferate & thicken. The end result is asynchronous breakdown of endometrial lining at
different level of maturation leading to different types of bleeding (i.e.; menorrhagia, oligomenorrhea & polymenorrhoea).

In the present study, mean TSH value in cases & controls were 6.88 μIU/ml & 2.49 μIU/ml respectively and this difference was found to be statistically highly significant. Mean T3 (7.37 μg/dl vs 8.76 μg/dl) values were compared between cases & controls. Mean T4 (1.03 ng/ml vs 1.12 ng/ml) levels were also compared but the difference was not significant. Based on serum values of T3, T4 & TSH, cases were classified into euthyroid, overtly hypothyroid, subclinically hypothyroid & hyperthyroid.

In our study 74% cases were having TSH levels within normal range (0.33-3.54 μIU / ml), 23% were having raised TSH levels above normal reference range & 3% were having TSH values below normal reference range. The difference were statistically significant.

Sharma Neelueet al 34 found increased TSH levels in 22% of DUB cases, while 14% were having decreased TSH levels. Percentage of TSH levels more than normal is same as seen in our study.

TSH forms important part of H-P-T axis. Any increase or decrease in TSH levels in the blood will disturb the balance between HPO & HPT axis, affecting normal ovarian & uterine cycle & will lead to abnormal uterine bleeding from uterus.

Thyroid dysfunction & uterine bleeding patterns: Thyroid dysfunction was commonest in menorrhagia (35.29%), followed by polymenorrhea (33.33%), hypomenorrhea (20%), acyclic bleeding (14.3%) & oligomenorrhea (10.5%). Our findings are in accordance with Moghal et al. 35 & Padmalalca et al. 36.

In case of hypothyroidism plasma binding activity of Steroid hormone binding globulin (SHBG) is decreased resulting in decreased plasma concentration of estradiol. Also there are decreased rates of clearance of androstenedione & estrone & further there is increase in peripheral aromatization of androstenedione. So, these increased levels of estrone along with anovulation leads to proliferation of endometrium. Asynchronised bleeding of endometrial lining at different levels of maturation leads to change in cycle length & duration & different types of bleeding i.e.; menorrhagia, (regular, prolonged duration & increased amount of bleeding), polymenorrhoea (increased frequency of bleeding) & acyclic bleeding (no discernable cyclic pattern)

Polymenorrhoea, a presumed luteal phase dysfunction, results in shortened cycles (less than 21 days), whereas oligomenorrhoea, a prolonged follicular-phase dysfunction, results in lengthened cycles (more than 38 days). Mid-cycle spotting occurs before ovulation as the estrogen levels decline 37

Menorrhagia is regularly occurring heavy menstrual bleeding (more than 80 ml per cycle) & may result from estrogen breakthrough bleeding. So, in the present study hypothyroidism seen in patients with menorrhagia & polymenorrhoea.

REFERENCES