



Comparative study of etiological factors of single early pregnancy loss with that of recurrent pregnancy loss

¹Dr. Digvijay Kadam, ²Dr. Nitin Kshirsagar, ³Dr. Manisha Laddad

¹Assistant Professor, ²Professor, ³Associate Professor, Department of OBGY, Krishna Vishwa Vidyapeeth, Karad, Maharashtra, India

Corresponding author: Dr. Nitin Kshirsagar, Professor, Department of OBGY, Krishna Vishwa Vidyapeeth, Karad, Maharashtra, India

Abstract

Background: This study was conducted to compare the etiological factors of single early pregnancy loss with that of recurrent pregnancy loss.

Material and methods: Overall 200 subjects were recruited in this research. They got divided into two groups of 100 each. Group A comprised of 100 female subjects with first single pregnancy loss whereas group B comprised of 100 females having RPL. The suggested investigations for causative variables had been performed in the two cohorts except karyotyping, and thrombophilia screening was done in females with unidentified cause.

Results: Sociodemographic factors and gestational age were similar in both the groups. Significantly more number of women with first single pregnancy loss (60%) had known etiological factors than women with RPL (40%).

Conclusion: A significant proportion of women with first early pregnancy loss had various etiological factors and endocrine factors were the most common causes.

Keywords: Endocrine cause, Etiology, First early pregnancy loss, Miscarriage

INTRODUCTION

Pregnancy loss is a distressing condition for both the patient and obstetrician. It can occur at any gestational period but most commonly during early pregnancy. The aetiologies for early pregnancy loss and late pregnancy loss are most often different.¹ Early pregnancy loss is defined as a nonviable intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without cardiac activity within the first 12 + 6/7 weeks of gestation. In the first trimester, the terms miscarriage, spontaneous abortion, and early pregnancy loss are used interchangeably as there is no consensus on terminology in the literature.²

Early pregnancy loss occurs in 10% of all clinically recognized pregnancies and approximately 80% of all cases of pregnancy losses occur within the first trimester. Pregnancy loss when occurs repeatedly is termed recurrent pregnancy loss (RPL). According to the European Society of Human Reproduction and Embryology (ESHRE), RPL is a distinct disorder defined by two or more failed clinical pregnancies.³ Whenever a woman suffers pregnancy loss, an explanation is sought for the same from the treating obstetrician. Sometimes women approach the clinicians after having suffered pregnancy loss and request for investigations, but the clinical practice recommendations are in place to investigate after two or more pregnancy losses and not for single pregnancy loss.^{4,5}

A significant proportion of women (20%) who experience a miscarriage become symptomatic for depression and anxiety.⁶ This warrants diagnostic workup and interventions. There are no studies with regard to the initiation of investigations after first early pregnancy loss. In this context, this study aims to find out the etiological factors in women with first early pregnancy loss and to compare it with women who had two or more than two early pregnancy losses (RPL).^{6, 7} Hence; the present study was conducted for assessing etiological factors of single early pregnancy loss with that of recurrent pregnancy loss.

MATERIALS AND METHODS

The present study was conducted for assessing etiological factors of single early pregnancy loss with that of recurrent pregnancy loss. Overall; 200 subjects were recruited in this research. They got divided into two groups of 100 each. Group A comprised of 100 female subjects with first single pregnancy loss whereas group B comprised of 100 females having RPL. Group A—Pregnant females admitted with first early pregnancy loss or nonpregnant women attending outpatient department with history of one early pregnancy loss and requesting investigations for pregnancy loss, and Group B—Women with two or more than two early pregnancy losses (RPL). Demographic information comprising age, occupation, education, socioeconomic status had been gathered by interviewing the subject. Clinical profile comprising gravidity, parity, past obstetric history, family history as well as treatment history had been recorded on a proforma after interviewing the subject as well as through medical records. Clinical evaluation was done to find out the etiology of pregnancy loss. If no reason was discovered, thrombophilia profile for acquired thrombophilias and congenital thrombophilias had to be performed. SPSS software was used for evaluation of level of significance.

RESULTS

100 female subjects were recruited in group A whereas 100 subjects were recruited in group B with RPL. Four women in group A (first pregnancy loss) and two women in group B (RPL) were in nonpregnant state, rest of the women were recruited immediately after pregnancy loss as inpatients. Table 1 shows the comparison of causes of first pregnancy loss with that of RPL. The proportion of known causes in group A women with single pregnancy loss was 55% as compared to 44% in group B. Among unknown causes, thrombophilia evaluation was positive in 9 cases of group A while it was positive in 12 cases of group B.

Table 1: Comparison of causes of first pregnancy loss with that of RPL.

| Etiological factors | Group A | Group B |
|---------------------|---------|---------|
| Unknown | 45(45%) | 56(56%) |
| Known | 55(55%) | 44(44%) |

Table 2: Comparison of known causes of first pregnancy loss with that of RPL

| Known causes | | Group A | Group B |
|--------------------|-----------------------------|---------|---------|
| Anatomical factors | Uterine anomaly | 12 | 8 |
| | Fibroid | 10 | 9 |
| | Cervical incompetence | 8 | 7 |
| Endocrine factors | Hypothyroidism | 8 | 7 |
| | Type 2 diabetes | 7 | 6 |
| | Polycystic ovarian syndrome | 5 | 4 |
| Infections | | 5 | 3 |
| Total | | 55 | 44 |

Table 3: Comparison of thrombophilia evaluation for unknown causes

| Thrombophilia evaluation | Group A | Group B |
|--------------------------|---------|---------|
| Negative | 36 | 44 |
| Positive | 9 | 12 |
| Total | 45 | 56 |

DISCUSSION

Spontaneous pregnancy loss is a surprisingly common occurrence. Whereas approximately 15% of all clinically recognized pregnancies result in spontaneous loss, there are many more pregnancies that fail prior to being clinically recognized. Only 30% of all conceptions result in a live birth. Spontaneous pregnancy loss can be physically and emotionally taxing for couples, especially when faced with recurrent losses. Recurrent pregnancy loss (RPL), also referred to as recurrent miscarriage or habitual abortion, is historically defined as 3 consecutive pregnancy losses prior to 20 weeks from the last menstrual period.⁸⁻¹⁰ Hence; the present study was conducted for assessing etiological factors of single early pregnancy loss with that of recurrent pregnancy loss.

In the present study, 100 female subjects were recruited in group A whereas 100 subjects were recruited in group B with RPL. Four women in group A (first pregnancy loss) and two women in group B (RPL) were in nonpregnant state, rest of the women were recruited immediately after pregnancy loss as inpatients. Our results were in concordance with the results obtained by previous authors who also reported similar findings. Luteal phase defect (LPD), polycystic ovarian syndrome (PCOS), diabetes mellitus, thyroid disease, and hyperprolactinemia are among the endocrinologic disorders implicated in approximately 17% to 20% of RPL. Traditionally, LPD has been proposed to result from inadequate production of progesterone by the corpus luteum and endometrial maturation insufficient for proper placentation. It is diagnosed when there is a persistent lag of longer than 2 days in the histologic development of the endometrium compared with the day of the menstrual cycle. Today, the true role of LPD in RPL is controversial and endometrial biopsies for LPD diagnosis are rarely indicated. Some studies have noted abnormal elevations in luteinizing hormone or in androgens (both features associated with PCOS) among patients experiencing RPL, suggesting that these abnormalities may result in premature aging of the oocyte and/or dyssynchronous maturation of the endometrium.¹⁰⁻¹²

In the present study, the proportion of known causes in group A women with single pregnancy loss was 55% as compared to 44% in group B. Among unknown causes, thrombophilia evaluation was positive in 9 cases of group A while it was positive in 12 cases of group B. Dasari P et al determined the identifiable causes and their proportion in women with first early pregnancy loss and to compare with that of women with recurrent pregnancy loss (RPL). Group A included 105 women with first single pregnancy loss and group B included 105 women with RPL. The recommended investigations for etiological factors were done in both groups except karyotyping, and thrombophilia screening was done in those with unknown etiology. Sociodemographic factors and gestational age were similar in both the groups. Significantly more number of women with first single pregnancy loss (58%) had known etiological factors than women with RPL (43%) ($p = 0.038$). Endocrine causes were commonest in both the groups (first pregnancy loss 36% vs RPL 21%; $p = 0.023$). Out of the women with unknown causes, 18% of women were positive for thrombophilia in each group and more than 50% of them were antiphospholipid antibodies (APLA) positive. Significant proportion of women with single first pregnancy loss have treatable etiological factors like those of RPL. Hence evaluation should be undertaken to achieve optimum outcomes during the next pregnancy and prevent RPL.¹³

CONCLUSION

A significant proportion of women with first early pregnancy loss had various etiological factors and endocrine factors were the most common causes.

REFERENCES

1. Wang X, Chen C, Wang L, et al. Conception, early pregnancy loss, and time to clinical pregnancy: a population-based prospective study. *Fertil Steril* 2003;79(3):577–584.
2. Bender Atik R, Christiansen OB, Elson J, et al. ESHRE guideline: recurrent pregnancy loss. *Hum Reprod Open* 2018;2018:hoy004.
3. El Hachem H, Crepaux V, May-Panloup P, et al. Recurrent pregnancy loss: current perspectives. *Int J Womens Health* 2017;9:331–345.
4. Nynas J, Narang P, Kolikonda MK, et al. Depression and anxiety following early pregnancy loss: recommendations for primary care providers. *The primary care companion for CNS disorders* 2015;17(1): 75- 78.
5. Nybo Andersen AM, Wohlfahrt J, Christens P, et al. Maternal age and fetal loss: population based register linkage study. *BMJ* 2000;320(7251):1708–1712.
6. Bhandari HM, Tan BK, Quenby S. Superfertility is more prevalent in obese women with recurrent early pregnancy miscarriage. *BJOG Int J Obstet Gynaecol* 2016;123(2):217–222.
7. Matjila MJ, Hoffman A, van der Spuy ZM. Medical conditions associated with recurrent miscarriage – is BMI the tip of the iceberg? *Eur J Obstet Gynecol Reprod Biol* 2017;214:91–96.
8. Cavalcante MB, Sarno M, Peixoto AB, et al. Obesity and recurrent miscarriage: a systematic review and meta-analysis. *J Obstet Gynaecol Res* 2019;45(1):30–38.
9. Shetty MB, Malyala M, Swarup A, et al. Recurrent pregnancy loss: challenge to obstetricians. *Int J Reprod Contracept Obstet Gynecol* 2017;6(8):3376.
10. Fox-Lee L, Schust DJ. Recurrent pregnancy loss. In: Berek JS, editor. *Berek and Novak's Gynecology*. Philadelphia: Lippincott Williams & Wilkins; 2007. pp. 1277–1322.
11. Bussen S, Sutterlin M, Steck T. Endocrine abnormalities during the follicular phase in women with recurrent spontaneous abortion. *Hum Reprod.* 1999;14:18–20.
12. Watson H, Kiddy DS, Hamilton-Fairley D, et al. Hypersecretion of luteinizing hormone and ovarian steroids in women with recurrent early miscarriages. *Hum Reprod.* 1993;8:829–833.
13. Dasari P, Garg S, Kar R, et al. Etiological Factors for First Single Early Pregnancy Loss: Are They Different from Recurrent Pregnancy Loss? *J South Asian Feder Obst Gynae* 2021;13(4):259–264.