PITUITARY GONADOTROPIC HORMONES IN WOMEN WITH OLIGO/AMENORRHOEA

Anwer Sultana, Shehnaz Nadir

Department of Gynaecology Obstetrics, Khyber Teaching Hospital, Peshawar, Pakistan

Background: Any abnormality of menstrual cycle makes women worried and requires proper evaluation. Oligomenorhea is one of the indicators of Polycystic Disease of the Ovary (PCO) which is associated not only with reproductive failure but it also has metabolic and cardiovascular complications. The recent study was conducted to find out the role of Pituitary Gonadotropins in the diagnosis. After diagnosing and finding out the cause for menstrual irregularities and chronic anovulation one can explain the prognosis and management of these disorders. **Methods**: Fifty patients were studied in the year 2005-06 in the outpatient department of Khyber Teaching Hospital Peshawar. A history Performa was duly completed in all subjects. Blood sample was collected for hormonal essay during first ten days of the cycle. Hormonal essay was performed by Microparticle enzyme immunoassay (MEIA) on AXSYM system of Abbott. **Results**: Age ranged from 13–45 years, 82% of the women were infertile, 60% had infrequent periods and 22% of the women had amenorrhea, 30% patients were overweight while 48% were obese. Physical examination revealed hersuitism in 24%, acne in 8% and galactorrhea in 6% of the patients. Ultrasound examination showed classical picture of PCO in 28% patients while 32% women had multiple small follicles and 16 % women were devoid of follicles. Elevated LH levels were found in 36% women. FSH level were found normal in 64% patients while in 16% women the levels were in menopausal range. LH/FSH ratio of more than two was observed in 52% women. Prolactin level was raised in 22% women. TSH level was below normal in 16% and higher in 22% women. **Conclusion:** Hormonal essays are mandatory in the evaluation of women presenting with Oligomenorhea/amenorrhea and chronic anovulatory infertility for finding out the cause and explaining the prognosis of the disease to the patient.

Keywords: Infertility, Gonadotrophins, PCO

INTRODUCTION

Irregular menses and/hersuitism, once thought to be of harmless occurrence, are no more considered to be benign.[1] Normal menstrual cycle indicates an overall reproductive health and its abnormalities requires evaluation.[2] Oligomenorhea and amenorrhea generally means anovulation and cause infertility. To find out the cause for irregular, infrequent cycles, with chronic anovulation, hormonal studies need to be carried out.[3]

Menstruation is dependent on the proper functioning of the chain made up of Hypothalamus-Pituitary-Ovary and uterus. Pituitary hormones, Follicle stimulating hormone (FSH), Leutinizing Hormones (LH), Prolactin and thyroid hormones are required for normal development of ova and need to be investigated in cases of chronic anovulation, oligomenorhea and amenorrhea.[4]

Chronic anovulation, oligomenorhea, amenorrhea, hyperandrogenism are features of Polycystic Ovarian syndrome. This syndrome is now recognized to be associated with obesity and insulin resistance, Type-II diabetes mellitus, dyslipidemia, hypertension, cardio-vascular disease and endometrial hyperplasia..[5,6]

Abnormal gonadotrophins particularly increased mean LH level is one of the common features of PCO. Follicle stimulating hormone may be low or normal. There is elevated LH/FSH ratio.[7]

This study was carried out to know the causes of infertility due to chronic anovulation, amenorrhea and to find out the role of studying Pituitary Hormones in those situations. We also wanted to know the role of these hormones in the diagnosis of PCO because pituitary dysfunction is also one of its features. By knowing the diagnosis we can better explain the prognosis and advise patients, the need for life style change in order to prevent the complications of the disease.

MATERIAL AND METHODS

This study was carried out from first January, 2005 to December, 2006 in outpatient clinic of Khyber Teaching Hospital (KTH), Peshawar. It is a descriptive type of study. The outpatient consultant clinic of KTH receives referred cases from general outpatient clinic. My consultant clinic was every week on Thursday.

In this study those patients who presented with infertility, amenorrhea, infrequent or scanty regular periods were included. Infrequent periods are defined as a cycle of more than 6 weeks. The term amenorrhea indicates no menses for more than 6 months. By scanty period we mean using less than one pad per day. Infertility was considered when the patient could not conceive in spite of her own regular unprotected marital relations for at least one year. Those unmarried patients with amenorrhea, obesity and hersuitism were also included in the study. Those infertile patients who had other reason for infertility like tubal blockade, male factor and systemic disorder like chronic disease were

excluded from the study. The age group 13–45 year was included in study. Women with primary amenorrhea were excluded from the study. Obesity was calculated according to body mass index (BMI). During detailed examination the hair distribution on the body, chin, chest, abdomen, and perineum was recorded on Performa. A History Performa was duly completed in each case with thorough examination. Written consent was obtained in each case to be included in the study. Following investigations were carried out in each case.

1. Follicle Stimulating Hormone (FSH)
2. Leutinizing Hormone (LH)
3. Serum Prolactin
4. Thyroid Stimulating Hormone (TSH)
5. Ultrasonography for Ovarian morphology.

The hormonal essay was performed in the first ten days of the cycle. For women with amenorrhea care was taken that they had not taken any hormones or withdrawal bleeding for at least six weeks before the essay. The hormone essay was performed by Microparticle enzyme immunoassay (MEIA) on AXSYM System of Abbott.

Serum Prolactin was reported in ηg/ml. Normal range was taken as less than 20 ηg/ml. Thyroid stimulating hormone was reported in μIU/ml. The normal range was 2–5 μIU/ml.

RESULTS

Total number of patients studied during two years was 50 who agreed to participate in the study. Twenty five patients refused to enter the study and some of them did not complete the investigations and hence could not be included in the study. Some of them wanted to take medicines for their complaints and refused to undergo investigations.

Age distribution of patients is presented in Table-1. Normal cycles were reported in 9 (18%) women, infrequent periods were reported by 30 (60%) of patients while 11 (22%) had amenorrhea. Scanty periods were present in 32 (64%) women and 6 (12%) women had heavy bleeding (Table-2).

Six women (12%) were underweight, 15 (30%) women were overweight, while 19 (38%) women were obese. Five women (10%) were having BMI of over 40 (Table-3).

Physical examination revealed that 12 (24%) women had hersuitism at different sites on the body, four (8%) had acne and 3 (6%) had galactorhea (Table-4). Ultrasound findings on morphology of ovaries are tabulated in Table-5.

Follicle stimulating hormone (FSH) level was in the normal follicular range in 34% women. Menopausal range of above 40 mIU/ml was observed in 8 (16%) women (Table-6). LH/FSH ratio was found higher in majority of cases. The ratio of 1:2 was observed in 22% women and a ratio of 1:3 was observed in 30% women.

Thyroid Stimulating Hormone levels are shown in Table-7. Prolactin levels were raised in 7 (14%) while one (2%) women had levels higher than 200 ηg/ml (Table-8).

Table-1: Age distribution

Age (Years)	Number of Cases	%age
13–20	8	16%
20–35	32	64%
36–40	8	16%
>40	2	4%

Table-2: Presenting symptoms of patients

	No.	Percentage
A. Infertility		
Primary	26	52.00
Secondary	15	30
B. Cycle		
Normal	9	18
Oligomenorrhoea	30	60
Amenorrhea	11	22
C. Amount of Bleeding		
Normal	12	24
Scanty	32	64
Heavy	6	12

Table-3: Body mass index (BMI)of women.

Body Mass Index	Number of Cases	%age
10–20	6	12%
21–25	5	10%
26–30	15	30%
31–40	19	38%
>40	5	10%

Table-4: Signs of hormone dysfunction in women.

Signs	No. of Cases	%
Galactorhea	3	6%
Androgenism	12	24%
Hair on Breast	1	
Facial Hair	5	
Abdominal Hair	2	
Acne	4	

Table-5. Ovarian Morphology on Ultrasound.

Findings on Ultrasound	No. of Cases	%age
Normal	10	20%
Polycystic Ovary	32	64%
Few or no follicle	8	16%

Table-6: showing LH, FSH levels & their ratio

	LH (μIU/ml)		FSH(μIU/ml)		Ratio		
	No.	%	No.	%		No.	%
<2	0	0%	3	6%	1:1	11	22%
2–10	15	30%	22	44	1:2	13	26%
11–25	17	34%	17	34%	1:3	14	28%
25–50	13	26%	0	0%	>3	12	24%
>50	5	10%	8	16%			

Table-7: Levels of thyroid stimulating hormones

TSH Level (μIU/ml)	Number of Cases	Percentage
<2	8	16%
2–5	30	60%
>5	12	24%

Table-8: Prolactin levels in women

Prolactin Level	Number of Cases	Percentage
0–20	39	78%
20–100	7	14%
100–200	3	6%
>200	1	2%

DISCUSSION

Irregular, infrequent periods are quite embarrassing for women. Their periods are unpredictable, sometimes heavy and painful. Women with infrequent cycles are at three fold risk of endometrial carcinoma.[8]

Infrequent periods (oligomenorrhoea and amenorrhoea) are also associated with infertility due to chronic anovulation. Various factors collectively play role in the process of child bearing and chronic anovulation. In the present era of developing technology emphasis has now changed from diagnosis to explaining prognosis.[9]

We found that 16% of our women had menopausal level of FSH. However in order to prove this diagnosis of primary ovarian failure FSH level need to be repeated. FSH levels are higher in resistance ovarian syndrome, which occurs, very rarely in younger menstruating infertile women. It is only distinguished from primary ovarian follicle by intermittent resolution of the ovaries and normalization of FSH levels.[10]

Polycystic ovarian syndrome has been said to be due to ovarian dysfunction and its prevalence range is 8-33% in different ethnic groups. Menstrual irregularities, hyperandrogenism and obesity are its cardinal features. In our study obesity was found in 78% of the patients which corresponds to the findings of Balen *et al.*[11]

According to the NIH criteria for diagnosing PCO 1990[8,12] ovarian sonography was not included in the criteria. However non US experts are continuing to use sonography for the diagnosis of PCO because of the subjectivity of hersuitism and insensitivity of the androgen assays.[13]

Ultrasonographic evidence of PCO was found in 22% of 257 healthy women. In that study however the irregular menses and hersuitism were found to be at higher rates in association with PCO compared with normal ovaries.[14]

Elevated LH/FSH ratio, a cardinal feature of PCO is no more considered to be the diagnostic test for PCO. It has been shown in one study that variability in LH/FSH ratio is at least as large for normal women as it is for those with clinical PCO and has little diagnostic value.[15]

In spite of the attempts to reach consensus on diagnosing PCO, only minority of endocrinologists/gynaecologists adhered to National Institute of Health or Rotterdam diagnostic criteria. This was because two groups were approaching different subgroups of heterogeneous population.[16]

According to NIH criteria both androgenism and ovarian dysfunction need to be present while in Rotaderm consensus 2003, PCO was considered a syndrome of ovarian dysfunction, hyperandrogenism and PCO morphology. In our study we could not measure the androgens because of the heterogeneity of this differential. Therefore we cannot include or exclude PCO on this evidence.

Hyperprolactinaemia is a common endocrine disorder with an incidence of 9–17%.[17,18] Increased Prolactin and TSH levels are also the feature of PCO. Our patients however did not report with visual symptoms or headache. Thyroid hormones were raised in 6% women though no clinical features of the disease were present. Aykut Bayrak *et al* have reported the incidence of 1.9% for hypothyroidism in his study on Hyperprolactinaemic women.[19]

CONCLUSION

in the present study we were able to diagnose hyperprolactinaemia, menopause and thyroid disorders in ladies presenting with Oligomenorrhoea/amenorrhoea and infertility and hence for proper management and prognosis, the women with these disorders we need to do baseline pituitary hormones levels as a first line investigations in the first ten days of the cycle to reach the diagnosis. Because of the controversies in the diagnosis of PCO, ultrasound should be included as one of the investigation in the evaluation of women with menstrual disorders and infertility. As the women with PCO are at increased risk of diabetes, dyslipidemia and cardiovascular complications, they need life style changes to prevent the complications of PCO.

REFERENCES

1. Michael T, Sheehan MD Polycystic ovarian Syndrome: Diagnosis and management Clin Med Res 2004;2(1):13–27.
2. Adams-Hillard, PJ, Deitch, HR. Menstrual disorders in the College age females. Pediatr. Clin North Am 2005;52:179–97.
3. Infertility and sub fertility. In: Jeffcoate's Principles of Gynaecology Victor Tindall Ed. 5th ed. Butterworth–Heinemann Ltd: Oxford; 1987. p587–597.
3. Amenorrhea: Scanty and Infrequent menstruation. In: Jeffcoate's Principles of Gynaecology. Victor Tindall Ed. 5th ed. Butterworth – Heinemann Ltd: Oxford; 1987. p 495–511.
4. Carmina. E and Lobo R.A. Polycystic ovary syndrome Arguably the most common endocrinopathy is associated with Significant morbidity in women. J Clin Endocrinol Metabolism 1999,84:1897–9.
5. Duhlgren E, Janson PO, Johansson S, Lapidus I, Oden A. Polycystic Ovary Syndrome and risk for myocardial Infarction. Evaluated from, A risk factor model based on a prospective population study of women. Acta Obstetricia Gynecologica Scandinavica 1992;71:599–604.
6. 7. Waldstreicher J. Santoro NF, Hall JE, Filicori M, Crowley WF. Jr. Hyperfunction of the hypothalamus–Pituitary axis in women with polycystic ovarian disease: Indirect evidence for partial gonadotrophic desensitization. Clin Endocrinal Meta. 1988;66:165–72.

7. Zawadski, JK, Dunaif, A. Diagnostic criteria for Polycystic ovarian syndrome: towards a rational approach. In: Polycystic Ovary Syndrome A. Dunaif. JR, Givens, FP, Haseltine GR, Merriam eds, Blakwell: Boston; 1992. p 337–84.
8. Rana, S. Controlled Ovarian Stimulation: The present strategies. Pak J Obstet Gynecol 2005;13(1):1–4.
9. M.G. R Hul, Ovarian failure an induction. Progress in obstetric and Gynecology Vol. 4. John Studd ed. London: 1984. p 272–8.
10. Balen A, Michelmore K. What is Polycystic Ovary Syndrome? Are National Views important? Human Reprod 2002;17:2219–27.
11. The Rotterdam ESHRE/ASRM-Sponsored PCO consensus workshop group. Revised 2003 consensus on diagnostic criteria and long term health risks related to Polycystic Ovary Syndrome. Fertil Steril 2004;81:19–25.
12. Gilling–Smith C, Willis DS, Beard RW Fr, Fanks S. Hypersecretion of adnrostenedione by isolated theca cells from polycystic ovaries. J Clin Encrinol Metab 1994;79:1158–65.
13. Polson D.W, Adams J, Wadsworth J. Franks, S. Polycystic ovaries–A common Finding in normal women. Lancet 1988;1:870–2.
14. Li Wei Cho, Jayagopal V, Kipatrick E S, Holding S and Atkin SL. The LH/FSH ratio has little use in diagnosing polycystic ovarian syndrome. Ann Clin Biochem 2006;43:217–9.
15. Cusson A.J, Stuckey BGA, Walsh JP, Walsh JP, Burke V, Normans RJ. Polycystic ovarian syndrome; Marked difference between Endocrinologists and gynaecologist in diagnosis and management. Clin Endocrinol 2005;62:289–95.
16. Miyia K, Ichihara K, Kondo K, Mori S. Asymptomatic hyperprolactinaemia and prolactinoma in general population: mass screening by paired assays of serum prolactin. Clin Endocrinal 1986;43:549–54.
17. Biller BM, Luciano A, Crosignani PG, Molitch M, Olive D, Rebar R, *et al*. Guidelines for the diagnosis and treatment of hyperprolactinemia. J Rep Med 1999; 44(12 Suppl):1075-84.
18. Bayrak. A, Saadat P, Mor E, Paulson RJ, Rebecca Z. Pituitary imaging is indicated for the evaluation of hyperprolactinemia. Fertility and sterility 2005;84:181–5.

Address for Correspondence:

Dr. Anwer Sultana, 15-Aabdara Road, University Town, Peshawar. Tel: +92-91-5842263