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Ovarian Reserve: A Critical Indicator of Female Reproductive Health

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Abstract

Introduction*:* Ovarian reserve, defined as the quantity and quality of a woman's remaining oocytes, is a critical determinant of fertility potential. The finite pool of oocytes established in utero declines progressively throughout life, which is a natural process but may result in diminished ovarian reserve (DOR) in some women. DOR can affect personal and demographic outcomes, as it is closely tied to reduced fertility potential. The global trend of delayed motherhood has further highlighted the need for accurate assessment tools and interventions to manage fertility challenges. This review aims to provide a concise overview of current knowledge on ovarian reserve, Moreover, it explores the factors affecting it to contextualize these insights within the broader challenges faced by women with diminished ovarian reserve. It also explores emerging potential interventions as well as innovative assessment tools that could enhance diagnostic accuracy.
Materials and Methods*:* This narrative review was conducted using PubMed and Scholar database with following search terms: "ovarian reserve", "diminished ovarian reserve", "ovarian aging", "ovarian insufficiency". Relevant publications were analyzed. Only articles in english were considered.
State of Knowledge*:* Key markers for assessing ovarian reserve include anti-Müllerian hormone (AMH), antral follicle count (AFC), follicle-stimulating hormone (FSH), and inhibin B, each providing unique insights into ovarian function. AMH has emerged as a reliable marker due to its stability across the menstrual cycle, but the lack of standardization in assays limits its clinical utility.

Factors such as obesity, thyroid dysfunction and endometriosis significantly impact ovarian reserve. Newly approaches, like machine learning models and AMH-based screening programs in countries like Portugal emerge. Additionally hormonal oral contraceptives affect the ovarian reserve marker values. DOR serves as an early marker for cardiovascular risk. Appropriate supplementation with folate and vitamin D may support ovarian reserve.
***Conclusions**:* Assessing ovarian reserve is crucial for predicting pregnancy outcomes, optimizing ART protocols, and guiding reproductive decisions. The diverse influence of discussed factors on ovarian function underscores the need for individualized evaluation. Emerging interventions, such as electro-acupuncture and autologous platelet-rich plasma injections, show promise for improving fertility outcomes. Further research and widespread screening programs are essential for advancing fertility management and understanding ovarian reserve globally.

Keywords: Ovarian reserve, diminished ovarian reserve, ovarian aging, female infertility

Introduction

Ovarian reserve is a complex clinical phenomenon defined as the quantity and quality of a woman's remaining oocytes. It is a critical determinant of fertility potential. As more women seek fertility counseling and treatment, the development of methods to assess and preserve ovarian reserve - and ultimately to slow ovarian aging - has gained critical research importance. Unlike men, who continually produce spermatogonial cells, women possess a finite pool of oocytes established in utero, which declines progressively throughout life due to a natural process of atresia. While some studies suggest the possibility of postnatal oocyte formation [1], the clinical viability of this finding remains uncertain. During fetal development, the number of oocytes peaks at 6–7 million, decreasing to approximately 2 million at birth. By the time of puberty, only 400,000 oocytes remain, and this number further declines to around 1,000 by menopause [2]. This ongoing depletion signifies a time-limited window for fertility, with diminished ovarian reserve typically becoming a concern as women reach their late 30s and early 40s [3]. Numerous mechanisms contribute to ovarian aging, including chromosomal cohesion deterioration, DNA damage, mitochondrial dysfunction, telomere shortening, genetic mutations, and alterations in protein metabolism and the ovarian stromal microenvironment [2].

The advancement of modern society and a prevailing trend toward delaying childbirth have brought diminished ovarian reserve (DOR) into focus as a critical factor impacting fertility. Female fertility begins to decrease after age 30, with a rapid drop in the mid-40s, making conception rare without younger donor oocytes. For women with DOR, assisted reproductive techniques (ART) often become necessary, though success rates are generally lower as ovarian reserve declines. DOR not only affects personal and reproductive goals but also has broader implications for societal demographics, as fewer women may achieve successful pregnancies without ART. Demographic shift toward older motherhood has been documented globally. In the United States, birth rates among women aged 35–39 and 40–44 more than doubled between 1990 and 2015, with similar trends observed across OECD countries, where the average maternal age has increased by approximately 2–5 years since 1970 [4]. Alongside these trends, DOR has emerged as a contributing factor to infertility, accounting for nearly 30% of cases in women [5]. Infertility is defined as a disease of the

reproductive system, characterized by the inability to achieve a clinical pregnancy after 12 months of regular, unprotected intercourse [5].

State of knowledge

Terminology

While there is general agreement on the concept of DOR, its definition remains somewhat ambiguous. A clear and consistent definition of ovarian reserve is essential for accurately assessing and predicting reproductive potential. One proposed approach is to use the term *ovulatory potential* to describe the actively growing follicle pool, which supports regular follicle development, ovulation, and the maturation of follicles in assisted conception. However, this *ovulatory potential* only indirectly reflects the size of the resting primordial follicle pool, which is the main determinant of reproductive lifespan and constitutes what some researchers consider the *true ovarian reserve* [6]. Distinguishing between *true ovarian reserve*, referring specifically to the resting pool of primordial follicles, and *functional ovarian reserve*, representing the actively growing follicle pool, may enhance the accuracy and application of these biomarkers in both clinical and research contexts. It is crucial to distinguish DOR from premature ovarian failure (POF) and poor ovarian responders (POR), both of which are clearly defined.

Markers

Ovarian reserve markers provide essential insights into a woman's reproductive potential, guiding fertility planning and intervention. Key markers include biochemical indicators such as follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), inhibin B, and antimüllerian hormone (AMH), as well as imaging-based assessment- antral follicle count (AFC), each contributing valuable perspectives on response to ART as well as providing patients with a realistic understanding of their reproductive potential.

AMH, produced by granulosa cells of pre-antral and antral follicles, is among the most reliable indicators of ovarian reserve. AMH outperforms FSH in predicting ovarian response to stimulation, though its ability to forecast pregnancy rates, particularly in younger women, remains limited [7]. The clinical utility of AMH lies primarily in its ability to estimate the quantity rather than the quality of ovarian follicles. For example, AMH levels tend to decline before FSH levels rise, making it a sensitive marker for detecting early declines in ovarian reserve. This decline correlates with the natural reduction in follicle numbers that accompanies reproductive aging [8]. The main issue concerning AMH is the lack of standardization assay, which is urgently needed to enable consistent reporting of AMH values and reliable clinical interpretation. A meta-analysis of existing patient data or large-scale studies using a standardized assay would facilitate the creation of reference ranges and normograms.

Functionally, AMH influences ovarian follicle dynamics by suppressing the recruitment of primordial follicles into the growing pool. Additionally, AMH reduces follicular sensitivity to FSH, lowering aromatase activity and consequently inhibiting estrogen production by granulosa cells during follicular maturation [9]. The fluctuations in AMH levels throughout the menstrual cycle are closely aligned with changes in AFC, especially in antral follicles of 2–8 mm in diameter, further reinforcing the relevance of AMH as a dynamic yet consistent marker of functional ovarian reserve [10].

AFC is assessed through transvaginal ultrasound and measures the number of visible antral follicles, typically 2–10 mm in diameter, present in the ovaries at the beginning of the menstrual cycle. AFC directly reflects the pool of recruitable follicles and correlates strongly with ovarian reserve, making it a cornerstone for predicting response to ovarian stimulation. Age-related declines in AFC are well-documented, with an AFC below five suggesting diminished ovarian reserve [11]. Despite its reliability, AFC can vary depending on the sonographer's expertise and subjective interpretation, introducing variability into its use in clinical practice. Nevertheless, when paired with AMH, AFC enhances predictive accuracy regarding ovarian reserve and treatment response.

FSH, typically measured on day 3 of the menstrual cycle, serves as an indirect indicator of ovarian function. High FSH levels are indicative of decreased ovarian hormone production and reduced follicular reserve, as insufficient ovarian hormone feedback prompts increased FSH release [7]. Elevated FSH has long been associated with poorer responses to ART and lower pregnancy rates, though it is less sensitive than AMH for detecting subtle declines in ovarian reserve. Additionally, FSH is sensitive to short-term fluctuations in hormone levels, limiting its reliability as a sole predictor of ovarian reserve.

LH is primarily recognized for its role in triggering ovulation and supporting corpus luteum function. While LH itself is not a primary marker for ovarian reserve, imbalances in LH and FSH levels can reflect underlying endocrine disorders that impact ovarian health and fertility potential [12]. Therefore, evaluating LH alongside other markers can enhance understanding of ovarian function, especially in cases where PCOS or other ovulatory dysfunctions are present.

Inhibin B, secreted by granulosa cells of growing follicles, plays a regulatory role in FSH secretion. As a marker, inhibin B rises in the early follicular phase, peaking as follicles reach 8–10 mm, and serves as a reliable indicator of granulosa cell function and follicular growth [13]. Its levels correlate well with AFC in the 5–7 mm range [14], making it particularly useful in assessing smaller follicle pools. However, inhibin B's episodic secretion pattern requires careful timing for optimal clinical interpretation.

Other Tests: Though historically used, dynamic tests like the clomiphene citrate challenge test (CCCT) and basal estradiol measurement have been largely phased out due to limited predictive value compared to static markers like AMH and AFC. For instance, the CCCT, which involves measuring FSH before and after clomiphene administration, has been found to offer no substantial advantage over basal FSH and AFC in predicting IVF outcomes, leading to a decrease in its clinical use [15].

Together, these markers establish a comprehensive framework for assessing ovarian reserve, enabling informed patient counseling and individualized treatment strategies. The ideal ovarian reserve test should be convenient, reproducible, exhibit minimal intracycle and intercycle variability, and have high specificity to reduce the risk of misdiagnosing women. By offering distinct yet complementary insights, the combined use of AMH, AFC, FSH, and inhibin B can enhance ART success rates, and facilitate proactive fertility management.

Marker	Description	Typical Range	Role in Ovarian Reserve Assessment
AMH	Produced by granulosa cells of antral follicles	1.0-4.0 ng/ml	Stable throughout menstrual cycle, main marker of follicle quantity

AFC	Count of antral follicles at the start of the cycle	> 5	Direct indicator of recruitable follicles
FSH	HPO axis function indicator, typically measured on day 3	< 10 mIU/ml	High levels indicate reduced ovarian response
Inhibin B	Produced by growing follicles, regulates FSH	45-200 pg/ml	Assesses granulosa cell function

Table 1: Ovarian reserve markers

Factors affecting ovarian reserve

Thyroid dysfunction

Ovarian reserve assessment is particularly relevant for certain patient groups where health conditions or hormonal imbalances may impact reproductive potential. For instance, thyroid dysfunction has been closely linked to ovarian reserve, as thyroid hormones play a critical role in female reproductive health [16]. Adolescent girls with autoimmune thyroiditis often experience reduced ovarian reserve, indicated by lower serum AMH levels associated with thyroid autoimmunity and hypothyroidism [17]. Monitoring ovarian reserve in these patients may therefore be necessary to manage reproductive outcomes proactively
In broader populations of women with thyroid dysfunction, both high and low levels of thyroid-stimulating hormone (TSH) correlate with reduced AMH levels, suggesting that deviations from an optimal TSH range can negatively affect ovarian reserve. In a population of infertile women, a TSH level around 2.88 mIU/L was associated with the highest AMH levels, highlighting the importance of optimal thyroid function in maintaining ovarian reserve [18].

Diet

Diet plays a significant role in overall health. While dietary supplements can offer health benefits, it is essential to use them in appropriate dosages, as excessive intake may have counterproductive effects. One nutrient with a noted impact on ovarian reserve is folate. Higher intake of folate, particularly from supplements, has been associated with modest improvements in ovarian reserve, as reflected by AFC. Benefits are observed up to a daily intake of 1200 μg, beyond which no additional advantages have been noted [19]. The Centers for Disease Control and Prevention (CDC) recommends a minimum daily intake of 400 μg of folic acid for women planning pregnancy, with potential benefits up to 800 μg. In contrast, supplemental iron intake exceeding 45 mg/day has been linked to a reduction in ovarian reserve in women seeking fertility care [20]. However, dietary iron intake itself did not show a general effect on ovarian reserve, though it may positively influence AFC in women over 35 [20]. The consumption of alcoholic, caffeinated, sugar-sweetened, and artificially sweetened beverages has not been found to affect ovarian reserve as measured by AFC. Likewise, specific beverages such as coffee, tea, soda, beer, wine, or liquor showed no relationship with AFC [21]. These findings further suggest that previously

reported links between these beverages and fertility are unlikely to stem from effects on ovarian reserve

Soy intake and its effects on female fertility remain inconclusive, despite being a widely discussed topic. No consistent association between soy or isoflavone intake and ovarian reserve has been observed [22].. Thus, patients may be informed that their ovarian reserve test results are unlikely to be impacted by dietary soy, although the effects of soy on other reproductive aspects are still uncertain

Vitamin D is another nutrient of interest in the context of ovarian reserve. Supplementation has been shown to increase levels of AMH while also reducing depressive symptoms and related risks [23]. These findings suggest that vitamin D plays a role in reproductive health and the mitigation of reproductive depression. The American Society of Endocrinology recommends a vitamin D intake of 400-1000 IU per day for infants, 600-1000 IU per day for children over one year old, and 1500-2000 IU per day for adults. For individuals with a body mass index (BMI) over 30 kg/m², a threefold increase in the standard dose is advised. However, the optimal dosage for women with PCOS is still under debate, with some studies suggesting that lower doses of 400-800 IU per day may be beneficial

PCOS and menstrual cycle characteristics

Women diagnosed with polycystic ovary syndrome (PCOS) also benefit from monitoring, as they may experience a unique pattern of ovarian reserve decline. Although traditionally considered to have an extended fertility window due to higher ovarian reserve markers, recent research indicates that women with PCOS may actually experience a more rapid decline in ovarian reserve and a similar age-related decrease in fecundity compared to women without the syndrome. Additionally, long or irregular menstrual cycles—common in PCOS are often anovulatory and correlated with decreased fecundability, while short menstrual cycles can signal ovarian aging and poor ovarian response to stimulation [24]. The features of the menstrual cycle itself (including length and regularity) regardless of the diagnosis of PCOS also provide insight into ovarian reserve. Menstrual cycles that are long (exceeding 35 days) or irregular are are more likely to be anovulatory and correlate with reduced fertility [25]. Prolonged menstrual cycles and oligomenorrhea (fewer than nine cycles per year) are diagnostic criteria of PCOS, while short cycles (less than 21 days) may indicate ovarian aging, as they tend to occur more frequently as menopause approaches. Evidence suggests that lower ovarian reserve is associated with shorter cycles and earlier ovulation, independent of age [24].

Oral hormonal contraception

Oral contraceptive (OC) use has been shown to significantly reduce ovarian volume and moderately decrease AFC and AMH, particularly affecting mid-sized antral follicles (5–7 mm and 8–10 mm), where AMH production is highest. The suppressive effect of hormonal contraception is believed to be reversible within 3–6 months [26]. High exposure to androgenic OCs appears to suppress functional ovarian reserve and lower. Given that OCs are frequently used in preparation for IVF, this practice may require reconsideration, particularly for women with already diminished ovarian reserve. High androgenic progestin OCs, in particular, should be avoided in these cases [27]. Hormonal contraceptives suppress AMH, complicating the accurate assessment of functional ovarian reserve. Women using long-term hormonal contraceptives who experience premature ovarian aging often remain undiagnosed until they discontinue contraception, at which point they may present with amenorrhea, menstrual disorders, or infertility. With increased awareness of ovarian reserve, more patients are opting to test AMH levels while still on contraceptives. It is crucial that

AMH levels can be interpreted appropriately for such group without interrupting safe and effective contraceptive use. Harrison et al. present guidance for clinicians on how to correctly interpret AMH in the abovementioned population [28].

Chronic inflammation

Women of reproductive age with inflammatory bowel disease (IBD) exhibit a lower ovarian reserve compared to healthy individuals, with a particularly marked reduction observed in those undergoing thalidomide therapy. Furthermore, transmural inflammation associated with IBD can lead to local inflammation of the oviducts and ovaries, further impacting reproductive health. As long as their disease course and medications permit, these patients should not delay conception, ideally considering pregnancy during their 20s [29]. Similarly, women with sickle cell anemia show higher rates of DOR than age-matched controls, likely due to the combined effects of chronic inflammation and associated medical treatments. [30].

Hypogonadotropic hypogonadism

Patients with hypogonadotropic hypogonadism present with elevated AMH levels, but have a similar AFC compared to other populations. Despite the need for prolonged stimulation and increased doses of gonadotropins during controlled ovarian stimulation, ovarian response and reproductive outcomes remain unchanged [31]. This phenomenon is particularly interesting given that women with hypogonadotropic hypogonadism maintain high AMH levels regardless of ovarian suppression, highlighting the complex interaction between hormone levels and ovarian function in this patient group.

Precocious puberty

The incidence of precocious puberty is increasing, posing both short-term and long-term health risks. This condition, which can lead to reduced adult height, is also associated with increased risks of diabetes, hypertension, and certain malignancies in adulthood. There are two types of precocious puberty: central, which is more common and linked to early activation of the hypothalamic-pituitary-gonadal axis, and peripheral. Girls are ten times more likely than boys to develop central precocious puberty, with most cases being idiopathic. Its standard treatment f aims to delay skeletal maturation by inhibiting pubertal development, with gonadotropin-releasing hormone agonists (GnRHa) currently being the primary medical intervention. Girls treated with GnRHa reach menarche at a similar age to that of healthy peers, and their menstrual cycles remain regular. Importantly, GnRHa treatment influences ovarian reserve markers, which are inhibited compared to pre-treatment levels but gradually recover and exceed pre-treatment levels after menarche [32]. This suggests that while GnRHa has an inhibitory effect on ovarian reserve during treatment, this effect is reversible, allowing for the restoration of ovarian function post-menarche

Obesity

Obesity can contribute to reproductive challenges, as AMH levels, a key indicator of ovarian reserve, tend to decrease with increasing BMI [33]. Obesity results in adipocyte hyperplasia and hypertrophy, leading to greater adipose tissue volume. Excess adipose tissue functions as an endocrine organ, secreting adipokines that shift cytokine profiles toward pro-inflammatory markers such as interleukin-6 and tumor necrosis factor-α. This chronic, low-grade inflammation contributes to insulin resistance in muscle and liver tissues,

making obese women more vulnerable to reproductive impairments and increasing their risk of late spontaneous abortion following ART. Furthermore, obesity-driven upregulation of enzymes involved in androgen metabolism within adipose tissue can result in hyperandrogenism. The subsequent increase in peripheral aromatization of androgens to estrogens, coupled with a reduction in sex hormone-binding globulin (SHBG), disrupts the hypothalamicpituitary-ovarian (HPO) axis, further inhibiting folliculogenesis and compromising ovarian function in obese women [34].

SARS-CoV-2

The COVID-19 pandemic has added new dimensions to fertility concerns, as infection has been shown to negatively impact female fertility and potentially cause ovarian damage [35]. Vaccination thus represents a logical and cost-effective approach for safeguarding ovarian reserve. Awareness campaigns that highlight the vaccine's neutral effect on fertility could encourage higher vaccination rates among women of reproductive age. Beyond fertility effects, COVID-19 poses increased risks for pregnant women, with elevated chances of ICU admission, placentitis, stillbirth, and maternal mortality.

Lifestyle

It is also crucial to consider the emotional and psychological impact of infertility. It often leads to distress, depression, and social stigmatization. On the other hand, stress itself negatively affects fertility probably by activation of the hypothalamicpituitary-adrenal axis. Perceived stress is associated with lower AFC and serum AMH levels, [36] creating a vicious cycle of stress and reduced fertility potential. Interestingly, [36] et al. observed that stress was negatively associated with ovarian reserve only among women with higher education. One possible explanation for this finding is the high level of stress professional women encounter daily, balancing personal and professional responsibilities. Women with higher education often hold positions with greater responsibilities and, consequently, higher stress levels compared to those with lower educational attainment. Exercise-related reproductive abnormalities are primarily rooted in hypothalamic dysfunction. Athletes, especially those involved in weight-sensitive sports, often exhibit of hypoestrogenism due to disruptions in the hypothalamic-pituitary-ovarian axis, potentially leading to a prolonged follicular phase or absence of a mid-cycle LH or estradiol surge, causing mild or intermittent menstrual suppression. Miller et al. indicated that while exercise combined with caloric restriction can suppress LH, exercise alone does not alter LH pulsatility [37] . By focusing on women with a normal BMI and excluding those with eating disorders, researchers effectively isolated the impact of physical activity on ovarian reserve, finding that athletic, normo-ovulatory women generally have ovarian reserves comparable to those of the general population [37].

Vaginal and uterine environment

Infertility linked to uterine abnormalities can arise from factors such as cervical incompetence, abnormal uterine contractions, reduced blood flow to the ovaries, and decreased overall uterine and ovarian volume [38]. Ovarian blood supply may be disrupted by variations in vascular contributions from the uterine and contralateral utero-ovarian arteries or uterine leiomyomas. These fibroids deform the endometrial cavity and alter blood flow direction toward the fibroid tissue, thereby diminishing endometrial blood supply. Given the interconnected blood flow between the uterine and ovarian arteries, leiomyomas may thereby also reduce blood supply to the ovaries [39]. Vaginal microbiota

is also relevant. Certain bacterial strains show associations with hormonal markers. Specifically, elevated levels of Actinobacteria, Atopobium, and Gardnerella correlate negatively with AMH and inhibin B concentrations, while also positively correlating with FSH and LH. In contrast, Bifidobacterium is positively associated with AMH and negatively associated with FSH and LH, indicating a more supportive role in reproductive health [40].

The intrauterine environment during pregnancy is critical for establishing ovarian reserve in offspring. Maternal testosterone treatment, excessive gestational weight gain or smoking are unfavorable factors that may hinder the formation of primordial follicles in the developing fetal ovary. [13] Research further suggests that diet has intergenerational effects, with evidence linking low-protein grandmother diet with DOR and accelerated telomere attrition in the ovarian cells of future generations. [41] Also, an obesogenic (high-fat or high-sugar) maternal diet [42] as well as caffeine intake during pregnancy may increase the likelihood of DOR in offspring as they mature [43].

Endometriosis

Endometriosis is one of the leading causes of female infertility, with numerous pathomechanisms contributing to decreased chances of conception. One such mechanism is the formation of ovarian endometriomas. Induction of local inflammation disrupts the normal ovarian cortical structure, damaging its function as a reservoir for dormant follicles [44]. Surgical interventions, particularly cystectomy of endometriomas, have been found to cause a greater reduction in ovarian reserve compared to removal of other benign ovarian cysts. Statistical analyses reveal a significant decrease in AMH levels post-cystectomy relative to conservative treatments like ultrasound-guided puncture and ethanol sclerotherapy [45].. Given the less invasive nature of these conservative approaches, they should be considered as primary options for managing ovarian endometriomas to preserve ovarian function.

Ovaian reserve and cardiovascular disease risk

The correlation between early menopause, DOR, and cardiovascular disease (CVD) is increasingly recognized [46]. Menopause before age 40 and surgical menopause due to bilateral oophorectomy have been associated with heightened cardiovascular mortality [47, 48]. While CVD has traditionally been viewed as a postmenopausal concern, risk factors are now being identified in younger women, particularly those with accelerated ovarian aging. Premenopausal women with DOR show lower estrogen levels than healthy counterparts. Prolonged estrogen deficiency has been tied to increased CVD risk, whereas cumulative estrogen exposure, including pharmacological replacement, correlates with reduced risk [49]. Although postmenopausal hormone therapy outcomes remain inconclusive, estrogen replacement appears to mitigate cardiovascular mortality. Therefore, DOR serves as an early marker of elevated CVD risk in women

Asessment tools

The diagnosis of DOR is not straightforward, as most women have no signs or symptoms. To aid in the assessment of ovarian reserve, various tools and technologies have emerged. For example Yong Han et al. created an online website-based tool for assessing the score of ovarian reserve assessment http://121.43.113.123:9999/ [50]. Such solutions can provide women with accessible insight into their ovarian reserve. Furthermore, advanced

mathematical models, particularly those utilizing machine learning techniques such as LightGBM, have demonstrated high accuracy in estimating ovarian age by integrating multiple variables, including biochemical tests, imaging metrics, and BMI. One model achieved impressive 99.49% accuracy in predicting ovarian age in women under 35, highlighting its potential as a reliable tool for ovarian reserve assessment [51].
Remaining on the subject of practical applications, a screening project to assess ovarian reserve based on AMH levels has been implemented in Portugal [5]. Such a program could be adapted and expanded to other countries, potentially evolving over time to incorporate advancements in testing and screening methodologies. An additional benefit of widespread AMH screening would be the accumulation of a more comprehensive dataset on AMH levels across diverse patient groups, supporting the creation of comprehensive meta-analyses. This, in turn, could further refine reference ranges and enhancing our understanding of ovarian reserve on a global scale.

Management

The extreme form of DOR is primary ovarian insufficiency (POI), a condition with distinct diagnostic criteria. The European Society of Human Reproduction and Embryology (ESHRE) has published guidelines for diagnosing primary and secondary POI, which could serve as a framework for developing similar guidelines specifically addressing DOR [52]. Such standardized protocols could further aid clinicians in the accurate identification and management of patients with varying degrees of ovarian reserve depletion.
Various strategies have been established for managing DOR, aiming to improve reproductive outcomes and provide support to affected patients. Ovarian cryopreservation, initially developed for fertility preservation in postmenarchal patients undergoing gonadotoxic treatments, is now available as a proactive solution for age-related infertility and conditions associated with early decline in ovarian reserve. Patients who pursue fertility preservation at a younger age generally achieve a higher oocyte yields with fewer ovarian stimulation cycles and see better live birth rates, emphasizing the importance of its timing. Interestingly, when asked about what they would do about unused cryopreserved oocytes 62% of patients would consider donating unused cryopreserved oocytes to research, while 14% would consider donating to other patients, reflecting a willingness to contribute to the field and assist others in need [53]. Quantitative assessments of ovarian reserve also play a key role, as blastocysts from women with DOR are less likely to be euploid [54]. The corresponding decline in euploid rates with fewer oocytes suggests that ovarian reserve measurements provide valuable insights into ovarian aging, which can be instrumental in counseling patients. This information allows both patients and physicians to set realistic expectations about the number of cycles potentially required to obtain a sufficient number of euploid embryos for successful transfer and cryopreservation.
Additionally, acupuncture, specifically electro-acupuncture, has shown excellent potential as a non-pharmacological treatment for patients with DOR. This intervention may positively influence ovarian function by modulating the intestinal microbiota and reducing Fe^{2+} accumulation, as observed in premature ovarian failure models [55]. Another promising intervention involves intraovarian injections of autologous platelet-rich plasma. The aforementioned method has been associated with improvements in ovarian reserve markers, including increased AFC and AMH levels, along with decreased FSH levels. Furthermore, it correlated with better IVF outcomes [56].

Conclusions

In clinical practice, assessing ovarian reserve is essential for predicting pregnancy outcomes, determining the optimal dosage for ovarian stimulation. Accurate and reliable assessment is vital not only for optimizing ART protocols but also for providing patients with a realistic understanding of their reproductive potential. and guiding them in their reproductive choices. It is crucial to educate women about. Patient-specific factors—ranging from endometriosis and thyroid dysfunction to occupation and obesity - significantly influence ovarian reserve, pointing to the need for individualized evaluation. Additionally, innovative interventions, including electro-acupuncture and PRP, offer promising avenues to enhance fertility outcomes. Through early identification and proactive management, both patients and healthcare providers can better navigate the challenges associated with DOR, ultimately supporting women in achieving their reproductive goals. Clinicians should be aware of the fact that DOR serves as an early marker of elevated CVD risk. While folate and vitamin D show promise for supporting ovarian reserve, it is essential to consider the appropriate dosages to maximize benefits and avoid potential drawbacks. Further research is needed to clarify the impacts of other dietary factors, including iron, soy, and common beverages, on ovarian reserve and reproductive health. Implementing widespread screening programs could further enhance our understanding of ovarian reserve across diverse populations, supporting more effective fertility management on a global scale.

Disclosures

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