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Original Research Article

## Correlation of prolactin and thyroid disorders in infertile women

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### ABSTRACT

**Background:** The objective of the study was to review the impact of thyroid status on the fertility and to study the prevalence of hyperprolactinaemia in infertility.

**Methods:** A total of 150 subjects were divided into 3 groups: 50 primary infertility, 50 secondary infertility and 50 controls. The incidence of hyperprolactinaemia and thyroid disorders was studied in all the three groups.

**Results:** The incidence of hyperprolactinaemia was 41% in all infertile subjects (60% with primary and 22% in secondary infertility) and 6% in controls. The incidence of hypothyroidism was 17% in infertility (18% in primary and 16% in secondary infertility) and 8% in controls.

**Conclusions:** In this study there is a positive correlation between increased prolactin levels and hypothyroidism and such patients' exhibit ovulatory failure. All patients with infertility should undergo prolactin levels and thyroid profile.

**Keywords:** Galactorrhoea, Hypothyroidism, Hyperprolactinaemia, Infertility, Oligomenorrhoea

### INTRODUCTION

One in every four couples in developing countries had been found to be affected by infertility. The prevalence of primary infertility was higher among women aged 20-24 yrs (2.7% in 2010) compared to women aged 25-29 yrs (2.0%) and women aged 30-44 yrs (ranging from 1.6% to 1.7% in 2010). Prevalence of secondary infertility increased sharply with age; from 2.6% in women aged 20-24 yrs to 27.1% in women aged 40-44 yrs.<sup>1</sup>

Hyperprolactinaemia adversely affects the fertility potential by impairing pulsatile secretion of GnRH and hence interfering with ovulation. Serum prolactin levels are mandatory in all infertile women especially those with oligomenorrhoea and amenorrhoea.<sup>2</sup> Thyroid hormones have profound effects on reproduction and pregnancy. There is a known association of

hyperthyroidism and hypothyroidism with menstrual disturbances and decreased fecundity.<sup>3</sup>

This study was designed to know the prevalence of hyperprolactinaemia and thyroid disorders in infertile women attending the OPD in KNSH Shimla.

### METHODS

A controlled prospective study was conducted in the Department of Obstetrics and Gynaecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College, Shimla on 100 infertile women (50 with primary and 50 with secondary infertility) and 50 control women attending the gynaecology OPD, w.e.f 1<sup>st</sup> July, 2013 to 30<sup>th</sup> June, 2014. The study has been approved by the ethical committee of the institution and informed consent of patients has been obtained.

**Method**

Primary infertility is infertility in a couple who have never had a child even after 12 months or more of regular unprotected sexual intercourse

Secondary infertility is failure to conceive following a previous pregnancy

**Inclusion criteria**

Diagnosis of infertility, Age between 20-40 years, Duration of marriage more than one year

**Exclusion criteria**

Male factor infertility, Tubal factor, Any congenital anomaly of the urogenital tract, Any history of thyroid disease or previous thyroid surgery or being on thyroid medications

The control group includes fertile females in the same age group attending the gynaec OPD for other complaints and having no menstrual irregularities

- A detailed medical, menstrual and obstetric history was taken
- Detailed general physical examination and gynecologic examination was done
- Complete infertility work up and following investigations were done

Complete haemogram with ESR, Chest X ray, TFTs, serum prolactin, pelvic ultrasound, semen analysis of the husband, endometrial sampling and whenever indicated hysterosalpingography and diagnostic laparoscopy.

- The hormonal profile was taken on day 3 of menstrual cycle.

- The normal range of serum prolactin and TSH was 2-25ng/ml and 0.5-4.7µIU/ml respectively
- Women with serum prolactin levels >100ng/ml were advised to undergo CT scan or MRI to rule out any pituitary pathology
- Hyperthyroidism was diagnosed if serum TSH is <0.5µIU/ml
- Hypothyroidism was diagnosed if serum TSH is >4.7µIU/ml
- Patients with subclinical hypo and hyperthyroidism were not included in the study
- The results of this study were subjected to statistical analysis and p-value <0.05 was considered statistically significant
- TFTs and Prolactin levels were measured in serum samples using Beckman Coulter Access II Immunoassay analyzer

**RESULTS**

The subjects were divided into Group I (50 women with primary infertility), Group II (50 women with secondary infertility) and Group III (50 women in control group). Groups I + II is taken as study group and Group III as controls.

In Group I the duration of infertility was less than 5 years in 66% subjects and in Group II it was 6-10 years in 56% subjects (Table 1). Other presenting symptoms in the study group were obesity; abnormal hair growth and pain abdomen were present in 30%, 17% and 15% subjects. 44% subjects in study group had regular cycles and 57% had menstrual irregularities. Oligomenorrhoea, amenorrhoea and menorrhagia were seen in 51%, 3% and 2% subjects respectively. Galactorrhoea was the commonest clinical findings in the study group followed by acne and hirsutism. In the study group majority of subjects (63%) had BMI of 19-24.9 kg/m<sup>2</sup>.

**Table 1: Distribution of cases according to duration of infertility.**

Duration in years	Group I (n=50)		Group II (n=50)		p value (Group I and II)	Group I+II (n=100)	
	No.	% age	No.	% age		No.	% age
1-5yrs	33	66%	12	24%	0.000	45	45%
6-10yrs	15	30%	28	56%	0.008	43	43%
>10yrs	2	4%	10	20%	0.013	12	12%

In this study the maximum number of subjects in all the 3 groups was in the age group 26-30 years. Out of all the subjects 84% subjects were literate and maximum had completed secondary education. In study group 68% subjects were from rural area. In all the groups maximum subjects belonged to class III. The prevalence of hyperprolactinaemia in infertility was 41%. The mean

prolactin in Group I and II was 32.7 and 26.1 ng/ml respectively (Table 2).

82% subjects in study group were euthyroid. The prevalence of hypothyroidism was 17% in infertility. The mean TSH I Group I and II was 3.84 and 3.67 µIU/ml respectively (Table 3). The incidence of hypothyroidism

in hyperprolactinaemia was 17.07%, hence seen in 1 in 5.8 subjects. Galactorrhoea was seen in 58.53% hyperprolactinaemic subjects. The majority of subjects with hyperprolactinaemia had BMI 19-24.9 kg/m<sup>2</sup>,

maximum hypothyroid subjects had BMI 25-29.9 kg/m<sup>2</sup> and majority of subjects with PCOS had BMI 25-29.9 kg/m<sup>2</sup> (Table 4).

**Table 2: Incidence of hyperprolactinaemia.**

Prolactin levels (ng/ml)	Group I (n=50)		Group II (n=50)		p-value between Group I and II	Group I+II (n=100)		Group III (n=50)		p-value between Group I + II and III
	No.	% age	No.	% age		No.	% age	No.	% age	
0-20	20	40%	39	78%	0.000	59	59%	47	94%	0.000
21-100	29	58%	11	22%	0.000	40	40%	3	6%	0.000
>100	1	2%	0	0	1.000	1	1%	0	0	1.000

Majority of subjects with hyperprolactinaemia had irregular cycles and oligomenorrhoea was commonest pattern observed. Majority of subjects with hypothyroidism also had irregular cycles and all presented with oligomenorrhoea (Table 5). On

ultrasonography 82% subjects had normal findings. In the study group maximum subjects had features suggestive of proliferative phase on endometrial biopsy. Majority of subjects with hyperprolactinaemia and hypothyroidism also had findings of proliferative phase.

**Table 3: TSH levels in infertile subjects.**

TSH levels (ng/ml)	Group I(n=50)		Group II (n=50)		p-value between Group I and II	Group I+II (n=100)		Group III (n=50)		p-value between Group I + II and III
	No.	% age	No.	% age		No.	% age	No.	% age	
<0.4	1	2%	0	0	1.000	1	1%	0	0	0.722
0.4-4.7	40	80%	42	84%	0.602	82	82%	46	92%	0.163
>4.7	9	18%	8	16%	0.790	17	17%	4	8%	0.212

**Table 4: Relationship between BMI and hormonal disorders.**

BMI (kg/m <sup>2</sup> )	Hyperprolactinaemia (n=41)		Hypothyroidism (n=17)		PCOS (n=10)	
	Group I + II		Group I + II		Group I+II	
	N	% age	N	% age	N	% age
<19 (underweight)	-	-	1	5.8%	-	-
19-24.9 (normal)	23	56.09%	7	41.1%	3	30%
25-29.9 (overweight)	17	41.46%	8	47.05%	7	70%
>30 (obese)	1	2.4%	1	5.8%	-	-

**Table 5: Menstrual cycles and hormone disorders.**

	Normal prolactin (n=59)		Hyper-prolactinaemia (n=41)		Euthyroid (n=82)		Hypo thyroid (n=17)		Hyper thyroid (n=1)	
	N	% age	N	% age	N	% age	N	% age	n	% age
Regular	27	45.7%	32	54.23%	36	43.9%	7	41.2%	1	100%
Irregular	16	39%	25	61%	46	56.09%	10	58.8%	-	-

During follow up 16 infertile subjects conceived with different modalities of treatment. 2 (2.22%), 3 (3.33%), 5 (5.55%), 5 (5.55%) and 1 (1.11%) subjects conceived

spontaneously, after EB, after hormones, after ovulation induction and after IUI respectively.

## DISCUSSION

In the present study 45%, 43% and 12% subjects had duration of infertility 1-5 years, 6-10 years and >10 years. These results were different from the study by Agrawal<sup>4</sup> et al where the results were 32.5%, 40% and 27.5% respectively. In the present study the commonest chief complaint of the infertile subjects was obesity (30%). The next common complaint in the present study was abnormal hair growth seen in 17% subjects and this was comparable to the study conducted by Zargar<sup>5</sup> et al (14.4%) whereas it was 4.47% in the study conducted by Emokpae<sup>6</sup> et al.

In present study the subjects with regular cycles and with menstrual complaints were 44% and 56% respectively. Oligomenorrhoea, amenorrhoea and menorrhagia were seen in 51%, 3% and 2% respectively. These results are comparable to the study conducted by Avasthi<sup>2</sup> et al which had similar pattern of cycles. Regular cycles in 42% and oligomenorrhoea, amenorrhoea and menorrhagia in 50%, 6% and 2% subjects respectively.

The present study showed acne, hirsutism, galactorrhoea and obesity in 12%, 20%, 24% and 28% in Group I and in 6%, 16%, 28% and 32% in Group II respectively. These results were comparable to the study conducted by Akhter<sup>7</sup> et al which showed acne, hirsutism and obesity in 13.95%, 24.42% and 30.23% in primary and 7.41%, 25.93% and 33.33% in secondary infertility respectively.

In the present study the incidence of hyperprolactinaemia was 41% in infertility and 6% in control group. The incidence of hyperprolactinaemia was 60% in primary infertility and 22% in secondary infertility. All the results were statistically significant. These results were comparable to the studies conducted by Goswami<sup>8</sup> et al 41%, Mohan<sup>9</sup> et al 42% and Avasthi<sup>2</sup> et al 46%. The studies by Akhter<sup>7</sup> et al showed 37.5% and Sharma<sup>10</sup> et al showed 38% incidence. The incidence of hyperprolactinaemia in primary and secondary infertility were 43% and 22% in study conducted by Akhter<sup>7</sup> et al and 46% and 40% in study by Avasthi<sup>2</sup> et al. All the studies including ours showed a higher incidence of hyperprolactinaemia in primary infertility. The present study showed that in infertile females 1% were hyperthyroid, 82% euthyroid and 17% had hypothyroidism. The results of our study were comparable to the studies conducted by Mishra<sup>11</sup> et al and Rijal<sup>3</sup> et al where hypothyroidism was seen in 14.3% and 19.45% subjects. The incidence of hyperthyroidism was also similar. In the present study the incidence of hypothyroidism in hyperprolactinaemia was 17.07%. Results are comparable to the results of studies conducted by Avasthi<sup>2</sup> et al (19.6%) and Emokpae<sup>6</sup> et al (14.9%).

The present study shows the incidence of galactorrhoea in hyperprolactinaemia to be 58.53%. The association between galactorrhoea and hyperprolactinaemia reported in various studies is highly variable ranging from 25% in

study by Emokpae<sup>6</sup> et al to as high as 90% reported by Avasthi<sup>2</sup> et al. The association between galactorrhoea and hyperprolactinaemia is well known. In the present study the BMI in hyperprolactinaemic subjects shows that none were underweight, 56.09% had normal BMI and 43.9% were obese or overweight. The results of the study conducted by Pereira Lima<sup>12</sup> et al in Brazil show even higher incidence of overweight and obesity 65.2% in subjects with hyperprolactinaemia. In the present study the 52.9% subjects with hypothyroidism were overweight or obese, 41.1% were having normal weight and 5.8% were underweight. In the study conducted by Verma<sup>13</sup> et al the subjects that were overweight or obese were 66% and 34% were with normal weight. Our study showed 70% subjects with PCOS to be overweight and obese and 30% subjects to be of normal weight. These findings were comparable to the study by Alnakash<sup>14</sup> et al who reported 36.45% subjects with normal BMI and 63.55% subjects with BMI > 25kg/m<sup>2</sup>.

In the present study 39% had regular and 61% had irregular cycles with hyperprolactinaemia. In study by Avasthi<sup>2</sup> et al 37% and 63% subjects with hyperprolactinaemia had regular and irregular cycles. Oligomenorrhoea was commonest finding in both.

In the present study the endometrium was non secretory in 72% subjects with primary and 58% subjects with secondary infertility. 65% of infertile subjects had non secretory endometrium. In study by Avasthi<sup>2</sup> et al the incidence of non secretory endometrium is 49.5% which is quite high though less compared to our study.

Out of 90 subjects in Group I and Group II total conceptions occurring with different modalities of treatment were 16 (17.78%) and can be attributed to the fact that our study was a one year study and not all subjects could be followed up for conception. In both the Groups two (2.22%), three (3.33%), five (5.55%), five (5.55%) and one (1.11%) subjects conceived spontaneously, after EB, after hormones, after ovulation induction and after IUI respectively.

## CONCLUSION

Problems in infertility are challenging and taxing to the clinician which can be solved just by tackling some simple endocrinological conditions like hyperprolactinaemia and thyroid disorders. The problem of infertility is seen in women with higher age groups due to the trend of late marriages. Obesity and hirsutism are commonly observed in infertile subjects.

Hyperprolactinaemia is a common finding in infertile population. Presence of hyperprolactinaemia should be looked for in subjects with oligomenorrhoea, amenorrhoea and galactorrhoea. Subjects with prolactin >100ng/ml should undergo further evaluation to rule out pituitary pathology.

Thyroid hormones have profound effects on reproduction and pregnancy. Thyroid dysfunction is implicated in a broad spectrum of reproductive disorders, ranging from menstrual irregularities and infertility. Hypothyroidism is more commonly associated with infertility.

There is also a positive correlation between increased prolactin levels and hypothyroidism and such patients exhibit ovulatory failure. All patients with infertility should undergo prolactin levels and thyroid profile.

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