

Premature Ovarian Insufficiency (POI)

Dr Ashraf.Moini.MD

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- ▶ POI is a state in which ovarian function decreases irreversibly beyond the extent of the normal range for the women's age. It can manifest as primary or secondary amenorrhea. In cases with secondary amenorrhea, menstrual cycle changes may precede the amenorrhea.

- ▶ Thus, diagnostic accuracy for POI is low, though early diagnosis is mandatory in the treatment of all phases of problems associated with POI. The diagnosis of POI should be based on the presence of a menstrual disturbance with biochemical confirmation.

Premature Ovarian Insufficiency (POI)

► Definition

Premature ovarian insufficiency (POI) is defined as a cessation of ovarian function before the age of 40 years. It is associated with hypoestrogenism and loss of residual follicles, both of which lead to menstrual abnormalities, pregnancy failures, and decreased health-related quality of life. The prevalence of POI is estimated at 1% in the general population.

Current European Society of Human Reproduction and Embryology (ESHRE) diagnostic criteria include: amenorrhoea or oligomenorrhoea for at least four months and increased follicle-stimulating hormone (FSH) levels > 25 IU/l measured twice (with a four-week interval). The aetiopathogenesis of the disease in most cases remains unexplained.

- ▶ Thus, the most appropriate diagnostic criteria proposed so far are those of the European Society of Human Reproduction and Embryology (ESHRE) POI guideline development group's guideline, which are as follows: oligo/amenorrhea for at least 4 months and elevated FSH levels >25 mIU/ml on two occasions >4 weeks apart.

- ▶ On the other hand, a meta-analysis of the global prevalence of POI found a rate of 3.7% .

ETIOLOGICAL FACTORS

- ▶ **A-**Whereas the cause of POI is unknown in many cases, a familial trait has long been recognized. The prevalence of familial POI has been reported to be 4 to 31% in various studies.
- ▶ **B-**Most of the genetic factors related to the etiology of POI are unknown. The etiological factors known to cause familial POI are chromosomal abnormalities and some gene mutations.

Chromosomal Abnormalities

- ▶ Among the women with abnormal karyotypes and secondary amenorrhea, a significant proportion of patients were older than 35 years at the onset of amenorrhea, so an age limit for testing for chromosomal abnormalities should not be set in diagnosing patients with POI.

Genetics

- ▶ Over 50 genes have been found to be involved in the etiology of POI, and many others have been implicated.

Autoimmunity

- ▶ **A-**POI is frequently associated with autoimmune disorders, more than in the general population, and autoimmune disorders are more frequently seen in POI patients than in the general population.
- ▶ **B-**The autoimmune disorder most frequently associated with POI in our data was hypothyroidism, followed by hyperparathyroidism.
- ▶ **C-**Thus, screening for thyroid (TPO-Ab) antibodies should be performed in women with POI of unknown cause or if an immune disorder is suspected.

Iatrogenic POI

- ▶ **A-** Of the iatrogenic POI cases, 64% occurred following ovarian surgeries.
- ▶ **B-** We found that cystectomy of endometriotic cysts is a potential risk factor for ovarian insufficiency after surgery, with, at times, the onset of ovarian insufficiency long after cystectomy.
- ▶ **C-** Some patients may be unaware that their menstrual disturbance is causally related to the ovarian surgery. Therefore, it is important to monitor ovarian reserve for an extended period of time after ovarian surgery.
- ▶ **D-** It is particularly important to monitor ovarian reserve over the long-term in patients who wish to conceive in the future and to suggest a variety of infertility treatments appropriate for their ovarian reserve.

Radiotherapy and chemotherapy

- ▶ Radiotherapy and chemotherapy used to treat malignant or benign diseases can cause POI
- ▶ The risk of developing POI after radiotherapy is dependent on the radiation therapy field (abdominal pelvic radiation, total body irradiation) and on dose and age
- ▶ In addition, the gonadotoxic effect of chemotherapy is largely drug and dosedependent and related to age
- ▶ Alkylating agents are a typical type of gonadotoxic agent in childhood, as well as in adulthood

Infectious Disease

- ▶ It has been shown in case reports that viral infections can be followed by ovarian failure. However, only mumps oophoritis has been considered to be a cause of POI, accounting for 3-7% of POI cases.

SYMPTOMS AND COMPLICATIONS

- ▶ Vasomotor Symptoms and Psychological Impact
- ▶ Neuro-Psychological Symptoms
- ▶ Urogenital Symptoms
- ▶ Cardiovascular Disease
- ▶ Bone Mineral Density
- ▶ Type 2 Diabetes

CONCLUSIONS

- ▶ The etiology of POI is basically genetic, including chromosomal abnormalities, overlapped by autoimmunity, which is also partly related to genetic causes. In most of the idiopathic cases, the genetic background is unknown.
- ▶ Initially, it was reported that its prevalence was 1%, but some new studies reported 1.8% or higher. Its regional and ethnic differences, which may be related to genetic differences, are still largely unclear.
- ▶ Due to the tendency for late childbearing, infertility caused by POI along with the age-related decrease in ovarian reserve is a serious problem in all developed countries.
- ▶ These attempts are important because they can be generalized to the infertility treatment of age-related diminished ovarian reserve.