

# Evaluation of Symptomatology in Hyperprolactinemic Infertile Women

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## Summary

A prospective study of 200 cases of infertility was carried out from June 1997 to July 1999 for detailed work up of symptomatology and serum prolactin estimation. Fifty parous women with normal menstrual cycles and non-lactating for last one year were taken for control to have mean serum prolactin.

There were 11% cases of hyperprolactinemia in the study group. Amongst these 90% had menstrual problem and 59% had galactorrhoea.

Cases of infertility presenting with menstrual disorders should be subjected to have serum PRL estimation, as hormonal imbalance in these women is due to high level of prolactin leading to anovulation.

## Introduction

The association between hyperprolactinemia and suboptimal reproductive functions has long been recognized (Blackwell et al, 1990). It has been postulated that prolactin blocks the action of gonadotropins on the ovary, inhibits production of progesterone by the human granulosa cells and leads to anovulatory infertility along with various menstrual abnormalities.

The following study was aimed at to find out the incidence of hyperprolactinemia amongst the infertile women and evaluation of symptomatology.

## Material and Methods

This was a prospective study carried out in the Department of Gynaecology, MGIMS, Sewagram, Wardha, over a period of 2 years from June 1997 to June 1999. The study group comprised of 200 cases of infertility (both primary and secondary). These 200 cases were subjected to serum prolactin estimation and detailed work up.

Fifty parous women, with normal menstrual cycles (26 to 30 days), 20 to 30 years of age, non lactating for at least one year and not ingesting drugs, were selected as control group to establish the normal range and mean of serum prolactin levels.

The complete history of all the patients regarding their marital status, duration and type of infertility, menstrual pattern, especially the presence of any irregularity, complete obstetric history in case of secondary infertility, any history of drug intake including oral contraceptives was recorded. History regarding galactorrhoea, thyroid dysfunction and visual disturbances was recorded.

The patients following thorough examination subjected for the investigations including serum PRL. The values of prolactin above 25ng/ml were taken as hyperprolactinemic and values below 5ng/ml were taken as hypoprolactinemic.

The data obtained, was evaluated by Chi square test.

## Observations

## Levels of Serum Prolactin (SPRL)

There were 22 (11%) cases of hyperprolactinemia in the study group as compared to none in the control group (Table I). This higher value of prolactin in the study group was found to be statistically significant ( $p < 0.05$ ). SPRL levels in primary & secondary infertility.

The present study has shown that amongst the hyperprolactinemic group, maximum number of both primary and secondary infertility cases had SPRL values between 26-75 ng/ml and only 1 case had serum

prolactin value more than 76 ng/ml (Table II).

## Presenting complaints

On analyzing the presenting complaints the study group had shown various manifestations like menstrual problems, galactorrhoea, dyspepsia, pelvic pain, weight loss and gain etc., which is depicted in (Table III). Menstrual problems were commonly observed in 20 (90.90%) hyperprolactinemic cases.

## Presenting complaints and serum prolactin levels

In patients with serum prolactin more than 25

**Table I**  
PRL in Control Group and Study Group

Levels of serum	Study group		Control group	
	No	%	No	%
PRL (ng, ml)				
< 05	004	02.00	—	—
05-25	174	87.00	50	100
> 25	022	11.00*	—	—
Total	200	100	50	100

\*  $P < 0.05$

**Table II**  
Levels of SPRL Primary & Secondary Infertility

Age in years	Primary infertility		Secondary infertility		Total	
	No	%	No	%	No	%
< 05	004	02.00	—	—	004	02.00
05-25	110	55.00	64	32.00	174	87.00
26-50	009	04.50	04	02.00	013	06.50
51-75	006	03.00	02	01.00	008	04.00
76-100	001	00.50	—	—	001	00.50
Total	130	65.00	70	35.00	200	100

**Table III**  
Presenting Complaints in Cases of Hyperprolactinemia and Other Cases in the Study Group

Complaints	Hyperprolactinemic cases (n=22)		Other cases # (n=178)		Total (n=200)	
	No	%	No	%	No	%
Menstrual Problem	20*	90.90	50*	28.08	70	35.00
Galactorrhoea	13*	59.09	05*	02.81	18	09.00
Dyspareunia	04	18.18	22	12.35	26	13.00
Pelvic pain	02	09.09	30	16.85	30	15.00
Weight gain	—	—	18	1.11	18	09.00
Weight loss	—	—	28	15.73	28	14.00
No complaints	02	19.09	74	41.57	76	38.00
Total	41	15.30	227	84.70	268	100.00

$P < 0.001$ ; \* : Menstrual problem and galactorrhoea had significantly higher Hyperprolactinemia as compared to other complaints.

# other cases include normoprolactinemic and hypoprolactinemic cases.

ng/ml, the main problem was in the menstrual cycle in 20 (10.00%) cases followed by galactorrhoea in 13 (06.50%), dyspareunia in 4 (02.00%) and pelvic pain in 2 (01.00%) cases. Only infertility, as the presenting complaint was found in majority; 74 (37%) cases with serum prolactin levels less than 25 ng/ml. It was observed that with increasing prolactin value, number of complaints too increased. Thus a statistically significant association between serum prolactin levels and number of complaints was found in the present study ( $p < 0.001$ ) (Table IV).

Of the 200 cases in the study, 18 (9.09%) cases had galactorrhoea. Of these, 13 (72.22%) belonged to the hyperprolactinemic group and remaining 5 (27.78%) belonged to normoprolactinemic group. Thus a highly significant association between galactorrhoea in hyperprolactinemic group as compared to galactorrhoea in normoprolactinemic group, was found in the present

study ( $p < 0.001$ ) (Table V).

## Discussion

In the present study, serum prolactin value was raised in 11% of the cases of the study group as compared to the none in the control group (Table I). Thus a significant association ( $p < 0.05$ ) between hyperprolactinemia and infertility was established in the present study. The incidence of hyperprolactinemia in the infertility group was reported ranging from 1.48% to 41.0% by various workers (Kredenster et al 1981, Pillai et al 1991, Pratibha et al 1993).

It was seen that amongst the hyperprolactinemic group, majority viz. 72.72% were of primary and 27.27% were of secondary infertility. Sinha et al (1989) reported the incidence of primary infertility in 65.81% and secondary infertility in 34.10% of the cases. The reason

**Table IV**  
Levels of Serum Prolactin and Presenting Complaints

Complaints	Serum prolactin levels in ng/ml (n=200)					Total
	< 5	5-25	26-50	51-75	76-100	
Menstrual problems	06 (03.00)	11 (22.00)	11 (05.50)	08 (04.00)	01 (00.50)	70 (35.00)
Galactorrhoea	-	05 (02.50)	05 (02.50)	07 (03.50)	01 (00.50)	18 (09.00)
Dyspareunia	02 (01.00)	20 (10.00)	—	03 (01.50)	01 (00.50)	26 (13.00)
Pelvic pain	—	30 (15.00)	—	02 (01.00)	—	32 (16.00)
Weight gain (09.0)	— (09.00)	18	—	—	—	18
Weight loss (14.0)	— (14.00)	28	—	—	—	28
No Complaints	—	74 (37.00)	02 (01.00)	—	—	76 (38.00)

Figures in parenthesis indicate percentages.

**Table V**  
Galactorrhoea and Serum Prolactin Levels in Study Group

Serum PRL levels (ng/ml)	Galactorrhoea present No	Galactorrhoea absent No	Total No
< 5	—	04 (02.00)	04 (02.00)
5-25	05 (02.50)*	169 (84.50)	174 (87.00)
26-50	05 (02.50)*	08 (04.00)	13 (06.50)
51-75	07 (03.50)*	01 (00.50)	08 (04.00)
76-100	01 (00.50)*	—	01 (00.50)
Total	18 (09.00)	182 (91.00)	200 (100.0)

\* $P < 0.001$

Figures in parenthesis indicate percentages

for hyperprolactinemia in parous women leading to secondary infertility was due to oestrogen of pregnancy which is enough to stimulate the growth of a small silent tumor of pituitary leading to amenorrhoea, persistent galactorrhoea and secondary infertility (Sherman et al, 1978). It is believed that the main cause of infertility associated with hyperprolactinemia is anovulation due to the impairment in the gonadotrophin release pulsatility - interference in the positive feedback of oestrogen on the mid cycle LH surge and direct inhibition of ovarian steroidogenesis (Salvi 1998).

On analyzing the presenting complaint along with infertility it was seen that the maximum cases had menstrual problems (90.90%) followed by galactorrhoea in 59.09% of infertile group (Table III & IV). There were only 2 (9.09%) cases who had no complaint other than infertility but were still hyperprolactinemic. The presence of multiple complaints in the infertile hyperprolactinemic cases was significantly more ( $p < 0.001$ ) than in normoprolactinemic infertile cases. According to Franks et al (1977), the characteristic reproductive disturbances associated with hyperprolactinemia include primary or secondary amenorrhoea, symptoms and signs of oestrogen deficiency (vasomotor symptoms, decreased breast size, vaginal dryness, vaginal atrophy and osteoporosis). Various workers state that hyperprolactinemia may present with galactorrhoea, menstrual disturbances, infertility or they may be asymptomatic (Conner and Fried, 1998 and Salvi, 1998). The present study is in complete agreement with the above workers.

Galactorrhoea, which is one of the commonest complaint reported by hyperprolactinemic cases in the present series was present in 59.09% of the hyperprolactinemic cases (Table III). Similar findings have also been reported by various authors (Takkar et al 1986, Sinha et al 1989, Rajan 1990, Pillai et al 1991 and Sheth & Sheth, 1992).

Hyperprolactinemia is not always associated with galactorrhoea. Out of 200 study cases, 182 (91%) cases and out of 22 hyperprolactinemic cases, 9 (41%) cases did not have galactorrhoea (Table V). Katz and Adashi (1990) commented that absence of galactorrhoea in hyperprolactinemic cases may be due to the presence of an immunoreactive and therefore measurable prolactin referred to as "big" prolactin and "big-big" prolactin which may lack bioactivity. In view of the fact that the hyperprolactinemic cases had highly significant

association with galactorrhoea ( $p < 0.001$ ) in our study, we believe that galactorrhoea is a typical marker of hyperprolactinemia.

An attempt was made to correlate the association of amenorrhoea and galactorrhoea with hyperprolactinemia. In our study 83.33% cases having both amenorrhoea and galactorrhoea had hyperprolactinemia.

Quigley & Haney (1980) reported, that of the cases with amenorrhoea and galactorrhoea between 79% - 97% have hyperprolactinemia. Also according to Kredentser et al (1981), when infertility was combined with abnormal menstruation or galactorrhoea or both the incidence of hyperprolactinemia increased. The present study also showed close association of amenorrhoea and galactorrhoea in infertile women with hyperprolactinemia.

Amongst the various menstrual abnormalities in hyperprolactinemic cases, oligohypomenorrhoea was commonest & present in 41% case, followed by oligomenorrhoea in 41% cases and secondary amenorrhoea in 23% of the cases. Rajan (1990) found the incidence of secondary amenorrhoea and oligomenorrhoea in hyperprolactinemic cases to be 23% and 16% respectively. Katz and Adashi (1990) attribute oligomenorrhoea and amenorrhoea in hyperprolactinemic cases to a compensatory increase in hypothalamic dopamine in response to hyperprolactinemia, which in turn inhibits GnRH production reducing gonadotropin production and causing amenorrhoea and hypoeostrogenism. We believe that though amenorrhoea does not always occur in hyperprolactinemic cases, variety of alterations like hypomenorrhoea, oligohypomenorrhoea, hypermenorrhoea may be present.

Cases of infertility presenting with amenorrhoea, oligomenorrhoea and hypomenorrhoea should be subjected to SPRL estimation, as higher SPRL level causes hormonal imbalance related to anovulation.

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