

# A Study on Subfertile Women Suffering from Polycystic Ovarian Syndrome with Hyperprolactinaemia and Hypothyroidism as Associated Factors

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## Summary:

**Objective:** This study tried to evaluate association of other factors of subfertility in women suffering from polycystic ovarian syndrome (PCOS).

**Methods:** Fifty subfertile women suffering from PCOS attending infertility unit of the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during July 2010 and June 2011, were evaluated.

**Results:** In out study, Age, BMI and duration of marriage range was 20-38 years, 17.70-33.20 kg/m<sup>2</sup> and 1-16 years,

respectively. Serum FSH was normal (1.0-10.0 mIU/ml) in all 50 (100%) women. Hyperprolactinaemia (serum prolactin >25 ng/ml) was seen in 60%. Hypothyroidism (serum TSH >4 iIU/ml) was seen in 74% women. Serum LH (>10 mIU/ml) was raised in 74%. USG finding of lower abdomen was abnormal in 75% cases.

**Conclusion:** This study concludes that hyperprolactinaemia and subclinical hypothyroidism were associated causes of subfertility other than PCOS.

**Key words:** PCOS, Subfertility.

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## Introduction:

The polycystic ovary syndrome (PCOS) is one of the most common cause of infertility due to anovulation. The prevalence is estimated to be between 5 to 10%<sup>1</sup>. The PCOS is a heterogenous condition which is defined by the presence of two out of the three following criteria: (1) oligo and/or anovulation, (2) hyperandrogenism (clinical and/or biochemical) and (3) polycystic ovaries, with the exclusion of other aetiologies<sup>2</sup>. According to

the National Institute of Health (NIH), USA, basic diagnostic criteria should be the presence of hyperandrogenism and chronic oligoanovulation, with the exclusion of other causes of hyperandrogenism, such as adult onset congenital adrenal hyperplasia, hyperprolactinaemia and androgen secreting neoplasms<sup>3</sup>. A consensus conference held in Rotterdam agree on the appropriateness of including ultrasound morphology of the ovaries as a further potential criteria to define the PCOS but also established that at least two of the following criteria are sufficient for the diagnosis: oligo and/or anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries at ultrasound<sup>4</sup>. The pathophysiology of PCOS may have a genetic component although it can be suggested that the main factors responsible for the increasing prevalence of PCOS are related to the influence of the environment, including dietary habits, behaviour and other still undefined factors<sup>1</sup>.

A baseline assessment of the endocrine status should include measurements of serum prolactin and gonadotropin concentrations and an assessment of thyroid function. Prolactin levels may be elevated in response to a number of conditions, including stress, a recent breast examination, or even having a venipuncture. The elevation, however, is moderate and transient. A more permanent, but still moderate elevation (greater than 700 mIU/L) is associated with

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hypothyroidism and is also a common finding in women with PCOS, where prolactin levels up to 2500 mIU/L have been reported<sup>5</sup>.

The present study was carried out to evaluate association of hyperprolactinaemia and hypothyroidism as other factors of subfertility in patients diagnosed as having PCOS who attended the outpatient department of infertility at Bangabandhu Sheikh Mujib Medical University, Dhaka.

### Materials and Methods:

The study was carried out at the infertility unit of the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during July 2010 and June 2011, on 50 primary and secondary subfertile women suffering from PCOS. Inclusion criteria: Women suffering from primary and secondary subfertility with PCOS. Exclusion criteria: Women suffering from PCOS with PID, endometriosis and tuberculosis. Approval for the study was obtained from the institution and informed written consents were obtained from all study subjects.

The collected data included age, menstrual history, body mass index, duration of marriage, parity and history of abortion. Routine laboratory investigations included hormonal status like serum follicle stimulating hormone, serum luteinizing hormone, serum prolactin level, blood sugar 2 hours after 75 g glucose load and serum thyroid stimulating hormone. Specific investigations included ultrasonography of lower abdomen including both ovaries and fallopian tubes. Collected data was compiled and analyzed using computerbased software (SPSS).

### Results:

Fifty women suffering from PCOS with hyperprolactinaemia and hypothyroidism were recruited for evaluation as other associated factors for subfertility. Table I shows that the age range was 20-38 years (mean±SD 26.78±3.83 years) and BMI range was 17.70-33.20 kg/m<sup>2</sup> (mean±SD 25.63±3.38 kg/m<sup>2</sup>). Menstrual cycle was regular in 12 (24%) and irregular in 38 (76%) patients, 46 (92%) were nulliparous and 4 (8%) were primiparous. History of abortion was present in 6 (12%) and absent in 44 (88%) patients. In 28 (56%) patients duration of marriage ≤5 years, in 19 (38%) was 5-10 years and more than 10 years in 3 (6%) (mean±SD 5.77±3.26, range 1-16 years).

**Table I**

*Characteristics of the study women (n=50)*

Parameters	Frequency	Percentage
<b>Age (years)</b>		
≤25	19	38.0
26-30	25	50.0
>30	6	12.0
Mean±SD	26.78±3.83	
Range	20.0-38.0	
<b>BMI (kg/m<sup>2</sup>)</b>		
Low (<19)	1	2.0
Normal (19-25)	21	42.0
Overweight (>25)	28	56.0
Mean±SD	25.63±3.38	
Range	17.70-33.20	
<b>Menstrual cycle</b>		
Regular	12	24.0
Irregular	38	76.0
<b>Parity</b>		
Nulliparous	46	92.0
Primiparous	4	8.0
<b>History of abortion</b>		
Present	6	12.0
Absent	44	88.0
<b>Duration of married life (years)</b>		
≤5	28	56.0
>5-10	19	38.0
>10	3	6.0
Mean±SD	5.77±3.26	
Range	1.00-16.00	

Table II shows laboratory investigation findings. Serum FSH was normal (1-10 mIU/ml) in all 50 (100%) patients (mean±SD 3.76±1.23, range 1.50-7.00 mIU/ml). Serum LH was normal (1-10 mIU/ml) in 13 (26%) and raised (>10 mIU/ml) in 37 (74%) patients (mean±SD 12.50±4.33, range 6.70-27.00 mIU/ml). Serum prolactin was normal (1.9-25.0 ng/ml) in 20 (40%) and raised (>25 ng/ml) in 30 (60%) patients (mean±SD 64.98±135.48, range 7.20-930.80 ng/ml). Serum TSH was normal (0.4-4.0 μU/ml) in 13 (26%) and raised (>4.0 μU/ml) in 37 (74%) patients (mean±SD 9.23±5.84,

range 1.80-25.80  $\mu$ IU/ml). Serum level of blood glucose 2 hours after 75 g glucose load was normal ( $<7.8$  mmol/L) in 30 (60%) and raised ( $\geq 7.8$  mmol/L) in 20 (40%) patients (mean $\pm$ SD 7.60 $\pm$ 1.77, range 4.30-13.40 mmol/L). Ultrasonogram finding of lower abdomen was normal in 13 (26%) and abnormal (polycystic ovaries) in 37 (74%) patients.

**Table-II***Investigation findings (n=50)*

Parameters	Frequency	Percentage
<b>Serum FSH (mIU/ml)</b>		
Normal (1.0-10.0)	50	100.0
Raised ( $>10.0$ )	0	0
Mean $\pm$ SD	3.76 $\pm$ 1.23	
Range	1.50-7.00	
<b>Serum LH (mIU/ml)</b>		
Normal (1.0-10.0)	13	26.0
Raised ( $>10.0$ )	37	74.0
Mean $\pm$ SD	12.50 $\pm$ 4.33	
Range	6.70-27.00	
<b>Serum prolactin (ng/ml)</b>		
Normal (1.9-25.0)	20	40.0
Raised ( $>25.0$ )	30	60.0
Mean $\pm$ SD	64.98 $\pm$ 135.48	
Range	7.20-930.80	
<b>Serum TSH (iIU/ml)</b>		
Normal (0.4-4.0)	13	26.0
Raised ( $>4.0$ )	37	74.0
Mean $\pm$ SD	9.23 $\pm$ 5.84	
Range	1.80-25.80	
<b>Blood sugar 2HAB (mmol/L)</b>		
Normal ( $<7.8$ )	30	60.0
Raised ( $\geq 7.8$ )	20	40.0
Mean $\pm$ SD	7.60 $\pm$ 1.77	
Range	4.30-13.40	
<b>USG of lower abdomen</b>		
Normal	13	26.00
Abnormal	37	74.0

**Discussion:**

The present study was designed to investigate the associated causes of subfertility in PCOS patients. In this observational study, serum FSH was normal in all 50 (100%) patients. Raised level of serum prolactin was found in 30 (60%), serum LH in 37 (74%) and serum

TSH in 37 (74%) patients. Our study population included both primary and secondary subfertile women.

In our study, we observed that the prolactin level was high (mean $\pm$ SD 64.98 $\pm$ 135.48 ng/ml) in 60% cases, which is concordant with Kalsum and Jalali, where 69.51% of subfertile women suffered from hyperprolactinaemia<sup>6</sup>. Nizam *et al.* also showed that hyperprolactinaemia is a major cause of subfertility, and treatment with drugs which lowers prolactin level showed that 24% infertile women became pregnant<sup>7</sup>. This finding is consistent with ours.

In our study, increased level of serum TSH ( $>4$  iIU/ml, mean $\pm$ SD 9.23 $\pm$ 5.84 iIU/ml) was found in 74% women. This is an indication of subclinical hypothyroidism. In a study by Joshi *et al.* (1993), reproductive history was related chronologically to symptoms and signs of thyroid dysfunction. Reproductive failure (infertility, pregnancy wastage, lactation failure) occurred in 45% of cases with menstrual abnormality, which was antecedent to other clinical features by a variable period of two months to ten years. Reproductive failure also precedes thyroid dysfunction which is concordant with the present study. This finding is also consistent with the study by Hollowell *et al.* (2002), who found women with both clinical and subclinical hypothyroidism in early pregnancy and found miscarriage rate was higher in both groups and treatment with hormones could reduce the miscarriage risk<sup>8</sup>. These findings are also consistent with the findings by Trokoudes *et al.* who found subclinical hypothyroidism is associated with ovulatory dysfunction and adverse pregnancy outcome<sup>9</sup>.

Present study is also similar to a case control study by Joshi *et al.* (1993), who found 34% subclinical thyroidism was associated with infertility and pregnancy wastage. Elder (2007) in his cohort study found 20.5% infertile women had associated subclinical hypothyroidism<sup>10</sup>. Yasmin *et al.* showed an association between subclinical hypothyroidism and infertility. One quarter (25%) of the infertile group had subclinical level of serum TSH ( $>5$  mIU/L) compared to 10% of the control group ( $P<0.05$ ). Computation of risk ratio revealed that the infertile group had 3 times (1.3-6.6) higher risk of being subclinically hypothyroid than that of the control group ( $P<0.01$ )<sup>11</sup>.

**Conclusion:**

The present study was carried out to find out an association of other factors for subfertility in women

suffering from PCOS. In this study we found that hyperprolactinaemia and subclinical hypothyroidism were the other associated causes of subfertility. In the light of our findings it is recommended to undertake further large scale study to find out whether therapy with thyroxine and drugs for decreasing levels of prolactin increases the fertility rate in women suffering from PCOS.

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