

THE ROLE OF EARLY DIAGNOSIS IN MANAGING AND TREATING INFERTILITY SECONDARY TO ENDOMETRIOSIS:A LITERATURE REVIEW

Abstract :

The goal is to encourage good medical practices so that the emotional and psychological stigma associated with the common occurrence of infertility related to endometriosis in females of reproductive age may be adequately treated simultaneously with the fundamental cause. The failure of a male and female partner to conceive following frequent, unprotected sexual activity for a period of 12 months is a fairly strict definition of infertility. As a result of the fact that 85% of women are seen to become pregnant within a year of engaging in regular, unprotected sexual activity, the length is significant and commonly stressed in this context. The remaining 15% of couples may encounter a variety of obstacles to conceiving, and those issues are what spark this entire discussion about infertility. The presence of endometrial tissue outside of the uterine cavity is referred to as endometriosis. In the event that the female does not engage in sexual activity to conceive, it typically lines the uterine cavity and is shed off during the monthly menstrual cycle. Endometriosis is diagnosed only on the basis of histology, with the criteria focused on finding endometrial glands and stroma anywhere beyond the uterine cavity. The presence of endometrial tissue outside of the uterine cavity is referred to as endometriosis. In the event that the female does not engage in sexual activity to conceive, it typically lines the uterine cavity and is shed off during the monthly menstrual cycle. Endometriosis is diagnosed only on the basis of histology, with the criteria focused on finding endometrial glands and stroma anywhere beyond the uterine cavity.

Keywords: Infertility, endometriosis, endometrial glands, early diagnosis, unprotected intercourse

INTRODUCTION

In a very literal sense, the term infertility is defined as the inability of a male and female partner to conceive after having regular, unprotected intercourse for a period of 12 months. The duration here is very important and more frequently emphasized, mainly because 85% of the women are seen to conceive within a year of having regular, unprotected intercourse. The remaining 15% of couples may have a myriad of reasons for facing a failure in doing so, and those factors are the ones that start this whole debate of infertility. (1)

According to the World Health Organization (WHO), approximately 40% of infertility stems due to factors present in female partners. In 35% of the remaining couples, both the male and female partners were found to be the causes behind it, whereas the male partners were found to be solely responsible in only 8% of the cases. (2)

Since female-only causes are seen to be the major reasons, it is an established factor that whenever a couple faces problems in conceiving, it is ultimately the female partner who is asked to get her consultation done first, before other factors are excluded. In these female-related causes, there are several ovulatory and other reproductive causes that are the culprit behind infertility in a female. (3)

Endometriosis has been found to be the causative factor behind infertility in about 15% of females. (4) It is a chronic inflammatory condition that affects women of reproductive ages and leads to them developing pain and infertility in the long run. All the women who suffer from endometriosis are seen to face a lot of problems due to the presence of this condition. It is also an understood fact that once a woman has been diagnosed with this condition, she will ultimately

have to face the consequences in the form of difficulty conceiving, and even facing issues such as infertility. (5)

Therefore, this review aims to reflect on the causes and reasons why endometriosis affects fertility rates in women. In addition, this review will also reflect on what could be done to effectively manage and somewhat reverse the condition.

The aim is to promote healthy and effective practices in medical science so that the emotional and psychological stigma attached to the prevalence of infertility secondary to endometriosis in females of reproductive ages could also be cured alongside the primary reason effectively.

ENDOMETRIOSIS AND ITS ROLE IN CAUSING INFERTILITY IN FEMALES

Endometriosis is defined as the presence of endometrial tissue outside the uterine cavity. It normally lines the uterine cavity and is shed off during the monthly menstrual cycle, in case the female does not undergo sexual intercourse to conceive. The diagnosis of endometriosis is done purely on histological grounds, where the criteria are set on identifying the presence of endometrial glands and stroma anywhere outside the uterine cavity. (6)

Although the presence of these endometrial glands is mostly found to occur within the pelvis, it was also seen that this condition could involve the other body organs and cavities as well. These other locations may involve the ovaries, the posterior broad ligament, the anterior and posterior cul-de-sac, and the uterosacral ligament. (7) Sometimes, the ureter, the bladder, and other visceral organs in relation to both the urogenital and the intestinal tract may also be seen to be involved in endometriosis. Moreover, the extra-pelvic locations might include the pleura, the pericardium, and the central nervous system. However, these locations are usually infrequent and rare but could be very much encountered in any of the cases with atypical features.

As far as the incidence and prevalence of endometriosis are concerned, it is seen that this condition is very easy to be evaluated in both these respects since the diagnosis is only declared when it has been confirmed accurately through a laparoscopic examination, which is indeed very authentic. It is seen that endometriosis affects typically 10-15% of females in their reproductive ages. Among these women, about 50% are bound to experience infertility in the course of this chronic disease. (8)

According to the American Society of Reproductive Medicine, there are four stages of endometriosis that are clinically seen in patients. These stages vary in their features and presence in different ways from patient to patient. Stages I and II are characterized by the presence of inflammation and increased production of cytokines, macrophages, natural killer cells, and prostaglandins. In these stages, tubal and ovarian function gets impaired due to the blockage of these ducts. This impairs fertilization and later on, even implantation. Stage III and IV of endometriosis is concerned with the presence of pelvic adhesions that affect the anatomy of the pelvis and once again, impair the fertility factor of the affected females. So, to understand it in a better way, it could be said that it is the series of changes that occur due to the presence of endometrial tissues outside the uterine cavity that leads to the development of all those factors that further give rise to infertility in the long run. (9)

The most problematic part of being affected by this disease is that it often gets too late before it is diagnosed for the better. It has been researched and concluded by experts that if endometriosis gets diagnosed at an earlier stage or before it starts taking a turn for the worse, there is a lot that could be done to reverse the ongoing changes, and all this could also help in reversing the infertility factor to some extent in some of the females who have not been affected so severely by this disease. (10) However, the unfortunate part is that this concept remains misunderstood and

miscommunicated, and as a result, women are seen to suffer from the chronicity and long-standing course of this disease with pain and other side effects. The pain that is associated with endometriosis is severe and unbearable for some women, yet they have to suffer from it if they are not getting the right treatment for it.

Although there are a few predisposing factors that link the development of endometriosis in certain women, not every layperson is aware of these symptoms and thus, has to suffer from the adversities of this situation. These predisposing factors consist of early menarche that occurs before the age of 11 years, women having shorter periods ranging less than 28 days on average, women having extremely heavy periods or menorrhagia, and disturbed hormonal levels, mainly low progesterone and higher estrogen levels. These hormones play an important role in regulating the menstrual cycle and when their levels would be out of balance or lesser than the actual amount, this is when the problem arises. (11)

There are many mechanisms by which endometriosis could affect the fertility status of a woman. In some earlier studies, it was found that endometriosis ends up damaging the tissues of the ovaries, which in turn affects ovarian function, as highlighted above. The whole process of ovulation might get affected due to this. Some studies have also highlighted how endometriosis could affect the ovarian reserve, thereby leading to lesser chances of a female getting pregnant with time. The ovaries face a chronic fibrotic change, which ultimately decreases the ovarian reserve and keeps them in a compromised state.

THE ROLE OF EARLY INTERVENTIONS AND MANAGEMENT OF ENDOMETRIOSIS IN REDUCING INFERTILITY IN WOMEN

It has been analyzed that if endometriosis is diagnosed within its early stages and simultaneously, steps are taken to control and manage the condition effectively, then it could be

possible for the affected women to conceive and overcome their infertility issues. However, like every other theory and assumption, it is required for this concept to get backed up by evidence as well to prove its authenticity. (12)

The definitive treatment of endometriosis involves removing the lesions that might be present in the pelvis or elsewhere to relieve the pain of the patient. This surgery is complex and requires the expertise of the most competent of all surgeons to ensure that maximum results could be achieved from it. In a very systematic way, it is appropriate to treat the infertility caused by endometriosis stage-wise. This also helps in understanding how much damage has been caused to the uterus and the ovaries.

For Stages I and II of endometriosis, it has been suggested that ovulation should be suppressed for a fixed period of time. This could be achieved through multiple drugs such as Danazol, Gestrinone, Medroxyprogesterone acetate, or combined oral contraceptive pills. (13)

Using this to suppress ovulation for a small time, provided that the couple complies with the following conditions, including the age of the female partner less than 39 years, a female partner with a normal ovulatory and menstrual cycle, and normal sperm analysis of the male partner. All these conditions act as favorable circumstances for the treatment to act and induce fertility in such couples. However, there is always a need to monitor any side effects that the female partner may experience from the use of the drugs that were used to stop ovulation. (14)

For couples in whom the female partner is suffering from Grade III or IV endometriosis, it has been recommended that the definitive treatment plan lies in the surgical excision of these cysts. Furthermore, trials may also be given for the coagulation of endometriotic peritoneal implants. Studies have found that doing so can help these couples with spontaneous conception within a

period of 3 years. Such successful couples were found to be approximately 50% out of the total couples who were selected for this purpose. (15)

However, for any method that has been devised appropriate for a couple, it is highly important that proper counseling is done for that couple along with making them aware of the possible outcomes, side effects, and complications that might arise with the usage of those treatments. (16)

Although not exactly incurable, endometriosis could prove to be a hindrance in people who are not wishing to conceive, but with a timely diagnosis and management protocols, it could very much help the couple conceive in the majority of cases.

It has been noted in various cases that the difference between the early and late interventions play an important role in altering the quality of life, while at the same time also affecting the mental health of both the male and female partner. The delay in treatment is also seen to negatively impact the fertility factors, since long-term waiting time could either exacerbate the symptoms or cause the stage of endometriosis to progress further. (17)

CONCLUSION

Endometriosis is a chronic inflammatory condition in which the endometrial lining is seen to develop outside the uterus. It may involve any location either within the pelvis or outside it. Endometriosis causes a wide range of symptoms in the females who are affected by it, with the most prevalent symptoms being pain and infertility in the long run. The latter side effect is what is of great concern to couples who wish to conceive and start a family of their own.

Although endometriosis is a condition that could be managed well with the appropriate medicines, however, its effects such as infertility might be irreversible in extreme cases. Therefore, it has been concluded through extensive studies that the early diagnosis and

management of endometriosis in women could help treat their condition effectively with promising results. Early management has seen to cause favorable effects on both the male and the female partner, as it makes both of them conceive within a short time. On the other hand, unnecessary delays could worsen to condition while also negatively impacting the patient's life for the worse in the long run.

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REFERENCES

1. Walker MH, Tobler KJ. Female Infertility. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Jul 24]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK556033/>
2. Elhussein OG, Ahmed MA, Suliman SO, Yahya leena I, Adam I. Epidemiology of infertility and characteristics of infertile couples requesting assisted reproduction in a low-resource setting in Africa, Sudan. *Fertil Res Pract.* 2019 Jul 18;5:7.
3. Recent advances in medically assisted conception. Report of a WHO Scientific Group. *World Health Organ Tech Rep Ser.* 1992;820:1–111.
4. Parasar P, Ozcan P, Terry KL. Endometriosis: Epidemiology, Diagnosis and Clinical Management. *Curr Obstet Gynecol Rep.* 2017 Mar;6(1):34–41.
5. Filip L, Duică F, Prădatu A, Crețoiu D, Suciuc N, Crețoiu SM, et al. Endometriosis Associated Infertility: A Critical Review and Analysis on Etiopathogenesis and Therapeutic Approaches. *Medicina (Mex).* 2020 Sep 9;56(9):460.
6. Tsamantioti ES, Mahdy H. Endometriosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Jul 28]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK567777/>
7. Jenkins S, Olive DL, Haney AF. Endometriosis: pathogenetic implications of the anatomic distribution. *Obstet Gynecol.* 1986 Mar;67(3):335–8.
8. Macer ML, Taylor HS. Endometriosis and Infertility: A review of the pathogenesis and treatment of endometriosis-associated infertility. *Obstet Gynecol Clin North Am.* 2012 Dec;39(4):535–49.
9. Lee SY, Koo YJ, Lee DH. Classification of endometriosis. *Yeungnam Univ J Med.* 2020 Aug 7;38(1):10–8.
10. Chauhan S, More A, Chauhan V, Kathane A. Endometriosis: A Review of Clinical Diagnosis, Treatment, and Pathogenesis. *Cureus.* 14(9):e28864.
11. Reis FM, Petraglia F, Taylor RN. Endometriosis: hormone regulation and clinical consequences of chemotaxis and apoptosis. *Hum Reprod Update.* 2013 Jul;19(4):406–18.
12. Lee D, Kim SK, Lee JR, Jee BC. Management of endometriosis-related infertility: Considerations and treatment options. *Clin Exp Reprod Med.* 2020 Mar;47(1):1–11.
13. Hughes E, Brown J, Collins JJ, Farquhar C, Fedorkow DM, Vandekerckhove P. Ovulation suppression for endometriosis. *Cochrane Database Syst Rev.* 2007 Jul 18;2007(3):CD000155.
14. Olive DL, Pritts EA. Treatment of endometriosis. *N Engl J Med.* 2001 Jul 26;345(4):266–75.

15. Vercellini P, Somigliana E, Viganò P, Abbiati A, Barbara G, Crosignani PG. Surgery for endometriosis-associated infertility: a pragmatic approach. *Hum Reprod Oxf Engl.* 2009 Feb;24(2):254–69.
16. Vercellini P, Fedele L, Aimi G, De Giorgi O, Consonni D, Crosignani PG. Reproductive performance, pain recurrence and disease relapse after conservative surgical treatment for endometriosis: the predictive value of the current classification system. *Hum Reprod Oxf Engl.* 2006 Oct;21(10):2679–85.
17. Kim MR, Chapron C, Römer T, Aguilar A, Chalermchockcharoenkit A, Chatterjee S, et al. Clinical Diagnosis and Early Medical Management for Endometriosis: Consensus from Asian Expert Group. *Healthcare.* 2022 Dec 12;10(12):2515.

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