

Prevalence of Diminished Ovarian Reserve in Sub-fertile Women Under 40 years of Age

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Submitted for Publication: 12-05-2023
Accepted for Publication: 22-11-2023

How to Cite: Anwar S, Shamsheer S, Saifullah S, Javed A, Bhattani KE, Ahmad S. Prevalence of Diminished Ovarian Reserve in Sub-fertile Women Under 40 years of Age. APMC 2023;17(4):427-430. DOI: 10.29054/APMC/2023.1228

ABSTRACT

Background: Diminished ovarian reserve defined as when woman ovaries lose their reproductive potential in terms of quality and quantity of eggs leading to reduced fecundability and poor ovarian response to stimulation. Female age is most common prognostic element but diminished ovarian reserve is quite common under 40 years old young sub-fertile women. It is best assessed by hormonal tests like FSH and AMH levels. **Objective:** To assess the prevalence of diminished ovarian reserve among sub-fertile women under 40 years age. **Study Design:** Cross sectional study. **Settings:** Department of Obstetrics and Gynecology, Mufti Mehmood Hospital, Dera Ismail Khan Pakistan. **Duration:** One year from January 01, 2022 to December 31, 2022. **Methods:** After meeting the inclusion criteria 593 sub-fertile women were enrolled. FSH level was performed on day 2 or 3 of menstrual cycle. if found more than 10 IU, it was repeated 4 to 6 weeks apart to satisfy the criteria of poor ovarian reserve. The primary outcome was to find the prevalence of diminished ovarian reserve in local population and secondary outcome was to assess the frequency of menstrual cycle pattern and type of subfertility in these women. The prevalence of diminished ovarian reserve and in respect to different age groups, menstrual cycle patterns like oligomenorrhea, and type of infertility (primary or secondary) were presented with frequency percentages. **Results:** The mean age of the females was 35.98 years with 84 (68%) women in age group 36-40.15 woman (12.29%) had amenorrhea of less than 4 months. 62 (50.8%) had oligomenorrhoea with scanty flow while 45 (36.6%) had regular menstrual cycle with normal flow or scanty flow. 92 women (75.4%) had primary infertility while 30 (24.5%) had secondary infertility. **Conclusion:** The prevalence of diminished ovarian reserve was 20% among sub-fertile women under 40 years age with mean age of 35.98 years with highest prevalence in age group 36-40 years. Oligomenorrhoea with scanty flow was the commonest menstrual pattern with more common primary subfertility.

Keywords: Prevalence, Secondary, Primary, Reproduction, Subfertility, Ovarian reserve.

INTRODUCTION

Fertility is a significant concern for many women, and understanding ovarian health is a crucial aspect of reproductive planning. Woman age is an important prognostic element in management of subfertility. With advancing female age, the ovarian follicular pool diminishes and fertility declines.¹

American society for reproductive medicine defines diminished ovarian reserve (DOR) as a reduced

fecundability (chances of conception per cycle) with suboptimal ovarian response to gonadotropin stimulation.² The diagnosis is applicable to women with subfertility who manifest poor ovarian stimulation to ovulation induction. This may cause significant distress among sub-fertile women. Therefore, its overdiagnosis must be avoided by careful interpretation of test result and additional sensitive investigations.³

One of the indicators used to assess ovarian reserve is the level of follicle-stimulating hormone (FSH) in blood. Follicle stimulating hormone is produced by the pituitary gland to stimulate the ovaries to produce mature eggs for ovulation. Women with a healthy ovarian reserve, the FSH level remains relatively low throughout the menstrual cycle. However, when ovarian reserve decreases, the body may produce more FSH to compensate for the diminished number and quality of eggs. To evaluate ovarian reserve, FSH tests involve a simple blood test taken on specific days of the menstruation, typically on day 2, 3, or 4. A higher-than-normal FSH level during these days may suggest a decreased ovarian reserve. While FSH levels can fluctuate from month to month, persistently elevated levels can be a concern.³

In women less than 40 years, a high Follicle stimulating hormone level is indicative with low ovarian reserve, which may impact their ability to conceive. Causes of diminished ovarian reserve are premature ovarian aging due to genetics, medical disorders, autoimmune disease like Hashimoto's thyroiditis or systemic lupus erythematosus and previous ovarian surgery or chemotherapy.⁴ Low ovarian reserve in women under 40, predicted by high FSH levels, is a challenging issue to address. It's essential for women concerned about their fertility to seek consultation from infertility expert about their plan for future reproductive health.⁵

While low ovarian reserve may present obstacles, advances in reproductive medicine offer hope and possibilities for many women who aspire to become mothers, even in the face of this challenge. Low ovarian reserve does not guarantee infertility, but it may significantly reduce a woman's chances of conceiving naturally. It may also lead to a higher chance of abortion.⁶

Options for women with diminished ovarian reserve are Assisted Reproductive Technologies (ART) like IVF, Egg donation with consultation of fertility specialist as women concerned about their ovarian reserve should seek advice from a reproductive endocrinologist who can provide individualized guidance.^{7,8}

Adequate data was not available about the actual prevalence of diminished ovarian reserve in Pakistani population, we aimed to assess the prevalence of DOR among sub-fertile females under 40 years of age attending Mufti Mehmood hospital, a public teaching hospital in Dera Ismail Khan. This will help to find out the real magnitude of problem, associated risk factors, its impact on fertility treatment and long-term health consequences.

The primary outcome measure in this study was to assess the prevalence of diminished ovarian reserve in sub-fertile women under 40 years age.

METHODS

This was a cross sectional study conducted from Jan 2022 to Dec 2022 in Gyn OPD of Mufti-Mehmood Hospital Dera Ismail Khan. A total of 630 sub-fertile women were seen in OPD. All sub-fertile women under age 40 years were included in study. Sub-fertile Women above 40 years of age, women with chromosomal or developmental abnormalities like Turner mosaic or congenital absence of uterus (MRKHS) or who fail to follow up were excluded from study. A total of 593 sub-fertile women below age 40 years were recruited by non-probability consecutive sampling.

A proforma was designed to collect the personal data and demographic data, previous obs. history if any, type of infertility primary or secondary, previous pelvic surgeries, chronic autoimmune diseases or family history of early menopause history was recorded. Menstrual history including oligomenorrhoea, regular cycle with normal flow or scanty flow were recorded. At day 2 or 3 of menstrual cycle FSH level was performed by a standard laboratory and if found more than 10 IU, it was repeated 4 to 6 weeks apart to satisfy the criteria of poor ovarian reserve.

All these women were advised TVS (transvaginal ultrasound) for antral follicle count and AMH level. The primary outcome was to find the prevalence of diminished ovarian reserve in local population and secondary outcome was to assess the frequency of menstrual cycle irregularities and type of subfertility in these women.

The data was entered and analyzed using SPSS version 21. The overall prevalence of diminished ovarian reserve within different age groups were presented with absolute numbers and percentages. Frequency, percentage calculated for menstrual cycle patterns like oligomenorrhoea, and scanty flow or regular cycle with normal flow and type of infertility (primary or secondary).

RESULTS

Out of 630 sub-fertile women presenting in OPD, 593 fulfilled the inclusion criteria. Among them 122 women (20.57%) had diminished ovarian reserve diagnosed by Day 2, 3 FSH level > 10 IU. repeated more than 4 weeks apart. The mean age was 35.98 years.

Among them 7 (5.7%) were in age group 20-30 years, 31 (25%) in age group 31 - 35 years and 84 (68%) in age group 36-40.

15 woman (12.29%) had amenorrhoea of less than 4 months. 62(50.8%) had oligomenorrhoea with scanty flow

while 45(36.6%) had regular menstrual cycle with normal flow or scanty flow.

18 patients went for AMH level which were below 1 IU. 92 women (75.4%) had primary infertility while 30(24.5%) had secondary infertility.

Table 1: Distribution of Subjects with Diminished Ovarian Reserve with Age

Age Group	Number	Frequency
20-30	7	5.7%
31-35	31	25%
36-40	84	68%
Total	122	100%

Table 2: Distribution of Subjects with Diminished Ovarian Reserve with Menstrual cycle Pattern

Menstrual pattern	Number	Frequency
Ammenorhoea <4 months	15	12.29%
Oligomenohoea with scanty flow	62	50.8%
Regular cycle with normal/scanty flow	45	36.8%
Total	122	100%

Table 3: Distribution of Subjects with Diminished Ovarian Reserve and Type of Subfertility

Type of infertility	Number	Frequency
Primary	92	75.4%
Secondary	30	24.5%
Total	122	100%

DISCUSSION

Diminished ovarian reserve is defined when woman ovaries reproductive potential is compromised. Ovarian reserve manifests the number and quality of eggs in both ovaries. The prevalence of DOR ranges from 3.8% to 28.6% in women aged between 20 to 40 years in various studies. It is a more common finding by infertility centers and a reason for poor response in ART.⁹In our study the prevalence was around 20.1% under age 40 yrs.

Our results states that diagnosis of DOR is increasing in sub-fertile women under 40 years age. The possible reasons could be advanced age at marriage, addition of ovarian reserve testing availability and counselling of reproductive health physicians about success of treatment regimens with good ovarian reserve for patients attending infertility clinics.¹⁰

A study conducted about prevalence of diminished ovarian reserve in Korean women of reproductive age using AMH and FSH levels in 2022 demonstrated that it markedly increases with age. They found the prevalence of 3.8%, 6.0%, 11.0%, 28.6%, 69.3%, and 95.0% in women aged 20-24, 25-29, 30-34, 35-39, 40-44, and 45-49 years, respectively. An overall 37.2% and 38.4% was observed for age adjusted prevalence of poor ovarian reserve. These results provide crucial information's about compromised ovarian reserve for use in ART services dealing with challenge of female aging.¹¹

Another study about prevalence of diminished ovarian reserve in Chinese women with follicular cysts and menstruation problems found that DOR was high in women <40 years with follicular cysts and abnormal menstruation pattern. Anti Mullerian hormone (AMH) was suggested as a sensitive marker to define DOR than FSH and Estradiol hormone levels. 117 women were categorized in various age groups and the prevalence was up to 50% in age group less than 40 years which was really alarming. of the Among 117 women, 34.2% were amenorrhic while 65.8% experienced irregular scanty menstruation.¹²

AUS study about diminished ovarian reserve and reproductive technology population found that DOR diagnosis is increasing. Its prevalence increased from 19% to 26% from 2004 to 2011 with basal FSH having greater specificity (92.2% vs. 81.6%) and positive predictive value (38.3% vs. 30.9%) for predicting DOR.¹³

Another study by A. Weld found 48% incidence of diminished ovarian reserve in relatively younger women with repeated pregnancy loss compared with known cause. This was more commonly observed in women younger than 38 years age while less significant in women older than 38 years. (22% vs. 12%, $p = .04$)¹⁴

In our study 57% of the patients had oligomenorrhoea while 42% had regular menstrual cycle with diminished ovarian reserve. A study conducted by Benjamin S Harris, in 2021 found that women whose FSH level is ≥ 10 mIU/mL had 0.32 (95% CI 0.15, 0.71) times the odds of having long menstrual cycles. These findings confirms that biomarkers like AMH and FSH plays a role in ovarian cycle regulation, proliferative and secretory phase lengths. After adjustment with age, they predicted shorter menstrual cycles and early ovulation. This adds to the understanding of reproductive physiology in woman with DOR.¹⁵

Another study conducted by Corry H found high FSH with poor ovarian reserve and higher FSH and LH pulse amplitude. The mean FSH was markedly raised in imminent ovarian failure group (15.4 ± 5.3 IU/l), then in control group (4.4 ± 1.1 IU/l, $P < 0.0001$).¹⁶

Butts et al. noted that although the prevalence of DOR was increasing in younger women but those less than 40 years age undergoing ART procedure had a >21% live birth rate. These comparatively successful ART cycles optimize the overall prognosis of DOR category. Therefore, a structured definition of DOR is needed to avoid over-diagnosis.¹⁷

CONCLUSION

The prevalence of diminished ovarian reserve was 20% in sub-fertile women under 40 years of age with mean age of 35.98 years with highest prevalence in age group 36- 40 years. Oligomenorrhea with scanty flow was the commonest menstrual pattern in these women mostly having primary subfertility.

LIMITATIONS

There were few Limitations of our study. Because of low resource hospital and poor socioeconomic status of sub-fertile women, very few went for confirmation by AMH and serum estradiol level, but still study provides a valuable reflection of diminished ovarian reserve arising at an alarming rate in sub-fertile women presenting in all communities as well as ART centers.

SUGGESTIONS / RECOMMENDATIONS

This study provides a reflection of diminished ovarian reserve in sub-fertile women under 40 years presenting in subfertility clinics with management challenges. More studies are required to assess the risk factors like dietary patterns, smoking, genetic and familial etc. Furthermore, other tests like AMH, serum estradiol levels and antral follicle counts by TVS must be in consideration while labelling a woman with diminished ovarian reserve.

CONFLICT OF INTEREST / DISCLOSURE

None.

ACKNOWLEDGEMENTS

None.

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