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Original Research Article

Premature ovarian failure incidence, risk factors and its relation to BMI and infertility

Smita Baheti[1]*, Anjana Verma[1], Medhavi Sharma[2]

[1]Department of Obstetrics and Gynaecology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India
[2]Department of Obstetrics and Gynaecology, Pacific Medical College and Hospital, Jodhpur, Rajasthan, India

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***Correspondence:**
Dr. Smita Baheti,
E-mail: smitasomani123@gmail.com

ABSTRACT

Background: Premature ovarian failure (POF) is cessation in the normal functioning of the ovaries in women younger than age 40 years. It is estimated to affect1% of women younger than 40 years and 0.1% of those under 30 years. Premature ovarian failure is a common cause of infertility in women.
Methods: Patient attending outpatient Department of Obstetrics and Gynecology with age less than 40 years and complaint of menstrual disturbances, symptoms of menopause were enrolled for the study for duration of 1year. This study is planned to calculate the incidence, risk factors, relation to BMI and infertility in patients attending outpatient department at Geetanjali medical college and hospital, Udaipur for all enrolled patient coming with complaints of menstrual disturbances. FSH levels were send for all the patients and those with FSH level more than 20 at day 2/3 for menstruating women and random FSH level for amenorrhea patient more than 20 were classified in to study group and all those women with FSH less than 20 are taken as control group.
Results: Present study strongly suggests that simple laboratory test FSH and symptoms of missed and irregularity of menstrual cycle help in early and prompt diagnosis of premature ovarian failure. And early diagnosis helps in avoiding unnecessary medications and helps in improving long term morbidity.
Conclusions: Disturbances in menstrual cycle like amenorrhea and infrequent cycles are the symptoms which are associated with premature ovarian failure after ruling out pregnancy and other hormonal and structural causes.

Keywords: Hypo-oestrogenism, Infertility, Premature ovarian failure, Primary amenorrrhoea, Secondary amenorrrhoea

INTRODUCTION

Premature ovarian failure (POF) is cessation in the normal functioning of the ovaries in women younger than age 40 years.[1,2] Overall, POF is responsible for 4-8% of cases of secondary amenorrrhoea and 10-28% of primary amenorrrhoea. It is estimated to affect1% of women younger than 40 years and 0.1% of those under 30 years.[3] Based on elevated FSH before the age of 40 years 0.9% of women will experience POF.[3] Premature ovarian failure is a common cause of infertility in women, and is characterized by amenorrhoea, hypo-oestrogenism and elevated gonadotrophin level in women under the age of 40. Known causes for POF are spontaneous in which no cause is identified other are due to auto immune (increased risk of having adrenal failure, thyroid failure, hypothyroidism), genetic disorder, cancer therapy, galactosemia, infectious agent (mumps, shigella, malaria, varicella).

Symptoms and presentation of POF depends on age as well as timing and rapidity of loss of ovarian function. POF before puberty do not experience the classic symptoms of oestrogen deficiency as loss of oestrogen appears to be necessary for development of symptoms. Young women who develop POF after puberty frequently experience hot flushes, night sweat, fatigue, mood changes, vaginal dryness and discomfort.

This study is planned to calculate the incidence, risk factors, relation to BMI and infertility in patients attending outpatient department at Geetanjali Medical College and Hospital, Udaipur for all enrolled patient coming with complaints of menstrual disturbances.

METHODS

Patient attending outpatient department of obstetrics and gynecology with age less than 40 years and complaint of menstrual disturbances, symptoms of menopause were enrolled for the study for duration of 1year from February 2016 till January 2017. FSH levels were send for all the patients and those with FSH level more than 20 at day2/3 for menstruating women and random FSH level for amenorrhic patient more than 20 were classified in to study group and all those women with FSH less than 20 are taken as control group. Further history of symptoms if present, demographic profile, family history, fertility history and any other illnesses such as autoimmune diseases were taken.

Exclusion criteria

- Women more than 40 years
- Primary amenorrrhoea
- Dysfunctional and organic causes of menstrual disturbances
- Secondary amenorrrhoea due to chemotherapy and radiotherapy.

Statistical analysis

There are different statistical methods for testing hypothesis. Based on these facts and with the help of biostatistician the statistical calculations for the present study involved the following tests. Incidence = no. of patient diagnosed to be premature ovarian failure % total no. of patient enrolled for study. For statistical analysis following methodology was applied percentage proportion. Chi square test SPSS 11.5 version. Once the values of chi square-tests are calculated the corresponding values of 'p' will be obtained using the standard tales are per degree of freedom and the significance graded as:

CL-p value: Results significance
95%-<0.05: Statistically significant
99%-<0.01: Highly significant
99.99%-<0.001: Very highly significant

RESULTS

Incidence of premature ovarian failure came out to be 3.62% which is slightly higher than the study primarily based on elevated FSH before the age of 40 years. Age group between 35-40 years have significant increase in risk of premature ovarian failure (p value <0.00001).

Table 1: Distribution of cases according to age in different groups.

Age group (years)	Case (26)		Control (65)	
	No.	%	No.	%
19-24	02	7.69	40	61.54
25-29	02	7.69	10	15.34
30-34	07	26.92	10	15.34
35-40	15	57.69	05	7.69

P value for age between 35-40 is<0.00001 which is highly significant

Based on present study we found significant association between amenorrrhoea (>6month) with premature ovarian failure (p value < 0.0009).

Table 2: Distribution of cases according to menstrual symptoms.

Menstrual symptoms	Case (26)		Control (65)	
	No.	%	No.	%
Irregular menses	06	23.07	35	53.84
Delayed menses	06	23.07	15	23.07
Amenorrrhoea	14	53.84	15	23.07

P value for amenorrhea <0.0009 which is highly significant

In present study there was no significant association seen between infertility (nulliparous) with premature ovarian failure.

Table 3: Distribution of cases according to association of POF with infertility.

Infertility	Case (26)		Control (65)	
	No.	%	No.	%
Present	10	38.46	20	30.76
Absent	16	61.53	45	69.23

P value >0.015which is insignificant

Based on present study we found significant association between higher BMI and premature ovarian failure (p value 0.004).

Table 4: Distribution and association of POF with BMI.

BMI	Case		Control	
	No.	%	No.	%
Normal (20-25)	12	46.15	50	76.92
Overweight+ obese (>25)	14	53.84	15	23.07

P value for BMI is 0.0044 which is highly significant

In present study we found significant association between endocrinal problems and autoimmune problems like diabetes type1, thyroiditis, systemic lupus erythromatosis, polyendocrine autoimmunity (p value< 0.0002).

Table 5: Association of POF with endocrinal and autoimmune disorder.

(Endocrinal and autoimmune problems)	Case		Control	
	No.	%	No.	%
Present	07	26.92	45	69.23
Absent	19	73.07	20	30.77

P value is < 0.00022 which is highly significant

No significant association was seen between symptoms of menopause like hot flushes, mood changes, irritability, decreased libido this might be because estrogen deficiency loss takes time to set in.

Table 6: Distribution of cases according to symptoms.

Symptoms (hot flushes, night sweat, irritability, vaginal dryness)	Case		Control	
	No.	%	No.	%
Symptoms	23	65.71	45	50
No symptoms	12	34.28	45	50

Chi square value is 2.508, P value is 0.113 insignificant

DISCUSSION

During 1-year study duration period of our study 2509 patients attended gynecology OPD. Out of which 91 were enrolled in the study who were complaining of disturbances in menstrual cycle. Their FSH levels were send, those with follicular stimulating hormone (FSH) more than 20 were grouped as cases of premature ovarian failure (POF) which were 26 and others were taken as control when FSH is less than 20, they were 65. Incidence of premature ovarian failure came out to be 3.62% which is slightly higher than the study primarily based on elevated FSH before the age of 40 years, (Table 1) Coulam et al, estimated that 0.9% of women experienced POF.[3] Likewise, in a population-based study of early ovarian failure by Cramer and Xu et al, the estimated prevalence of POF was 1.2%.[4] In this large study of middle-aged and elderly Chinese women, 2.8% of postmenopausal women experienced menopause before 40 years of age, a lower proportion than that was reported amongst Western women 3.7% (Table 2).[5]

Age group between 35-40 years have significant increase in risk of premature ovarian failure (p value <0.00001). Similar results were seen in spontaneous POI affecting 1% of women by age of 40 years and 0.1% by 30 years.[3] This suggested that as the age advances, factors such as demographic and environmental factors affect ovarian ageing, which needs to be studied in detail over a large population-based study. Based on present study we found significant association between amenorrrhoea (>6 month) with premature ovarian failure (p value <0.0009). Similar results were seen in Progetto menopausal Italian study group where risk of premature ovarian failure was higher in women reporting lifelong irregular menstrual cycle in comparison with women reporting menopause at age equal or more than 45, the odds ratio of premature ovarian failure was 1.3 (95% CI 1.0-1.7).[6] A similar association was found by Hanan et al.[7]

In present study there was no significant association seen between infertility (nulliparous) with premature ovarian failure, which was similar to results seen by Luborsky et al, based on multi-ethnic population study as compared to low parity which was related to earlier natural menopause as studied by Luoto et al, Do et al and Frohlich et al, Gold et al.[8-12]

Based on present study we found significant association between higher BMI and premature ovarian failure (p value 0.004). Similar results were seen by Luborsky et al, who also concluded that mean BMI is higher in cases with premature ovarian failure (Table 4).[8]

In present study we found significant association between endocrinal problems and autoimmune problems like diabetes type1, thyroiditis, systemic lupus erythromatosis, polyendocrine autoimmunity (p value< 0.0002) (Table 5). POF is associated with autoimmune diseases such as diabetes type 1 (Dorman et al), Addison's disease (Winqvist et al), polyendocrine autoimmunity (Myhre et al), and thyroiditis (Falsetti et al, Luborsky et al).[13-17] Alterations in the immune system may induce POF secondary to the deletion of follicles or a disruption of normal ovarian function.[18] It is estimated that 20% of patients with POF have been associated with autoimmune disease, most commonly type I diabetes mellitus, systemic lupus erythematosis (SLE), and rheumatoid arthritis.[19-22]

No significant association was seen between symptoms of menopause like hot flushes, mood changes, irritability, decreased libido this might be because estrogen deficiency loss takes time to set in. Some women with premature ovarian failure presenting with oligomenorrhea have persistent ovarian activity (Table 6).[8]

Limitation of present study was small sample size and single centric study. Further large population based, and longer duration studies are required to study the association and risk factors for causality association.

CONCLUSION

Present study strongly suggests that simple laboratory test FSH and symptoms of missed and irregularity of menstrual cycle help in early and prompt diagnosis of premature ovarian failure. And early diagnosis helps in avoiding unnecessary medications and helps in improving long term morbidity. Based on present study we conclude that disturbances in menstrual cycle like amenorrrhoea and infrequent cycles are the symptoms which are

associated with premature ovarian failure after ruling out pregnancy and other hormonal and structural causes. Spontaneous premature ovarian failure significantly affects the age group of 35-40 years which may result due to age and environmental stress. POI is significantly associated with high BMI and endocrinal and autoimmune diseases.

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