

OVARIAN ENDOMETRIOMA A CAUSE FOR DIMINISHING OVARIAN RESERVE - A REVIEW

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ABSTRACT

Female Infertility is considered as the 5th major global disability among population. There are multiple factors which may lead to female infertility like uterine factors, tubal factors, ovarian factors etc. Ovarian causes are one of the most frequent causes of infertility which includes anovulation, diminishing ovarian reserve, ovarian endometriosis etc. Diminishing ovarian reserve is a condition by which there is reduction in oocyte quantity quality and reproductive potential. Ovarian reserve test (AMH and AFC) is the credible markers to assess the ovarian reserve. Ovarian endometrioma affects 17–44% of women with endometriosis, endometrial implants on the surface of ovary is the causes for endometrioma. Which itself is a clinical predicament in infertility management. In OPD while observing cases of diminishing ovarian reserve, a casual association of ovarian endometriosis is repeatedly observed in patients of diminishing ovarian reserve. Main objective was to assess the association of ovarian endometriosis in DOR and to develop a mode of approach in management of similar cases. In Āyurvedic approach DOR is considered as *dhātukṣaya Vandyatwa*. But for these patients of DOR associated with endometriosis *Avaranacikitsā along with Dhātukṣayachikitsā* were giving a better outcome.

Keywords: Diminishing ovarian reserve, endometrioma, *Dhātukṣaya Vandyatwa*

INTRODUCTION

Infertility is defined as the inability to conceive naturally after one year of regular unprotected intercourse. About 8-12% of couples around the world have difficulty in conceiving at some point of time, and its level may vary in different countries. In India according to the Indian society of assisted

reproduction, infertility affects 10-14% of the Indian population. In Ayurveda this condition is explained under an umbrella term *Vandhvatva*. But in Ayurveda it is considered as a failure to achieve a child rather than pregnancy. Different acharya's had difference in opinion regarding the causes of *vandhyatwa*. Acharya

Caraka and Vagbhata had mentioned *Vandhya* as the result of *Pradusta Garbshayabija Bhaga of sonitha* (Ca.SaA/30) and also as a complication of *yoni vyapad*. (A.S.2/48). Acharya *Susrutha*, and *Bhavamishra* had mentioned *Vandhya* in *Vimshathi Yoni Vyapath* (Su.Ut.38/10, *Bhii.Pra.Ci.70/6*). In *Kashaypa Samhitha* Acharya explained *Vandhyatva* as one of the 80 disorders of *Vata* (Kash.Sam.Su.27). *Acharya Susrutha* had explained that chance of pregnancy depends upon normal functioning of factors like *ritu* (fertile period whether it can be ovulation or it can be considered as the appropriate age for conception) *kshetra* (it can be considered as healthy uterus and adequate endometrial factors supporting implantation), *ambu* (can be the normal hormonal supply as well as adequate blood supply especially the low resistance flow during the mid-luteal phase) and *beeja* (healthy ovum and sperms). If the normal functioning of these factors may affect it may lead to infertility. There are also so many factors which may contribute to infertility. Psychological factor also plays a major role. Most of the couples have one of these three major causes including a male factor, ovulatory dysfunction or tubal-peritoneal disease¹ as their cause of infertility. The social stigma of infertility weighs heavily on couples especially for women and it has a huge psychological impact in their life also.

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There are so many factors which may lead to female infertility like uterine factors, tubal factors, ovarian factors etc. Ovarian causes are one of the most frequent causes of infertility which includes anovulation, PCOS, diminishing ovarian reserve (DOR), ovarian endometriosis etc.

Considering the female infertility, age of female plays a major role in the fertility it is also an important variable affecting the success rate of ART² Female fertility decline after the age of 31 years and the decline accelerate after the age of 37 years leading to sterility³. As age advances the quality and quantity of oocyte reduces and they do not regenerate⁴. The rate of decline also varies among females of same age group considerably. Different factors such as lifestyle, environment, genetics and medical issues, including endometriosis,

ovarian cystectomy, oophorectomy, pelvic inflammatory disease, chemotherapy, and radiotherapy reduce the quantity and quality of oocytes⁵.

DOR (Diminishing Ovarian Reserve)

One of the major ovarian causes of female infertility is Diminishing Ovarian Reserve. Ovarian reserve (OR) is the term used to describe the functional potency of the ovary and reflect the number and quantity of oocytes. 10-30% of female infertility is caused due to DOR. It occurs approximately 1% of women worldwide. DOR is a complex phenomenon in which ovary loses its normal reproductive potential compromising fertility. In most of the cases the exact cause is unknown. It is unclear whether DOR represents a pathological condition resulting from abnormally rapid atresia in a normal pool of oocytes from normal atresia of an abnormally small pool of oocytes⁶. DOR is a common term refers to 3 related but three different parameters like

- a) The reduction of oocyte quantity
- b) The reduction of oocyte quality
- c) The reduction in oocyte reproductive potential⁷. As per ESHRE & Bolognas criteria for DOR at least any two of the following should be present.

- (1) Age > 38 years
- (2) Abnormal ovarian reserve test
- (3) Poor ovarian response in a previous stimulated cycle. Clinical presentation in a case of DOR are Primary or secondary infertility, Shortening of menstrual cycles, Vasomotor symptoms, Vaginal dryness and dyspareunia, Sleep disturbances and Osteoporotic changes.

Ovarian reserve test aims to predict how well the ovaries are still functioning at a certain point of time. AMH and AFC are the reliable markers to assess DOR.

- 1) **AMH** is formed from the primary follicles which are potentially capable of maturation. So AMH determines the ovarian functional reserve. (Ovarian reserve, really represents only small components of total ovarian reserve (TOR) which consists of Non growing primordial follicles (NGFs) arrested in meiotic prophase I, and remains quiescent until recruited for follicle maturation these recruited follicles are called functional ovarian reserve (FOR) which can be counted as AFC count. These

recruited in their antral follicular stage produces AMH. Normal range of AMH is 2.25- 4.08ng/dl

The value Below 1.5 ng/ml in diagnosed as DOR.

2) AFC is the Antral follicular count i.e. the sum of antral follicles in both ovaries by TVS during early follicular phase especially it is measured on day 2 or 3 of a cycle. A count of 5-10 AF per ovary is considered as a normal reserve.

Management of women with diminished ovarian reserve is challenging and generally depends on Assisted Reproduction Technologies (ART). Women with DOR has less oocytes for retrieval and have less embryos for transfer and their chances of pregnancy are also low.

The Effect of Endometrioma on DOR

Endometriosis is an enigmatic disease. The pathology of the disease is still hypothetical. Ovaries are a common site for endometriosis. Ovarian endometrioma or chocolate cyst is a common finding in clinics. The ovarian endometrioma may be a pseudo cyst that is formed by blood filled secretions from endometriotic lesion on ovarian surface adherent to broad ligament (pelvic peritoneum)⁸. The gold standard for the treatment of ovarian endometrioma is cystectomy. The damage of the stripping of cyst cause damage the ovaries is a major concern in the balance between reproductive risk and benefits. There are number of studies shows the adverse effect cystectomy on ovarian reserve⁹. Along with the removal of the cyst the non-growing follicles (NGF) may also loose. Certain studies also shows that even without conducting cystectomy patients with minimal / mild endometriosis present a decreased serum AMH level & AFC count denoting low reserve¹⁰. A study also demonstrated that the density of follicles in ovarian tissue from the endometrioma bed is approximately one- to two thirds of that adjacent to a non-endometriotic cyst in women younger than 35 years¹¹.

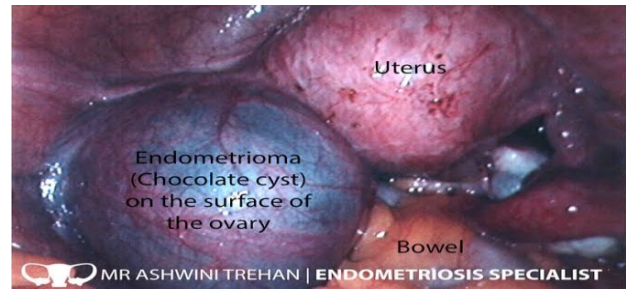


Fig 1: laproscopic image of endometrima

In OPD also while observing cases of diminishing ovarian reserve, a casual association of ovarian endometriosis is repeatedly observed in patients of diminishing ovarian reserve which needs further studies.

DISCUSSION

Both superficial and deep infiltrating endometriosis (DIE) decrease the ovarian reserve, ovulation rate and response to ovulation induction¹². Studies had also showed that women with untreated endometrioma showed decreased pre surgical AMH levels, especially those with bilateral lesions compared to women with another benign ovarian cyst¹³. The development of ovarian endometrioma may evoke marked inflammation in surrounding tissues which alter the normal physiological function. The primordial follicles maintain a dormancy which may also contribute to the DOR. Usually the maintenance of the quiescence is necessary for the survival of primordial follicles as females are concerned primordial follicles is formed during the embryonic stage of life and it remains quiescent until maturation of reproductive structures. The exact mechanism of the maintenance of such a long dormancy of the primordial follicles have remained unknown certain factors inhibitory factors may aid such dormancy. Certain studies reported that phosphatidylinositol 3 kinase (PI3K) pathway is important for the control of follicular activation¹⁴ This pathway is activated by the insulin and growth factors¹⁵ certain other factors like Neurotrophin, nerve growth factor (NGF0 and its tyrosine receptor kinase (NTRK1) are also needed follicular activation¹⁶. In subjects with ovarian endometriosis these follicular activating factors may be altered and affects the activation of functional ovarian reserve leading to diminishing ovarian reserve. One of the major challenge

clinicians are commonly facing is that patients with endometriosis may also have altered pelvic anatomy as a result of severe adhesion. In Āyurvedic approach DOR is considered as *dhātukṣayavandyatwa*. *Dhatukshaya Vandhyatwa* is due to depletion of *dhatu*s or due to inadequate formation of *dhatu*s mainly *arthava* and *sukradhatu* especially *streesukra* which in turn leads to reduction in fertility potential and ultimately cause *anapathyatha*. In the *poorvaroopaavastha rasa kshaya* and *arthavakshaya* occurs and there will be *kshaya* of *utharotharadhātukṣhaya*. In such subject *dhathukshaya chikitsa* should be done along with *rasāyanachikitsa*. But for those patients of DOR associated with endometriosis, *avarana cikitsā* especially (*pittavrihaapana chikitsa*) along with *dhātukṣaya cikitsā* will give a better outcome. Some of the commonly used drugs in the management are *Mahatik-takam kashyam*, *Hingutrigunatailam*, *Shad-palaghritam*, *Indukanthamghritam* etc

CONCLUSION

Ovarian endometrioma itself is a contributing factor for DOR especially in women with bilateral or multiple chocolate cysts. Surgical managements like cystectomy may also contribute to further loss of primordial follicles as a result there will be low AMH & AFC count. So female subjects under infertility treatment with the history of ovarian endometrioma or had done cystectomy as a part of its management should be evaluated for ovarian reserve.

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