HIGH LEVEL OF AMH

High Level Of Mih (Müllerian-Inhibiting Hormone)

Serum level of AMH (Anti-Müllerian hormone) above the upper limit of the reference range.

⚠️ Risk factor ♂️ Female

About High level of AMH

High level of AMH (Anti-Müllerian hormone) is a condition of blood levels of AMH above the upper limit of the reference range (Pic. 1). High levels of AMH are associated with several pathological conditions, most notably polycystic ovary syndrome (PCOS) and granulosa cell tumours, which have a significant detrimental effect on female fertility.

Anti-Müllerian hormone, or Müllerian-inhibiting hormone, is a glycoprotein hormone that has key roles in embryonal growth, differentiation, and in regulation of folliculogenesis (growth and development of ovarian follicles).

In females, AMH is secreted by granulosa cells of small follicles in the ovary. Serum values are almost undetectable during infancy and then rapidly increase with the onset of puberty, reflecting the initial recruitment of primordial follicles (the smallest form of ovarian follicles, small aggregations of cells that each contain an egg cell). AMH is produced in growing follicles until they reach a stage when dominant follicle is detached from a cohort of antral follicles (more mature stage of ovarian follicles).

The measurement of serum AMH levels during woman’s reproductive life represents an ideal tool for the assessment of the ovarian follicular reserve (the number of ovarian follicles that are still capable of producing an ovulation). The advantage of AMH in relation to the ovarian steroid hormones is that serum levels do not fluctuate significantly during the menstrual cycle. The strong correlation of AMH with the number of growing follicles is supported by the fact that its levels are reported very high in ovarian tumors and in polycystic ovaries, while undetectable levels are testified in postmenopausal women (women after their menopause, the natural cessation of menstrual cycle) and Turner syndrome (a genetic syndrome affecting only women, causing infertility) patients without gonadal tissue. As the number and quality of the oocytes diminish throughout the woman’s reproductive life, serum concentrations of AMH gradually decrease and fall below detectable levels in menopause (the definite cessation of woman’s menstrual cycle).

It has been reported that, in PCOS, AMH levels are elevated up to two- to threefold (Pic. 2), reflecting the load of growing follicles. This correlation with follicular growth implies the strength of AMH as a marker of severity of ovarian dysfunction and hyperandrogenism (elevated levels of male sex hormones) in women with anovulatory PCOS. Also, AMH was identified as the marker of ovarian tumors of granulosa cell origin. As it is exclusively secreted by granulosa cells (type of cell surrounding the oocyte in the ovarian follicle), it is a reliable marker for diagnosis as well as monitoring for recurrences (repeated peaks of activity) of tumor. Raised levels have been found in 76 to 93% of women with granulosa cell tumors. Moreover, AMH surge is observed up to 16 months prior to clinical recurrence of the tumor itself, suggesting it as a useful marker of granulosa cell activity.

Symptoms

High level of AMH is detected only biochemically by measuring the serum concentration of circulating AMH. Other symptoms that may be present in patients with high AMH levels depend on the underlying disease.

Granulosa cell tumors
In cases of granulosa cell tumours, the elevation of AMH levels may precede any noticeable clinical signs and symptoms in the patient, and in cases of tumor recurrence may serve as a sensitive marker of the tumor’s activity. When clinically manifest, the symptoms are various: abdominal pain (30 to 50%), abdominal distension related to mass effect and hormonal events (41%) such as irregular menstruation, intermenstrual bleeding, postmenopausal bleeding or amenorrhea (cessation of menstrual cycle). Endocrine manifestations are noted in 66% of the patients. These manifestations are related to estrogen secretion of the tumor. This explains why the granulosa cell tumors are frequently associated with endometrial hyperplasia (4 to 10%) or to endometrial adenocarcinoma.

**PCOS**

In patients with PCOS, who often have very high AMH levels, the most common symptoms of PCOS include amenorrhea or oligomenorrhea (weak or infrequent menstruation), abnormal uterine bleeding, androgenization (development of male characteristics due to elevated levels of male sex hormones), including hirsutism (facial hair growth), acne, oily skin, and the characteristic finding of polycystic ovaries on ultrasound examination (Pic. 3), with or without ovarian enlargement. Patients with polycystic ovary syndrome also usually appear obese.

**Associated diseases**

**Polycystic ovary syndrome (PCOS)**

Polycystic ovary syndrome is a condition attributable to elevated androgens (male sex hormones) in females. One of the most prominent symptoms in patients with PCOS is oligomenorrhea or amenorrhea, caused by lack of ovulation in the ovaries. Consequently, women with PCOS are highly likely to be infertile and potentially develop endometrial hyperplasia (abnormal thickening of the uterine cavity lining) due to continuing secretion of oestrogen without ovulation. Furthermore, emerging evidence has suggested that ~50–70% of patients with PCOS have insulin resistance (the need of higher insulin levels for its effect on peripheral tissues) regardless of their body weight or body mass index (BMI). Consequently, women with PCOS are at an elevated risk of developing various common metabolic disorders compared with the general population. In addition, many patients with PCOS exhibit symptoms of elevated androgen level, or hyperandrogenism, which leads to hirsutism (Pic. 4), alopecia (early hair loss) and acne. In women with PCOS, increased growth of ovarian follicles with no following ovulation causes two- or threefold increase in the blood level of AMH.

**Granulosa cell tumors**

Granulosa cell tumors are very rare ovarian malignancies; they represent 2 to 3% of all ovarian cancers. Unlike epithelial ovarian tumors, they occur in young women and are usually detected at an early stage. The mainstay of treatment is a complete surgery (hysterectomy with bilateral salpingo-oophorectomy) with staging for early stage and debulking surgery (removal of as much tumor mass as possible) for advanced stage or recurrent disease. Fertility-preserving surgery with unilateral salpingo-oophorectomy is an option in young patients with early stages of the tumor growth. Available data showed that there is not much difference in survival with a conservative approach when compared to the radical surgery (97% versus 98%, resp.). Although granulosa cell tumors have generally a good prognosis, they have a tendency for late recurrence.

**Risk factors**

- hyperandrogenism
- amenorrhea
- oligomenorrhea
- abnormal uterine bleeding
- irregular menstruation
- hirsutism
- acne
- obesity
- family history of PCOS or insulin resistance

**Complications**
Infertility

Conditions associated with elevated AMH levels may lead to female infertility. PCOS usually causes infertility associated with anovulation, and therefore, the presence of ovulation indicates absence of infertility. In patients with granulosa cell tumors, especially in advanced stages, the treatment includes bilateral salpingooophorectomy (surgical removal of the Fallopian tubes and ovaries), which renders the patient infertile.

Prevention

It has been reported that, in PCOS, AMH levels are elevated up to two- to threefold, reflecting the load of growing follicles. This correlation with follicular growth implies the strength of AMH as a marker of severity of ovarian dysfunction and hyperandrogenism (elevated levels of male sex hormones) in women with anovulatory PCOS. Although the exact cause of PCOS still remains unknown, certain ways of reducing the risk of developing the condition are known. If the patient has a family history of PCOS or increased insulin resistance (obesity, type 2 diabetes and related conditions), certain steps may be taken to lower the risk of developing PCOS or at least to prevent many of its associated health complications. These steps include regular exercise, walking or running 20 – 30 minutes a day to increase insulin sensitivity, and excluding processed and carbohydrate-rich foods from the diet. If the patient notices irregular menstrual periods, acne or facial hair growth, they should consult their physician.

![How it can affect fertility](image)

Polycystic ovary syndrome (PCOS)

Hormonal dysbalance in women with PCOS are one of the major causes of female infertility. Polycystic ovary syndrome causes more than 75% of cases of anovulatory infertility. Not all women with PCOS have difficulty becoming pregnant. For those who do, anovulation is a common cause. The mechanism of this anovulation is uncertain, but there is evidence of arrested antral follicle development, which, in turn, may be caused by abnormal interaction of insulin and luteinizing hormone (LH) on granulosa cells. Endocrine disruption may also directly decrease fertility, such as changed levels of gonadotropin-releasing hormone, gonadotropins (especially an increase in luteinizing hormone), hyperandrogenism, and hyperinsulinemia (increased insulin levels, resulting in insulin resistance).

Granulosa cell tumor

Granulosa cell tumors usually affects adults, juvenile forms are much rarer (usually up to 5% of granulosa cell tumors). Although in patients with early stages of the tumor, fertility-sparing surgery can be performed, in advanced stages of the disease, bilateral salpingo-oophorectomy and hysterectomy (surgical removal of the uterus, both Fallopian tubes and ovaries) has to be performed, resulting in sterility. The fertility-sparing approach does not, however, show a significantly lower rate of the overall patient survival, making it suitable especially for younger patients.

Prognosis

Polycystic ovary syndrome (PCOS)

There is no cure for PCOS. Lifestyle modifications and certain medications can, however, improve many of the associated conditions and health issues. Management of infertility in polycystic ovary syndrome includes lifestyle modification as well as assisted reproductive technology such as ovulation induction, oocyte release triggering and surgery. For overweight women with PCOS who are anovulatory, diet adjustments and weight loss are associated with resumption of spontaneous ovulation.

For those who after weight loss still are anovulatory or for anovulatory lean women, ovulation induction to reverse the anovulation is the principal treatment used to help infertility in PCOS. Clomiphene citrate is the
main medication used for this purpose, and is the first-line treatment in subfertile anovulatory patients with PCOS. Gonadotrophins such as follicle-stimulating hormone (FSH) are, in addition to surgery, second-line treatments. For patients who do not respond to diet, lifestyle modification and clomiphene, in vitro fertilization can be performed. This usually includes controlled ovarian hyperstimulation with FSH injections, and oocyte release triggering with human chorionic gonadotropin (hCG) or a GnRH agonist.

Granulosa cell tumors

Granulosa cell tumor patients have overall good prognosis. The 5-year and 10-year disease-specific survival was 97% and 94%. Granulosa cell tumors do have, however, a tendency for late recurrence, and the fertility of the patient may be impaired following treatment.

Find more about related issues

Diagnoses

Polycystic ovary syndrome
A condition in which a woman has an imbalance of female sex hormones. This may lead to changes in the menstrual cycle, cysts in the ovaries, trouble g
Learn more at: [www.fertilitypedia.org/therapy/diag/polycystic-ovary-syndrome](http://www.fertilitypedia.org/therapy/diag/polycystic-ovary-syndrome)

Gallery

<table>
<thead>
<tr>
<th>Females:</th>
<th>AMH blood level</th>
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<tr>
<td><strong>Age</strong></td>
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<tr>
<td>Younger than 24 months</td>
<td>ng/mL</td>
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<td>24 months to 12 years</td>
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<td>More than 45 years</td>
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Pic

Table of reference ranges of AMH serum levels for females.

Pic

AMH serum levels in adult females with their interpretation. High levels of AMH are often associated with PCOS.

Pic

A graphic showing the typical finding in PCOS patients – multiple cysts of varying size on both ovaries. These cysts are originally ovarian follicles that do not undergo ovulation.
A photograph of a female patient suffering from hirsutism, increased facial hair growth in females.

Sources

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