



Prevalence of Common Causes of Secondary Infertility Among Women

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ABSTRACT

Background: The research team examined irregular menstrual cycles along with tubal occlusion, dyspareunia, dysmenorrhea, and endometriosis as these conditions affect both reproductive ability and mental and social aspects of the afflicted females. The occurrence of secondary infertility affects numerous couples worldwide especially in locations with limited resources. **Materials and methods:** A six-month research study used descriptive cross-sectional methodology at Mayo Hospital Lahore. The researchers applied non-probability consecutive sampling to select 152 women from ages 18 to 40 years old with secondary infertility. Medical histories along with pelvic ultrasonography, hormonal profiling, vaginal discharge culture, hysterosalpingogram, and laparoscopy made up the data collection methods. The research analysis was conducted through SPSS version 24.0 software. **Results:** The time period of living with the husband influenced irregular menstrual cycles and dysmenorrhea whereas parity led to dyspareunia only. **Conclusion:** The research findings demonstrated that secondary infertility causes exist at high frequencies within a low- and middle-income country population. These study results demonstrate the necessity for full evaluation and treatment management of these issues to properly handle secondary infertility. More research is essential to establish specific interventions that will enhance reproductive health results in restricted resource settings. **Keywords:** LMIC, secondary fertility, dyspareunia, tubal occlusion, irregular menstrual cycle, and endometriosis.



INTRODUCTION:

Among all the different aspects of infertility, one of the substantial global health concerns is secondary infertility, which affects millions of couples around the world, especially those in resource-constrained countries. The causes of secondary infertility range from irregular menstrual cycles, tubal occlusion, dyspareunia, dysmenorrhea, and endometriosis. In addition to reproductive capacity, these conditions exert far reaching consequences for psychological and social well-being of the affected individuals. A common factor that can affect secondary infertility is dysmenorrhea or painful menstruation. The vast majority of primary dysmenorrhea is treatable by conservative measures, whereas secondary dysmenorrhea may be related to a number of underlying conditions such as endometriosis, uterine fibroid, pelvic inflammatory disease, or adenomyosis. Severe dysmenorrhea has the capability to interrupt normal menstrual cycles and ovulation and therefore has the potential to affect fertility.^(1, 2)

The inability to conceive can be significantly impeded by a couple's ability to engage in sexual intercourse due to the experience of pain, known as dyspareunia, during sexual intercourse. This condition is often associated with some forms of gynecological disorder, including endometriosis and pelvic inflammatory disease. However, such avoidance of sexual activity in the case of a persistent nature of dyspareunia may lead to relationship strain and exacerbation of existing fertility challenges.^(1, 3) Tubal occlusion that may occur for many reasons, such as pelvic inflammatory disease, past ectopic pregnancy, and complications

after prior surgical intervention, may cause secondary infertility. For instance, it has been demonstrated that *Chlamydia trachomatis* infection is a major causative agent of tubal damage and that there is a strong association between antibodies to chlamydial heat shock proteins and the development of tubal factor infertility.⁽⁴⁾ In low-and middle-income countries (LMIC) the burden of tubal factor infertility is great due to restricted access to timely diagnosis and treatment of sexually transmitted infections.

Irregular menstrual cycles might also lead to secondary infertility due to hormonal imbalance or other reasons associated with reproductive health issues. The females who are afflicted may have trouble predicting their ovulation and therefore the timing of sexual intercourse to achieve pregnancy. Irregular menstrual cycles also are a signal of anovulation or other ovulatory dysfunction, and thus confounds an already complicated fertility management.⁽²⁾

The secondary infertility might also result from endometriosis. It is estimated that 10% of women of reproductive age in the world suffer from this condition, and they present with several symptoms such as pelvic pain, dysmenorrhea and dyspareunia.⁽⁵⁾ ⁶⁾ Endometriosis may impair a female's fertility through several mechanisms including distorted pelvic anatomy, impaired peritoneal function, or poor embryo implantation.^(1, 7)

Clinical management of these conditions is very difficult to identify, especially in the context of resource constrained settings. Laparoscopy for



endometriosis evaluation, for example, may be restricted access to patients and lead to delay of diagnosis and/or to undiagnosed patients. In addition, underreporting of these conditions and, thus, the failure to optimize their treatments may be attributed to the healthcare providers' and patients' lack of knowledge.^(6, 8) The females afflicted with these conditions are not only adversely affected physically but also have their psychological and social aspects getting impacted as well. Both endometriosis and chronic pelvic pain are predisposing factors for severe anxiety and depression and vice versa, which can further aggravate gynecological problems and have a negative impact on the quality of life of women. The purpose of the current study was to provide data on the prevalence of these common causes of secondary infertility to provide a clinical setting with a better means to manage patients with patient-centered care. Additional information on the causes of secondary infertility will be added to the information already available. It will also help build the body of knowledge that will guide future interventions and research on reproductive health.

MATERIALS AND METHODS:

The descriptive cross-sectional study was carried out from August 2018 to February 2019 in the department of Obstetrics and Gynecology at Mayo Hospital Lahore following approval from the Institutional Review Board. The sample size of 152 was obtained with the use of the WHO sample size calculator, with the frequency of 11.1% of endometriosis obtained from a prior study.⁽⁹⁾ Patients

were recruited on a non-probability consecutive basis, aged between 18 and 40 years, diagnosed with secondary infertility, with a minimum of one successful childbirth, and practiced unprotected regular intercourse for at least one year. Participants using contraceptives, with BMI > 30 kg/m², or confirmed male factor infertility were excluded as per the exclusion criteria. Voluntary informed consent was obtained. Medical histories were recorded, and investigations like pelvic ultrasonography, hormonal profiling, vaginal discharge culture, hysterosalpingogram, and laparoscopy were the data collection strategies. The diagnoses of the causes of secondary infertility, such as irregular menstrual cycle, tubal occlusion, dyspareunia, dysmenorrhea, and endometriosis, were made by an obstetrics and gynecology consultant-supervised principal investigator. Data was analyzed using SPSS version 24.0, and means and standard deviations were computed for continuous variables, while frequencies and percentages were computed for categorical variables. Independent relevant factors were stratified to control for effect modifiers, and a Chi-Square test was carried out to determine the effect of the factors on the existence of different causes of secondary infertility. A p-value of <0.05 was statistically significant.

RESULTS:

A total of 152 females fulfilled the inclusion criteria and were enrolled into the study. Mean ($\pm$ SD) of age, weight, cohabitation with husband, and parity was 28.7 ($\pm$ 5.4) years, 70.2 ($\pm$ 15.4) kg, 3.3 ($\pm$ 1.6) years, and



2.16 (± 0.9). Out of 152 patients, dysmenorrhea (n=57; 38%) was the most frequent cause of secondary infertility followed by dyspareunia (n=54; 36%), tubal occlusion (n=50; 33%), irregular menstrual cycle (n=35; 23%), and endometriosis (n=26; 17%). The frequency of each cause encompassed both the cause alone as well as in combination with other causes. Association of factors revealed that age had a significant impact on the presence of tubal occlusion (p-value: 0.037) and endometriosis (p-value: 0.031), weight on irregular menstrual cycles (p-value: 0.039), tubal occlusion (p-value: 0.047), and endometriosis (p-value: 0.043), cohabitation with husband on irregular menstrual cycles (p-value: 0.041), and dysmenorrhea (p-value: 0.040), and parity on dyspareunia (p-value: 0.026) only (Table 1).

Table 1: Association of independent factors on the causes of secondary infertility

CAUSES OF INFERTILITY		Age (Years)		Weight (kg)		Cohabitation with husband (years)		Parity		p-value						
		18 – 30	> 30	42-70	> 70	1-4	>4	1-3	>4							
Irregular menstrual cycle	Yes	23 (15.1%)	12 (7.9%)	26 (17.1%)	9 (5.9%)	17 (11.2%)	18 (11.8%)	32 (21.1%)	3 (2.0%)	68 (44.7%)	58 (38.2%)	71 (46.7%)	55 (36.2%)	82 (53.9%)	44 (28.9%)	111 (75.0%)
	No	69 (45.4%)	48 (31.6%)	64 (42.1%)	53 (34.9%)	79 (52.0%)	38 (25.0%)	108 (71.1%)	9 (5.9%)	0.031*		0.043*		0.976		0.4
	p-value	0.474		0.039*		0.041*		0.866		* Statistically significant						

infertility, which is a major problem among women worldwide, and especially in countries with low and middle income. This investigation offers a detailed

DISCUSSION:

The overall objective of this study was to explore the serious reproductive health problem of secondary

analysis in the multiple factors associated with secondary infertility in this population.

The most prevalent cause of secondary infertility found in the current study was dysmenorrhea with 38% of the participants. This is clearly underlined by the high rate of importance of menstrual pain on reproductive health. According to the research of Vilšinskaitė et al.,⁽¹⁰⁾ the risk of menstrual pain is higher for nulliparous women and decreases with age. In addition, Liang et al.⁽¹¹⁾ study also suggested that acupuncture may be a cheaper option for treating endometriosis related pelvic pain and a feasible option in resource limited settings where access to Western medicine is limited. According to the study findings, healthcare providers should keep a watch for women with severe menstrual pain as it may be a sign of underlying fertility issues.

Dyspareunia was the second most common contributing factor in the current study (36% of study participants). This is noteworthy because dyspareunia can substantially impair sexual function and frequency of intercourse and therefore overall ability to conceive. Dyspareunia is biopsychosocial, as stated by Meana,⁽¹²⁾ meaning that it has physiologic, psychologic, relational, intergenerational, and sociocultural components. The recommendation of this study is that dyspareunia should be assessed and treated by combining sex therapy, gynecology, and physical therapy. The implementation of this comprehensive approach might be difficult in resource limited settings and adapted strategies are needed in low-and-middle income countries. The current study found that the sexual health problems should be taken into account in the routine service and treatment of fertility.

The study discovered that tubal occlusion was the third most common cause of infertility in the participants and that 33% of participants had tubal occlusion. This is consistent with the research that shows tubal factors as an important cause of infertility as per the research of Gu et al.⁽¹³⁾ who reported that 30% of infertile women have associated fallopian tube pathology and underlined the importance of TV 4D HyCoSy in assessing tubal status for the possibility of natural conception and for determining the requirement of assisted reproductive technology (ART). Yi et al.⁽¹⁴⁾ interestingly propose that stimulated intrauterine insemination (IUI) may be a reasonable initial treatment for women with unilateral tubal occlusion with pregnancy rates equivalent to those with unexplained infertility. This finding provides hope to women with tubal factor infertility in resource-constrained settings where access to advanced reproductive technologies may be limited. The study also noted that 23% of participants had irregular cycles. This may be due to ovulatory dysfunction which could also impact the fertility of the affected female. Vilšinskaitė et al.⁽¹⁰⁾ reported that 84.2% of women surveyed had pain during menstruation, and in particular, women under 25 years of age were more likely to have pain. Further, the research indicated that dysmenorrhoea was more prevalent among women with irregular menstrual cycle (92.5%) and among women who had bleeding duration between 4 – 7 days (90.7%). This emphasized the importance of menstrual irregularities in fertility. It may also indicate the presence of other underlying health conditions such as polycystic ovary syndrome (PCOS), thyroid related problems or any hormonal imbalance. Given this, hormonal evaluations and

monitoring of menstrual cycles should be done in women with secondary infertility. Furthermore, Rehan et al.⁽¹⁵⁾ study also revealed that women who had experienced pandemic-related stress had higher potential of change in menstrual duration (p-value=0.0008), heavy blood flow (pvalue=0.028) and higher incidence of painful periods (p-value<0.0001) that might affect menstrual health and, consequently, fertility.

The researchers of the present study found that 17 percent of the participants had endometriosis, which is a very high incidence considering the known impact of this condition on fertility. Moreover, in a prior research by Kotowska et al.⁽¹⁶⁾ on endometriosis reported a prevalence of 9.9% with common associated symptoms such as dysmenorrhea (83%), pelvic pain not associated with menstruation (72%), dyspareunia (68%) and painful defecation or dysuria (40%). Endometriosis can interfere with fertility by various mechanisms including changes of the pelvic anatomy, ovarian function and inflammation. The high prevalence of endometriosis in women with secondary infertility justifies its inclusion in the work up of women with secondary infertility, particularly when they have symptoms of dysmenorrhea or dyspareunia.

Several consequential relationships were found in the investigation of associated factors. Analysis of results showed that age was a significant factor in prevalence of endometriosis and tubal occlusion. This is consistent with the well-recognized relationship between reproductive health problems and elevated risk with age, especially tubal occlusion⁽¹⁷⁾ and endometriosis.⁽¹⁸⁾ However, this opens up the need for early fertility assessments and immediate action,

where appropriate, particularly, for women in the late reproductive stage in life.

The present research results indicate a very complex relation between body weight and various outcomes to reproductive health. For example, Micic et al.⁽¹⁹⁾ found that obesity had an effect on the regularity of the menstrual cycle and even on fertility, which could take place via disruption of the hypothalamic pituitary ovarian axis, leading to anovulation and infertility. Further study of morbidly obese women determined that metabolic factors, as with elevated insulin resistance, may contribute to functioning of the menstrual cycle.⁽²⁰⁾ In contrast, the study on young Korean women also found increased proportions of underweight as well as obese individuals in the group with irregular menstruation.⁽²¹⁾ This suggests the need for personalized weight management strategies in the context of fertility care to varying body composition profiles of each patient.

As observed in this current study, cohabitation with a spouse was also associated with irregular menstrual patterns and dysmenorrhea. As a compelling finding, this merit further investigation of the possible psychosocial and lifestyle determinants that may affect fertility and menstrual health in the context of marriage and cohabitation.

In the present study, an interesting observation was made regarding the significant association of parity with dyspareunia. Contradictory findings from the existing literature have been shown regarding the relationship between parity and dyspareunia. Gürel and Gürel's research showed that the parity level was higher in women with chronic pelvic pain (a disorder typically associated with dyspareunia) compared to the control group (p-value: <0.0001).⁽²²⁾ Moreover,

they reported that grand multiparity had a significant effect in chronic pelvic pain (p-value: <0.0001) and can be associated with a higher number of births that can consequently lead to pelvic pain and dyspareunia.⁽²²⁾ On the other hand, some studies have not been able to establish an important correlation between parity and sexual dysfunction, for example dyspareunia, following first vaginal delivery.^(23, 24) Several reasons for the inconsistency of these findings are possible, including the possibly significant effect of delivery induced changes in pelvic floor anatomy, as noted by Dixit et al.⁽²⁵⁾ in the observation of reduced sonographic measures of pelvic floor function after delivery. Mechanisms underlying such an association should be elaborated further.

The implications of the research findings demand the allocation of resources in low-and middle-income countries. As a result, more investment in pain and sexual health clinics in these settings is required as the prevalence of conditions such as dysmenorrhea and dyspareunia is high. In addition, the ample existence of tubal occlusion could prompt even more sophisticated reproductive technologies, e.g. in vitro fertilization, to be encouraged in such LMIC contexts. Nevertheless, there is a need to acknowledge the limitations of the study. Although a sample size of 152 women is certainly useful, but it cannot be generalized to a larger population. Furthermore, the study offers no information regarding male factor infertility, which is also an important factor in overall fertility evaluations.

CONCLUSION:

This is an important contribution to understanding the factors that contribute to secondary infertility in

women from low-and-middle-income countries. Dysmenorrhea, dyspareunia, tubal occlusion, irregular menstrual cycles and endometriosis are the predominant causes identified by the research, and the relationship with a number of determinants is examined for use in clinical practice and public health initiatives. These findings would need to be validated with larger populations and the potential mechanisms underlying these relations would need to be studied as well as work to improve the effectiveness of the interventions that are specifically targeted to the women in LMICs with secondary infertility.

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