Original Article

Association of Thyroid Profile and Prolactin Level in Patient with Secondary Amenorrhea

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Abstract

Background: **Amenorrhea is the absence of menstrual periods. It has multiple social consequences as it may leads to infertility. This case control study was conducted for determining the association of thyroid hormones with hyperprolactinemia in patient with amenorrhea.**

Methods: **We investigated 50 women with diagnosed cases of secondary amenorrhoea, who attended UCMS hospital, for hormonal evaluations. Fifty two healthy women were taken as the controls. The thyroid dysfunction and serum prolactin level were reviewed in cases and in the controls.**

Results: **Mean serum prolactin level was found to be significantly higher in the cases as compared to the controls. Mean serum fT3 and fT4 level in the hyperprolactinemic cases (mean = 2.67, SD = 1.04 pg/ml) and (mean = 1.38, SD = 0.51 ng/dl respectively) were slightly lower as compared to normoprolactinemic cases (mean = 3.21, SD = 1.86 pg/ml) and (mean = 1.73, SD = 1.37 ng/dl) respectively. Mean TSH of normoprolactinemic and hyperprolactinemic cases were comparable (P = 0.049). There was positive correlation between prolactin, BMI and TSH whereas negative correlation of prolactin was seen with fT3, fT4 and age. In hyperprolactainemic cases, prolactin was found to be negatively correlated with TSH (r = -0.155, P = 0.491) whereas prolactin was positively correlated with TSH (r = 0.296, P = 0.126) in normoprolactainemic cases.**

Conclusions: **Thus, hyperprolactinemia with thyroid dysfunction may be contributory hormonal factor in patient with amenorrhoea and as such, estimation of prolactin, fT3, fT4 and TSH should be included for diagnostic evaluation of amenorrhea.**

Keywords: *Amenorrhea, prolactin, Thyroid Stimulating Hormone (TSH)*

Introduction

Women having regular cycles but lack menses since three months or more and those having irregular or prolonged cycles but absence of menses since nine months or more are taken as secondary amenorrhoiec (1).

Thyroid dysfunctions affect menstrual cycle. Most of the studies have shown the association of thyroid disorder (hyperthyroidism or hypothyroidism) with menstrual disturbance and even anovulatory cycles (2, 3). Prolactin secretion is regulated by prolactin inhibitor factor secreted from hypothalamus. In addition, other factors like vasoactive inhibitory peptide (VIP) and Thyroid releasing hormone (TRH) also contribute in release of prolactin (4, 5).

Highly elevated levels of prolactin decrease the levels of estrogen in women (6). Pituitary hormones play a vital role in maintaining normal menstruation. Serum TSH, prolactin or growth hormone act synergistically with FSH and LH

that in turn enhance the production of growing follicles (7). Thus, there are certain changes occurred in the follicles in hypothyroidism and it may be due to higher prolactin production that in turn blocks both secretion and action of gonadotropins (8). It was found that even thyroid disorder alone may cause menstrual dysfunction as thyroid hormones are needed for the maximum production of steroid hormones like estradiol and progesterone (9). Hence, the present study can be the baseline data which can show the impact of hormonal changes in thyroid dysfunction and amenorrhea patient and can serve nationwide prevalence for further studies.

Materials and Methods

Case-control study were carried among 102 subjects (50 diagnosed secondary amenorrhoeic patients as cases and 52 healthy subjects as controls by expert Gynaecologist of UCMS from January 2015 to June 2015 in Department of Biochemistry with collaboration of Department of Gynaecology at Universal College of Medical Sciences (UCMS), Bhairahawa, Nepal. Thyroid disorders was classified as euthyroidism, TSH within the normal range, subclinical hypothyroidism, TSH > 4.7mIU/L but normal thyroid hormones, primary hypothyroidism, TSH > 4.7mIU/L and primary hyperthyroidism, TSH < 0.5mIU/L. Likewise, Prolactin level was graded as follows: Hyperprolactenemia, prolactin level more than 23.2ng/ml and normoprolactenemia 1.0 to 23.2ng/ml. Patients on medication that affects thyroid hormone levels, patient with primary amenorrhoea, anorexia nervosa (athletic amenorrhea), Functional Hypothalamic Amenorrhea (FHA), drug induced were excluded. Similarly, patient using any means of contraceptives were also excluded. The consent was taken from each subject and the ethical approval for the study was provided by institute review board of UCMS, Bhairahawa. Serum Prolactin and TSH along with fT_3 and fT_4 were measured by using Perfermed, Human and Diametra kits of ELISA immunoassays respectively.

Statistical analysis

The data generated from study were analysed using IBM SPSS Windows version 22. The data was expressed as mean and SD values. Independent *t*-test, One way Analysis of Variance (ANOVA) were used. Association between TSH and PRL was analysed with Pearson's correlation coefficient. A P value < 0.05 was considered statistically significant.

Results

Thyroid function along with different socio-demographic variables of cases and controls are depicted in Table 1. Out of 50 amenorrhoeic cases taken, 40 (80%) previously had regular cycles but lack menses since three months or more when sample was taken while 10 (20%) previously had irregular or prolonged cycles and lack menses since nine months or more. No significant differences were seen in the mean age (P = 0.665) and BMI (P = 0.604) between both groups.

Table 1: General characteristics of cases and controls

Characteristic	*n* (%)	
	Cases	Controls
Euthyroidism	31 (62)	41 (78.8)
Subclinicalhypo-thyroidism	9 (18)	7 (13.6)
Primary hypothy-roidism	4 (8)	2 (3.8)
Primary hyper-thyroidism	6 (12)	2 (3.8)
Normoprolacten-emia	22 (44)	52(100)
Hyperprolactine-mia	28 (56)	0 (0)
Age(yr)[a]	25.92 (7.97)	25.27 (7.12)
BMI (Kg/m^2) [a]	21.89 (3.56)	21.55 (2.91)

[a]Mean (SD)

Mean serum TSH levels in the amenorrhoeic cases (mean = 4.42, SD = 4.09 mIU/L) were found to be higher than controls (mean = 3.53, SD = 2.4 mIU/L). Likewise, the cases had higher prolactin levels (mean = 23.28, SD = 18.53 ng/ml) than in the controls (mean = 6.57, SD = 4.68 ng/ml) (Table 2). Higher serum prolactin levels were seen in the euthyroidism and subclinical hypothyroidism cases as compared to their respective control groups. Similarly, mean serum prolactin in cases of primary hypothyroidism and hyperthyroidism was found to be significantly higher. (P = 0.036) (Table 3).

When we compared fT_3, fT_4 and TSH levels in amenorrhoeic cases with normal and high

prolactin level, we observed that TSH level was higher in the later group whereas fT_3 and fT_4 levels were higher in the former group (Table 4).

There was positive correlation between prolactin, BMI and TSH whereas negative correlation of prolactin was seen with fT_3, fT_4 and age (P = 0.009). In hyperprolactainemic cases, prolactin was found to be negatively correlated with TSH (r = –0.155, P = 0.491) while positive correlation was seen with TSH (r = 0.296, P = 0.126) in normoprolactainemic cases (Table 5).

Table 2: Thyroid hormones, TSH and Prolactin levels in cases and controls

	Cases[a]	Controls[a]	*P*-value[b]
fT3 (pg/ml)	2.91 (1.46)	2.63 (0.79)	0.245
fT4 (ng/dl)	1.54 (0.99)	1.37 (0.35)	0.270
TSH (mIU/L)	4.42 (4.09)	3.40 (2.43)	0.334
Prolactin (ng/ml)	23.28 (18.53)	6.40 (4.60)	0.001

aMean (SD); bIndependent *t*-test

Table 3: Comparison of serum prolactin level incases and controls between different Thyroid disorders

	Prolactin level[a]		*P*-value[b]
	Cases	Controls	
Subclinicalhypothyroidism	18.53 (11.57)	5.68 (4.52)	0.001
Primaryhypothyroidism	35.31 (10.73)	10.21 (1.58)	0.036
Primaryhyperthyroidism	23.43 (19.90)	2.29 (0.29)	0.036

[a]Mean (SD). [b]Analysis of variance (ANOVA)

Table 4: Comparison of thyroid hormones and TSH in cases with high & normal prolactin level

	Prolactin [a]		*P*-value[b]
	Normal	High	
fT3 (pg/ml)	3.21 (1.86)	2.67 (1.04)	0.203
fT4 (ng/dl)	1.73(1.37)	1.38(0.51)	0.203
TSH (mIU/L)	2.72 (1.90)	5.40 (5.17)	0.049

[a]Mean (SD). [b]Independent *t*-test

Table 5: Correlation of prolactin with different parameters in cases

	r [c]	*P*-value
Age	-0.36	0.009
BMI	0.087	0.550
fT3	-0.90	0.535
fT4	-0.112	0.438
TSH	0.144	0.319

[c] Pearson's correlation coefficient

Discussion

In this study, serum prolactin in cases (mean = 23.28, SD = 18.53 ng/ml) was found to be significantly higher than in control group (mean = 6.40, SD = 4.60 ng/ml). Hyperprolactinemia was seen in 56% of the amenorrrhoeic cases. Similar finding was also observed in the study of Kumkum et al. (10).

Amenorrhea occurs in thyroid disorder due to hyperprolactinaemia as a result of LH and FSH suppression (11). TRH in addition to increasing TSH causes to raise prolactin level (12). Prolactin hinders FSH and GnRH thus

impairs ovulation. Thus, hyperprolactinaemia results to irregular menstrual cycles and infertility (13). Affia Tasneem stated that there was a higher prevalence of hyperprolactinaemia, together with a greater propensity for thyroid disorders in infertile subjects (14).

Majority of amenorrrhoeic cases as well as controls were euthyroid in our study. This is supported by study of Elahi et al. (15). In our study, hyperprolactainemia was seen in 75% cases of primary hypothyroidism whereas it was found to be 50% in primary hyperthyroidism. It might be due to small sample size. A study of Singh et al. (16) reported hyperprolactinemia in 57% of women with hypothyroidism. Subclinical hypothyroidism associated with hyperprolactinaemia was significantly higher in our cases than in controls.

Although some studies reported that hyperprolactinemia is rare disorder in subclinical hypothyroidism (17). Tasneem et al. (14) also observed in their study, that some of the women with high prolactin levels had thyroid disorder. In this study, the serum TSH concentration was increased in cases (mean = 4.42, SD = 4.09 mIU/L) as compared to that in the control group (mean = 3.40, SD = 2.43 mIU/L). This is similar to observations made in a study by Sharma et al. (18) Paul Isong et al.(19) and Turankar et al.(9) Positive correlation was found between serum TSH levels and high prolactin level (P = 0.049) unlike fT_3 and fT_4 levels in cases. During the regulation of TSH secretion the negative feedback on the hypo-thalamo pituitary axis results in increased secretion of TRH that stimulates thyrotrophs and lactotrophs thereby increasing the levels of both TSH and prolactin (20). Evidence from experimental and clinical studies have suggested that there is a close relationship of hypothalamic–pituitary–ovarian axis (HPO) with hypothalamic–pituitary–thyroid axis (HPT) (20). This study shown an association between amenorrhea and hyperprolactainemia (P = 0.0001).

Maximum percentage of the amenorrhoeic group had normal menses whereas 20% had oligomenorrhea. The mean serum levels of fT_3 and fT_4 of the hyperprolactinemic cases were slightly lower than those of normoprolactinemic one. But that was not statistically significant. Similar findings were reported by Poppe and Velkeniers (21).

A positive correlation was found between serum TSH and prolactin levels in cases. This finding is also consistent with the findings of other studies (22, 23). As we expected, TRH caused hyperprolactinemia in hypothyroidism, perhaps there is some unknown etiology that causes hyperprolactinemia in these cases. Hence, thyroid profile mainly serum TSH and prolactin estimation are ordered clinical tests that are carried out in diagnosing as well as treating amenorrhoeic cases.

Conclusion

In our study, a higher incidence of hyperprolactinaemia was found in amenorrhoeic women. Likewise, thyroid disorders were found to be common in cases. Serum TSH was found to be altered i.e. significantly higher in hyperprolactinaemic subjects.

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Conflict of Interests

None

Authors' Contributions

Conception and design: NG
Analysis and interpretation of the data: RKD, ACJ
Drafting of the article: SS
Critical revision of the article for important intellectual content: NG
Provision of study materials or patients: NRD
Statistical expertise: RKD
Administrative, technical, or logistic support: AJ
Collection and assembly of data: SS, SN

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