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Short Communication

Hormonal Fluctuations of Serum Prolactin and Gonadotropins in Autoimmune Thyroid Patients

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Authors' Contribution
Khayyam and QK designed and performed the experiment. MZ and NA analysed the data. Khayyam and MZ compiled the results and wrote the article.

Key words
Hashimoto's thyroiditis, Grave's disease, Prolactin, Follicle stimulating hormone, Luteinizing hormonetome.

ABSTRACT

The present study was conducted to find the hormonal variations resulted after the autoimmune thyroid disease. Out of total eighty two autoimmune thyroid patients 50 were Hashimoto's thyroiditis patients (HT) (30 female, mean age=34±1.43 years, 20 males mean age =38.35±1.17 years) and control group included 35 individuals (20 females mean age=31.65±1.77years, 15 males mean age=37.93±2.561 years). The 32 Grave's disease (GD) patients (24 females mean age=34.96± 2.18 years, 8 males mean age=33±5.385) while control included 20 females (mean age=32.3±2.28years) and 5 males (mean age=27.33±4.83years). The prolactin in HT females and males showed significantly high values (p=0.041, 0.025 respectively) but follicle stimulating hormone was significantly low *(p=0.0007)* in female HT patients. Follicle stimulating hormone and Luteinizing hormone concentrations were higher than normal range in both male and female Grave's disease patients. Prolactin and serum gonadotropin showed fluctuations in Hashimoto's thyroiditis patients but in Grave's disease patients only the gonadotropins showed abnormal values while prolactin was in the normal range. The study suggests that autoimmune thyroid diseases effect the pituitary-hypothalamic axis which needs to be further investigated to find the mechanism underlying it.

Thyroid hormones play an important role in the metabolism, gene regulation and reproductive function (Veeresh *et al*., 2015). Thyroid stimulating hormone (TSH) and prolactin (PRL) in combination with follicle stimulating hormone (FSH) and luteinizing hormone (LH) enhance the growth of follicle cells in the ovary. Hyperprolactinemia inhibits the action and release of gonadotropins adversely affecting the ovulation process (Goswami *et al*., 2009). Borba *et al*. (2018) reported that hyperprolactinemia was found in thyroid autoimmunity especially in Hashimoto's thyroiditis (HT) condition. Hypothyroid females have disturbed ovarian cycle showing various problems like delayed puberty, menstrual irregularities, infertility and increased risk of miscarriages. This is due to the stimulatory effect of thyrotropin releasing hormone (TRH) increasing PRL and TSH secretion (Nath *et al*., 2019; Soundarrajan and Kopp, 2019). At the same time in thyroid autoimmunity, TRH inhibits gonadotropins secretions in female of reproductive age (Poppe *et al*., 2008; Acharya *et al*., 2011). Ulrich *et al*. (2018) reported that autoimmune thyroiditis is more common in females having polycystic ovarian syndrome (PCOS). Similarly, the effect of Grave's disease (GD) and HT on pituitary gonadal axis has been reported by Romitti *et al*. (2018). Although a lot of studies are there on the role of PRL in autoimmune thyroid patients but cumulative effect of PRL, and serum gonadotropins is evaluated by very few studies. So the present study was conducted in order to see the hormonal fluctuations in the serum level of PRL, FSH and LH in autoimmune thyroid patients.

Material and methods

The present case control study was carried out at the Department of Endocrinology, Institute of nuclear medicine and radiotherapy (IRNUM), Peshawar, Khyber-Pakhtunkhwa, Pakistan, from January 2017 to December 2017. The committee for Advanced Study and Research Board (ASRB) approved the study. All patients and control subjects gave the consent before participation in the study.

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Abbreviations
HD, Hashimoto's thyroiditis; GD, Grave's disease; PRL, Prolactin; FSH, Follicle stimulating hormone; LH, Luteinizing hormone

A total number of 50 HT patients (30 females and 20 male patients) and 32 GD (of 24 females and 8 males). The total control female was 20 compared with HT female group while in comparison with GD female patients 15 control females were selected. In comparison with HT males 15 control males were selected while 5 males were selected in comparison with GD male patients. All the patients and control subjects were age matched as shown in the Table I and II. Patients who were having any systemic disease, pregnancy, and breast feeding or using steroid, psychiatric drugs were excluded. Those females were selected for the study who were in follicular stage of their menstrual cycle. The diagnosis of HT and GD patients were based on the clinical findings and biochemical tests.

The healthy control subjects were selected having no history of autoimmune diseases or any other major complication. Venous blood was taken from the patients in the morning. Hormonal evaluation of total thyroxine (TT4) and TSH was done by Elisa kit (Immunotech Beckman Coulter Company, Czech Republic). ATPO (thyroid peroxidase antibodies) and Anti TSHR antibodies were measured using Elisa kits, Anti-TPO (Aesku, Germany), E lisa Anti TSHR (Diametra, Italy) respectively. Serum PRL was measured by Elisa assay (Pishtazteb diagnostics, Tehran). Similarly, serum FSH and LH were determined by Elisa kits (Pishtaz tab diagnostics-Iran). Graph pad prism version 7 was used for Statistical analysis.

Results

The present study was conducted to see the hormonal fluctuations of PRL, FSH and LH in autoimmune thyroid patients. In case of HT patients the hormonal fluctuation was more pronounced as compared to the Grave's disease. Total 82 AITD patients were selected after the biochemical confirmation. These patients included 30 HT females with mean age 34± 1.43 years and 20 control female 31.65±1.77years. While 20 male HT patients with mean age =38.35±1.17 years and 15 male as control with mean age=37.93±2.56 years. The PRL concentration in HT females is significantly higher (p = 0.0414) than control. Similarly, the serum FSH for HT female patients showed significantly lower value (0.0007) than the control. No significant difference was found in LH level between HT patients and control. The serum PRL in male HT patients was significantly higher (p=0.0252) than control individuals. Similarly in GD patients FSH and LH showed insignificant P values (0.2669) and (0.0622), respectively. All the results for HT patients are given in Table I. For GD patients 24 females (mean age =34.96± 2.18 years) and 8 males (mean age =33±5.38 years) were selected after the biochemical confirmation. While the 20 control female (mean age=32.3±2.28 years) and 5 males (mean age=27.33±4.83 years) were selected. The serum concentration for PRL in GD females and males were 473.6±129 IU/L and 233 ± 66.06 IU/L showing the values with in normal range. While the control female and male also showed values within the normal range as shown in the Table II. Similarly, the serum concentration of FSH in GD females and males were 16.41±4.99 IU/L and 15.09 ± 5.82 IU/L, respectively. The FSH for control females and males were within normal range. While the LH concentration for GD females and males were 13.82±3.46 IU/L and 12.57 ± 4.22 IU/L, respectively. Similarly, the LH for control female and males were with in normal range. All the results for GD patients are given in Table II.

Discussion

The present study was conducted to see the hormonal fluctuations of PRL, FSH and LH in autoimmune thyroid patients. In case of HT the hormonal fluctuation was more pronounced as compared to the GD. The result showed hyperprolactinemia in both male and female HT patients while FSH concentration got reduced as reported by the previous studies. Kaur *et al*. (2018) reported hypothyroidism as one of the important cause of hyperprolactinemia. Sirohi and Singh, (2018) reported hyperprolactinemia (18%) due to subclinical hypothyroidism in New Delhi, India. Similarly, the positive correlation between hyperprolactinemia and hypothyroidism was confirmed in female patients suffering from primary infertility (Goswami *et al*., 2009; Bhandari *et al*., 2019). All these results supports our findings of hyperprolactinemia in HT patients. Rrupulli *et al*. (2018) also confirmed the correlation between LH and TSH in PCOS patients suggesting the thyroid dysfunction. Veeresh *et al*. (2015) reported that hypothyroid females had increased levels of serum PRL and LH which is similar to our results. Similarly, Acharya *et al*. (2011) concluded that low serum level of FSH and LH is due to hypothyroidism in females having reproductive abnormalities. It seems that thyroid hormones affect the PRL and serum gonadotropin levels in case of hypothyroidism suggesting that this hormonal axis is disturbed by abnormal thyroid gland. In case of GD hyperprolactinemia was not reported which suggest a different neuroendocrine mechanism of the disease. Conversely increase in the serum LH was reported in both male and female GD patients. While FSH was only increased in male GD patients. It suggests that pituitary hypothalamic axis in case of GD is more effected. Similarly, Csaba and Shahin (2018) said that hypothalamic pituitary axis is affected by GD. Moreover, they added that the females suffering from the PCOS showed positive correlation between TSH and LH hormones. It means that thyroid autoimmunity affects the production of LH as shown by our results.

Table I. Hormonal profile of Hashimoto's thyroiditis patients.

	Male			Female		
	Control (n=15)	Sample (n=20)	P-value t value	Control (n=20)	Sample (n=30)	P-value t value
ATPO (IU/L)	50.07±2.59	527.7±68.13	<0.0001**** 6.06	25.07±1.99	494±58.33	<0.0001**** 6.54
TSH (µIU/L)	3.40±0.267	15.91±1.12	<0.0001**** 9.42	2.21±0.37	5.83±1.349	0.0365* 2.15
TT4 (nmol/L)	108.3 ± 7.10	7.88±2.69	<0.0001**** 14.61	97.02 ± 6.87	16.49±0.82	<0.0001**** 14.2
PRL (IU/L)	134.4±19.59	450.7±115.4	0.025* 2.34	328.8 ± 46.7	637±115.8	0.041* 2.096
FSH (IU/L)	3.24 ± 1.50	5.06±0.82	0.266 1.129	13.38 ± 3.58	2.64±0.45	0.0007** 3.62
LH (mIU/L)	2.14±.57	9.01±3.72	0.062 0.062	9.35±3.19	17.31±3.59	0.128 1.55

P < 0.05 *; P < 0.01 **; P < 0.001***; P <0.0001****.

Table II. Hormonal profile of Graves' disease patients.

	Male			Female		
	Control (n=5)	Sample (n=8)	P-value t-value	Control (n=20)	Sample (n=24)	P-value t value
TSHR (IU/L)	1.501±0.30	20.56±5.38	0.0001**** 6.06	1.40±0.60	18.46± 2.9	<0.0001**** 5.28
TSH (µIU/L)	3.3 ± 0.75	0.35±0.11	0.0004* 4.95	2.49±0.36	0.21±0.05	<0.0001**** 6.78
TT4 (nmol/L)	78.4 ± 6.005	187.1± 10.37	<0.0001**** 7.70	118 ± 6.69	186.2±4.82	<0.0001**** 8.432
PRL(IU/L)	131 ± 32.01	233 ± 66.06	0.27 1.15	328.8±46.7	473.6±129	0.33 0.97
FSH (IU/L)	6.456 ± 4.18	15.09± 5.82	0.31 1.06	3.12± 0.47	16.41 ±4.99	0.02* 2.417
LH (mIU/L)	2.146±.57	12.57 ± 4.22	0.030* 1.02	5.65±2.607	13.82 ±3.46	0.075 1.82

The normal range for TSH is 0.5-5.0 µIU/L, TT4 is 62-165nmol/L and ATPO is 40-60 IU/mL and Anti TR >1.5 IU/L. The normal range for PRL are: Males: 425 mIU/L, Non pregnant females: 118-555 mIU/L. The normal range for FSH females (follicular stage) = 3-20 IU/L and FSH males =1-12 IU/L. The normal range of LH for females is (follicular stage) =1.9 to 12.5 IU/L and for males = 0.7 to 7.9 IU/L.

Previously Zahringer *et al.* (2000) reported increased level of LH in both male and female GD patients which is consistent with our data. Khan *et al.* (2018) found significant increase in serum PRL and LH in HT patients as reported in the present study. But they also reported increased FSH which is against the present study result. Similarly, normal level of PRL and FSH were reported in Grave's disease female patients as reported in present study. But in our study increased level of LH was reported which contradicts the khan results.

Conclusion

The alterations in the serum level of PRL and serum gonadotropin in autoimmune thyroid disease reveals the

effect of thyroid hormones on the pituitary hypothalamic axis. Our study suggests that thyroid hormones are actively involved in alterations of these hormones participating in the disease pathogenesis. But there is need of further research to further investigate the underlying mechanisms behind the fluctuation of these hormones in HT and GD patients.

Statement of conflict of interest

There is no conflict of interest between the authors.

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