

Perspective Article

Infertility (Non Conception) with Regular Menstruation Predisposes to Endometriosis – A Hypothesis

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Abstract

Endometriosis is the most challenging and intriguing gynecological enigma. The true incidence of pelvic endometriosis in women still remains largely unknown, despite several studies quoting variable figures. Chronic pelvic pain and infertility have been the most common features in women with endometriosis. However the cause/effect relationship is a subject of debate. Endometriosis is found to be more in nulliparous women & women with pelvic pain and rare among fertile women and women with amenorrhoea. We now believe that retrograde menstruation is probably the cause for the occurrence of pelvic endometriosis. We here propose that infertility or non conception with persistent menstruation most likely leads to endometriosis and not the other way around as is commonly believed.

Key Words: Endometriosis, Infertility, Retrograde menstruation, Cause/Effect

Introduction

Endometriosis is the most challenging and intriguing gynecological enigma. The true incidence of pelvic endometriosis in women still remains unknown, despite several studies quoting variable figures¹⁻³. It has been estimated as high as 25-60% in infertile women^{4,5}. Chronic pelvic pain and infertility have been the most common features in women with endometriosis⁶. It is not yet clear if infertility is the sequel of endometriosis per se or are these two conditions causally related.

Endometriosis almost always occurs only in women who are menstruating. Premenarchal endometriosis is almost unheard of and the case report by Erica E. Marsh et al also requires further substantiation⁷. Endometriosis and infertility remain as associated conditions and the causal link has not yet been convincingly proven⁸. In the following paragraphs, we are trying to substantiate our hypothesis-i.e. - infertility/non- conception predisposes to endometriosis and not vice versa.

Menstruation – a bio marker of failed physiology

Nature's intention is to have the following sequence of biological events to happen in a regular rhythm in all women i.e., onset of puberty → folliculogenesis → increasing levels of estrogen → priming of endometrium → implantation of embryo after ovulation and pregnancy. If the chain is disturbed by non – conception, either voluntary or involuntary, menstruation ensues with the shedding of the prepared endometrium. Hence, menstruation emerges as the biomarker of failed physiology⁹ i.e., non conception.

Known pathophysiology of endometriosis

Despite the myriads of theories postulating the genesis of endometriosis, retrograde menstruation theory is

believed to be the most tenable pathway for the occurrence of pelvic endometriosis. It is explained as, the retrograde flow of blood and endometrial cells into the peritoneal cavity occurring during menstruation via the patent fallopian tubes. The extruded blood and endometrial cells are normally dealt by the local defense mechanism. When the defense mechanism fails as in endometriosis, the endometrial cells adhere to the peritoneal cavity, implant, grow and bleed over the course of subsequent menstrual cycles leading to endometriotic implants. This is noted in women who are genetically prone & immunologically susceptible. This theory has gained strength by laparoscopic demonstration of efflux of menstrual blood during menstrual cycle in 76%-90% of women in the reproductive age group¹⁰. We hypothesize that retrograde menstruation probably happens in all women with patent fallopian tubes but those women with poor immunological competence alone develop endometriosis.

Substantiating the retrograde menstruation theory

Incidence of endometriosis is increased in women with early menarche, frequent menstrual cycles (polymenorrhoea), women with menorrhagia, obstructive congenital Mullerian anomalies like imperforate hymen and cervical stenosis. All these women have increased episodes of retrograde menstruation and hence increased risk of developing endometriosis. The endometrial cells in retrograde menstrual blood enter the peritoneal cavity, get absorbed by the lymphatic system and drain into the venous system, from where they spread to the distant sites explaining the extra pelvic endometriosis¹¹.

It has also been observed that endometriosis is rare in premenarchal girls and postmenopausal women. The incidence of endometriosis in postmenopausal women (without HRT) is only 2.2 %. Punnonen et al also quote the reason for postmenopausal endometriosis as

hyperestrogenic state in obese women or in women who gain weight with probably pre existing endometriotic lesion¹². So far no case has been documented in pre-pubertal girls. Endometriosis is very rare in complete Mullerian agenesis and in Turner's syndrome¹³ who present with primary amenorrhoea.

The incidence of endometriosis in multiparous women is relatively low around 3.7 %¹⁴ and probably because pregnancy and absence of menstruation ameliorate endometriosis. The prevalence of endometriosis in women who have undergone tubal sterilization is only 1% to 7%¹⁵, may be parity being the preventing factor, whereas the prevalence of endometriosis is more in women undergoing laparoscopy at the time of evaluation for infertility i.e., 25-60%^{4,5}.

Is infertility the actual cause for endometriosis?

To say "Menstruation is a pre requisite for the occurrence of endometriosis" -would be stating the obvious. The above statement is reinforced by the conspicuous rarity of endometriosis among amenorrhoeic/fertile women. Longer the duration from menarche to conception, greater is the risk for endometriosis. Uninterrupted continuous cyclical menstruation overwhelms the local defense mechanism and results in the implantation of endometrial cells. The endometrial cells grow further, bleed over the course of subsequent menstrual cycles leading to endometriosis (in genetically prone/ immunologically susceptible women¹⁶. Moreover, endometriosis has been documented more in women with excessive and persistent menstruation as in abnormal uterine bleeding irrespective of their parity¹¹.

Conclusion

We therefore hypothesize that retrograde menstruation happens in all women with patent fallopian tubes. Endometriosis develops in women who are infertile due to any cause or postpone pregnancy & have uninterrupted menstrual cycles. Prevalence of endometriosis has been noted to be high in the infertile women due to incessant menstruation overwhelming the local immunological defense mechanism. However, it does not have any deleterious effect per se on the reproductive outcome of these women, unless otherwise there is gross disturbance of the pelvic anatomy^{17, 18}.

These findings cast a serious doubt on the cause/effect relationship between endometriosis and infertility. Aggressive treatment of endometriotic lesions are known to result in impaired ovarian function¹⁹ thus making the remedy worse than the malady. Therefore, it is wise to treat the infertility and ignore the endometriosis. It may be that infertility predisposes to endometriosis and not vice versa.

Have we been putting the cart before the horse?

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INTERESTING ECG

A 50 year old female presented with complaints of giddiness on and off for the past ten days. She is not a known case of Diabetes Mellitus, Hypertension, and is not on any medications.

