ORIGINAL RESEARCH PAPER

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PREVALANCE AND ETIOLOGY OF RECURRENT PREGNANCY LOSS

KEY WORDS:
endocrinopathy, re-current pregnancy loss, etiology, management, miscarriage

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ABSTRACT

Recurrent pregnancy loss is an important reproductive health issue, affecting 15%–25% of couples. Common established causes include uterine anomalies, hormonal and metabolic disorders, psychological, infection and cytogenetic abnormalities. Other aetiologies have been proposed but are still considered controversial such as chronic endometritis, inherited thrombophilias, luteal phase deficiency, and high sperm DNA fragmentation levels. Over the years, evidence-based treatments such as surgical correction of uterine anomalies or metformin for PCOS have improved the outcomes for couples with recurrent pregnancy loss. However, almost half of the cases remain unexplained and are empirically treated using progesterone supplementation, anticoagulation, and/or immunomodulatory treatments. Regardless of the cause, the long-term prognosis of couples with recurrent pregnancy loss is good, and most eventually achieve a healthy live birth. However, multiple pregnancy losses can have a significant psychological toll on affected couples, and many efforts are being made to improve treatments and decrease the time needed to achieve a successful pregnancy. This article reviews the established and controversial etiologies, and the recommended therapeutic strategies, with a special focus on prevalence of unexplained recurrent pregnancy losses and their etiologies.

INTRODUCTION

Early loss of pregnancy is perhaps the most widespread obstetric problem that occurs in over two thirds of human conceptions (1). Clinically recognized pregnancy loss is widespread that influences about 15–25% of pregnancies (2). Miscarriage is the loss of foetus earlier than the 23rd week of gestation (3). Usually recurrent pregnancy loss (RPL) is defined as the failure of 3 or more successive clinically documented conceptions prior to 20 weeks of development.

The etiology of RPL includes genetic abnormalities, autoimmune related conditions, structural abnormalities, infections and endocrine disorders, is unknown in a significant number of miscarriages. Although chromosomal anomalies are identified in about 50%–60% of all miscarriages, they seem to occur less frequently in the products of conception (POC) from recurrent abortions than in those from spontaneous abortions (4).

Following the loss of wanted pregnancy, most women are likely to keep trying until a live birth is achieved. Thus, the chance of conception following a miscarriage should be higher than those following a live birth. In a cohort of 261 women followed up for 6 years after a miscarriage, natural conception occurred in 97.7% of these without known fertility problems (5). A significant proportion of cases of RPLremain unexplained despite detailed investigation. It affects about one in every hundred couples. Sometimes a treatable cause can be found, and sometimes not. But in either case, most couples are more likely to have a successful pregnancy next time than to miscarry again. The investigations and management of RPL is one of the most debated topics. This study is aimed to evaluate risk for future pregnancy among patients with recurrent abortion.

The management of RPL is a challenging clinical scenario with associated psychological trauma. It can be frustrating for both patients and clinicians. It is based on various limited evidence and several controversies exist.

MATERIALS AND METHODS

This was a prospective outpatient clinic-based cohort study carried out in 100 RPL patients enrolled for the study. Majority of the women (76) experienced two consecutive miscarriages and the remaining 24 had undergone more than two successive miscarriages. The patients who visited the antenatal clinics for regular health check were screened for eligibility criteria and data availability. All these couples have at least one year duration of married life. Detailed demographic and socio-economic characteristics were recorded using Performa. The clinical details were obtained from RPL patients via their diagnostic investigations and prescription cards as well as interview as per the pre-structured questionnaire for the study. The patients were tested for T3 (Triiodothyronine), T4 (Thyroxine), TSH (Thyroid Stimulating Hormone), prolactin, chromosomal analysis, HbA1C (Haemoglobin A1C), blood sugar, MRI (Magnetic Resonance Imaging) / 3D TVS, auto antibodies profile (antiphospholipid antibodies, anticardiolipin antibodies, lupus anticoagulant, antinuclear antibodies, anti-thyroid antibodies and β2 glycoprotein1), torch profile ,blood Vitamin D3 levels, psychological factors, BMI (body mass index) and hysteroscopy.

Inclusion criteria

The age of patients ranged between 18 and 45 years. Women with history of 2 or more spontaneous abortions. Those who willingly signed the consent form.

Exclusion criteria

Women with history of two or more induced abortion. A detailed clinical history, thorough clinical examination and investigations according to history with a certain group of pre-decided laboratory test, were done through a pre-structured Performa.

Psychological assessment for stress was performed using validated scales such as Fertility Problem Inventory (FPI). Polycystic ovarian syndrome (PCOS) was diagnosed on the basis of at least two of the three criteria: oligo-ovulation or an-ovulation, biochemical and/or clinical hyper-androgenism, and polycystic ovaries as visible on ultrasound.

All the patients were given different RPL management therapies during their pregnancy period for carrying the gestation successfully to full term. The therapies include levothyroxine, progesterone, folic acid, HCG (human chorionic gonadotrophin), LMWH (low molecular weight heparin), LDA (low-dose aspirin), vitamin D3, intravenous immunoglobulin (IVg), psychotherapy, genetic counselling. The therapeutic regimens were given either singly or combined on the basis of etiology (single or multiple). However, patients with idiopathic recurrent miscarriage were treated with progesterone supplementation, anticoagulation and immune modulatory agents. Informed consent in both English and vernacular was taken from the participants.

Table 1 showing different factors affecting RPL

Type of RPL(n=100)	Percentage (%)
Primary	68
Secondary	26
Tertiary	6
Trimester wise distribution	
First trimester	77
Second trimester	23
Age wise distribution	
<20 yrs.	2
21-30 yrs.	73
31 yrs.& more	25
Parity wise distribution	
G2	20
G3	36
G4 & more	44
Urban/rural	
Urban	67
Rural	33
Etiology wise distribution	
Anatomical	14
Endocrinal	22
Genetic	4
Immunological	8
Infection	2
Medical cause	6
Unexplained	44

RESULTS

In our study, nearly 73% women belonged to age between 20 to 30 years with only 25 patients being 31 yrs. or more. About 67% women belonged to urban population and 33% rural. We found that the incidence of primary RPL was 68 %. According to patient's history, 77% women had abortions in the first trimester (Table 1). We found that most women with first trimester abortions remained unexplained. Among identifiable causes, Endocrinal factors were the most common cause, (22%). Next were anatomical cause (14 %), followed by the Immunological factors (8%)

DISCUSSION

Recurrent Pregnancy Loss (RPL) also referred to as Recurrent Miscarriage or Habitual Abortion is a distinct disorder defined by two or more failed clinical pregnancies, and up to 50% of cases of RPL will not have a clearly defined etiology. Approximately 15-25% of clinically recognizable pregnancies end in spontaneous abortion. The incidence of chromosomal abnormalities in those abortions is as high as 50%.

RPL is not only distressing for the women, but frustrating for the clinician. We found that 73% women belonged to age between 20 to 30 years. The mean age in our study, was 26.2 yrs. whereas Bhattacharya et al, reported the mean age as 27.5 years (6). In our study, we found that the incidence of primary RPL was 68%, consistent with study by also reported higher rates of primary RPL (7-8).

Majority of 56% women showed identifiable causes. Among which endocrinal factors accounted for 22% in contrast to study (9-10) reported 6.9%, 6% and 10%, respectively. In another study, endocrine pathology was found in 13.5% (11).

Anatomical factors were very common (14%) in our study. Uterine anomalies remain one of the most common abnormalities found among patient with RPL and the detrimental effects of uterine anomalies on pregnancy are well documented. Studies have urged that uterine imaging be recommended for patients with only two consecutive miscarriages because there is no difference in the rate of anomalies between women with two and those with three or more losses.

The replacement of thyroid hormone therapy with levothyroxine improved the outcome of pregnancy in child bearing women affected with subclinical hypothyroidism (12). PCOS management with metformin or regulation of body weight appears to decrease the risk of miscarriages. The higher age of female partner has been reported to serve as an independent risk factor for spontaneous pregnancy loss (13-16). In the present study reproductive tract infections were found associated with RPL and affected 2% patients. In our study we reported stress as one of the factors responsible for RPL. Our data is support by Qu et al. (17) who reported higher prevalence of depression and anxiety in RPL women particularly during early stage of pregnancy.

CONCLUSION

Genetic abnormalities, immunological factors, anatomic defects, endocrinal factors, certain thrombophilia and infections are established causes of RPL and specific treatment improves pregnancy outcome. Women with unexplained pregnancy loss represented a heterogeneous group of patients and accounting for 44% of the cases in our study. Women with unexplained RPL should be encourage to continue attempts at pregnancy, because prospective studies show that these women, even with advanced maternal age, have a high rate of live births with their subsequent pregnancies. Despite innumerable investigations, sometimes or rather most of the times, the etiology remains obscure. It is this group of women who become a challenge to manage. Ultimately, most effective therapy for women with unexplained RPL is antenatal counselling, psychological support and tender loving care.

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