CLINICAL PROFILE OF WOMEN WITH PREMATURE OVARIAN INSUFFICIENCY ATTENDING A TERTIARY CARE CENTER: A CROSS SECTIONAL STUDY

Gynaecology

Anupama Bahadur	D.N.B, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Rishikesh, India.
Rajlaxmi Mundhra*	M.D, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Rishikesh, India. *Corresponding Author
Aditi Jindal	M.D, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Rishikesh, India.
Latika Chawla	M.D, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Rishikesh, India.
Kavita Khoiwal	M.D, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Rishikesh, India.
Amrita Gaurav	M.D, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Rishikesh, India.

ABSTRACT

Introduction: Premature ovarian insufficiency (POI) is a depletion of normal ovarian function before age of 40 years accompanied by cessation of menstruation. A couple must be counseled on the effect of POI on future fertility and once diagnosed a woman needs to be evaluated annually. She requires hormone replacement therapy for bone support, cardiovascular and sexual health.

Material and methods: A prospective study was conducted in department of Obstetrics and Gynecology at AIIMS Rishikesh from November 2016 to November 2018. We studied the sociodemographic profile, etiology, clinical presentation of 30 patients presenting with POI. Women less than 40 years of age with amenorrhea lasting for four months with two FSH levels in menopausal range (> 40 mIU/ml) obtained atleast one month apart were included in the study.

Results: 18 (60%) women presented with amenorrhea between 1 to 2 years. 17 (56.67%) women belonged to urban region and 13 (43.33%) resided in rural area. 22 (73.3%) women had infertility of which 17 (77.27%) had primary infertility and 5 (22.72%) had secondary infertility. For the rest 8 (26.66%) women hypoestrogenic symptom, including vasomotor was the major concern.

Conclusion: When POI is diagnosed in adolescent females, patient and her family are often unprepared for such news and its implications are compromised fertility and impaired self-esteem as well as long term hormonal therapy. As clinician we should be mindful of the sensitive nature of this medical condition.

KEYWORDS

hormone replacement therapy, premature ovarian insufficiency, infertility

INTRODUCTION:

Premature ovarian insufficiency (POI) previously known as premature ovarian failure (POF) is characterized by accelerated depletion of ovarian follicles causing oligomenorrhoea or amenorrhoea in women less than 40 years of age and is associated with raised gonadotropins. There has been considerable debate regarding the most suited nomenclature. Premature ovarian insufficiency has replaced all other nomenclatures since it encompasses the more unpredictable and sometimes intermittent nature of the disorder. Ovulation and at times pregnancy has also been reported in women diagnosed with POI [1]. Worldwide prevalence of POI is approximately 1% wherein ethnicity may affect the prevalence [2].

Ovarian dysfunction contributes to POI and has been classified into two types (spontaneous and iatrogenic) according to mode of onset [3]. In spontaneous POI, onset is insidious while in iatrogenic POI (following oophorectomy, chemotherapy, radiotherapy) onset is sudden and anticipated by clinician and patient. This division may actually not be necessary since endpoint of both is decreased circulating sex hormones. Iatrogenic POI is diagnosed and treatment is initiated earlier as compared to spontaneous POI.

The main cause of POI is not always depletion of follicles. It may also occur in women harboring mutations in the Follicular Stimulating Hormone receptor (FSHR), where follicles may be present in ovary in adequate number [1]. However, the etiopathogenesis of the disease in most cases remains unexplained. Factors contributing to POI include genetic abnormalities, metabolic disorders, autoimmunity, iatrogenic causes and environmental factors amongst many others [4].

The clinical presentation is variable with around 10 % of patients presenting with primary amenorrhoea, while the rest may have late onset menstrual irregularity after an uneventful pubertal development. Some women may even present with hypoestrogenic symptoms. In a

sub fertile couple it has been observed during investigation that POI may be a contributing factor. Patients may ignore their complaints leading to a delay in diagnosis and treatment causing various health consequences of estrogen deficiency including loss of bone mineral density, cardiovascular problems and psychosexual dysfunction.

Any woman diagnosed with POI requires a sensitive approach to her physical and emotional needs. Hormonal therapy helps in regaining menstrual cycles, addresses bone health and helps in building self-esteem.

The aim of this study was to identify sociodemographic profile, clinical presentation and probable etiology in patients with POI.

MATERIAL AND METHOD:

This was a prospective study conducted over a period of two years from November 2016 to November 2018 in Gynecology outpatient department at a tertiary centre in Uttarakhand India. Women less than 40 years of age with amenorrhoea of more than 4 months with two FSH levels in menopausal range (> 40 mIU/ml) obtained over a month apart and who gave consent for participation were included in the study. On initial evaluation a urine pregnancy test was done in all women with amenorrhoea. Once pregnancy was ruled out serum FSH and ultrasound was performed to exclude polycystic ovarian syndrome.

Patients recruited in the study were classified based on their sociodemographic profile including age at presentation, region and socioeconomic status. Varied clinical presentations and the probable etiology was documented. However, genetic testing could not be done as it was not available in our Institute.

RESULTS:

A total of 30 patients fulfilled the inclusion criterion and were enrolled in the study. Table 1 depicts the sociodemographic factors of women

included in the study. 18 (60%) women with POI were in age group of more than 30 years at the time of presentation. 17 (56.67%) women belonged to urban region and 13 (43.33%) resided in rural area. Majority of women (13) were from upper lower class while 12 women belonged to middle class.

Table 2 depicts presenting symptoms of patients. 18 (60%) women presented with amenorrhea between 1 to 2 years. 22 (73.3%) women had infertility of which 17 (77.27%) had primary infertility and 5 (22.72%) had secondary infertility that was their primary concern. In subfertile women on evaluation of the cause of infertility revealed POI. For the rest 8 (26.66%) women hypoeostrogenic symptom, including vasomotor was the major concern.

In Table 3 probable etiology has been discussed. In 19 (63.34%) women cause remained unknown. 3 women had history of ovarian surgery done for endometriosis and ovarian drilling for polycystic ovaries. 1 woman had history of radiation exposure for lymphoma while 2 had autoimmune thyroiditis. In 2 out of 30 subjects there was family history of POI in first-degree relative.

Table 1: Demographic profile

	Number of subjects(n=30)	Percentage %
Age at presentation		
<20 years	2	6.67%
20- 29 years	10	33.33%
30- 40 years	18	60%
Residence		
Rural	13	43.33%
Urban	17	56.67%
Socioeconomic status		
Upper	1	3.33%
Upper Middle	3	10%
Lower Middle	9	30%
Upper Lower	13	43.33%
Lower	4	13.33%

* Socioeconomic status was calculated on basis of occupation, education and income and classified into five classes.

Table 2: Presenting symptoms

	Number of subjects(n=30)	Percentage %
Duration of amenorrhea		
6 months- 1 year	7	23.33%
1 year - 2 year	18	60%
> 2 year	5	16.67%
Presenting symptom		
Infertility		
Primary infertility	17	56.67%
Secondary infertility	5	16.67%
Hypoeostrogenic symptoms	8	26.66%

Table 3: Probable Etiology

	Number of subjects(n=30)	Percentage %
Idiopathic	19	63.34%
Environmental factors(Smoking, pesticide exposure, chemical exposure)	4	13.33%
Iatrogenic	3	10%
Familial predisposition	2	6.67%
Autoimmune thyroiditis	2	6.67%

DISCUSSION:

In the present study 18 (60%) women had amenorrhea lasting between 1 to 2 years. In the initial years presentation may include menstrual irregularity, which perhaps goes unrecognized. It is only when amenorrhea sets in for varying periods that becomes worrisome enough for the patients to seek medical help. In a study by Alzubaidi et al 92 % patients had disturbance in menstrual pattern as the most common initial symptom [5]. The authors reported that over half of the patients had seen three or more clinicians before a diagnosis of POI was made and in a quarter them it took more than 5 years to establish the diagnosis [1,5]. In our study 18 patients had visited more than two clinicians. A vast majority of patients in our study presented with infertility.

Patients who belonged to the rural area mainly resided in the hilly region of Uttarakhand. In them high altitude may perhaps be a contributing factor. This cause needs to be further elucidated in a larger population from this region.

In our study 63.34%, the etiology of POI was idiopathic. However, iatrogenic causes of POI are on the rise and were seen as a contributing factor in 10% of women in our study. Better survival of childhood malignancy is an important contributory factor. In separate studies by Chemaitilly et al and Sklar et al it was observed that depending on the type of chemotherapy used and age at diagnosis of malignancy the incidence of acute ovarian insufficiency is 6.3% and another 8% developed POI in the lifetime [6,7] In a study by Kasteren et al [8] it was estimated about 10-15% women with POI had a first degree relative suffering from POI. The results were similar in our study where 10% had a first degree relative with similar complaints.

Before making a diagnosis of POI all secondary causes of amenorrhea must be ruled out including pregnancy, polycystic ovarian syndrome, hypothalamic and pituitary lesion and thyroid disorders.

Small sample size and a short duration of study were the major drawbacks of this study. Additionally, blood analysis for immunological disorders and genetic evaluation could not be done.

CONCLUSION:

POI is a life changing diagnosis causing emotional distress and impaired self-esteem in women. These patients may not be emotionally prepared for this eventuality in their lives. They should be explained about the long-term consequences of the disease. As clinicians the psychological aspect of the disease should be well understood and such women should undergo counseling regarding long term health related issues due to POI, regarding HRT and should also be offered psychological therapy if needed. Patients with POI should be followed up annually.

ACKNOWLEDGEMENT:

There is no financial support in this study. All authors certify they have no conflict of interest.

REFERENCES:

1. Maclaran K, Panay N. Current concepts in premature ovarian insufficiency. *Womens Health* 2015 11(2), 169–182.
2. European Society for Human Reproduction and Embryology (ESHRE) Guideline Group on POI, Webber L, Davies M, et al.: ESHRE Guideline: management of women with premature ovarian insufficiency. *Hum Reprod.* 2016; 31(5): 926–37.
3. Torrealday S, Kodaman P, Pal P. Premature Ovarian Insufficiency - an update on recent advances in understanding and management. *F1000Research* 2017, 6(F1000 Faculty Rev):2069.
4. Rudnicka E et al. Premature ovarian insufficiency – aetiology, epidemiology, and diagnostic evaluation. *Prz Menopauzalny*. 2018 Sep; 17(3): 105–108.
5. Alzubaidi NH, Chapin HL, Vanderhoof VH et al. Meeting the needs of young women with secondary amenorrhea and spontaneous premature ovarian failure. *Obstet. Gynecol* 2002; 99, 720–725.
6. Kaump GR, Spies JB. The impact of uterine artery embolization on ovarian function. *J. Vasc. Interv. Radiol.* 24, 459–469 (2013).
7. Chemaitilly W, Mertens AC, Mitby P et al. Acute ovarian failure in the childhood cancer survivor study. *J. Clin. Endocrinol. Metab* 2006. 91, 1723–1728.
8. Sklar CA, Mertens AC, Mitby P et al. Premature menopause in survivors of childhood cancer: a report from the childhood cancer survivor study. *J. Natl Cancer Inst* 2008. 98, 890–896.
9. van Kasteren YM, Hundscheid RD, Smits AP, Cremers FP, van Zonneveld P, Braat DD. Familial idiopathic premature ovarian failure: an overrated and underestimated genetic disease? *Hum. Reprod* 1999. 14, 2455–2459.