

Original article:

An observational study of causes of recurrent pregnancy loss in rural Population

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Abstract:

Introduction: Our aim was to identify causes of recurrent pregnancy loss in rural population in Maharashtra in Indian population

Method: A longitudinal observation study was carried out in the Obst and Gynae department , Pravara Hospital . The study enrolled 70 patients aged 18 to 44 years with history of at least two or more miscarriages less than 20 weeks gestation. They were divided into 3 groups -Group A patients with history of two or more pregnancy losses who reported to OPD immediately after abortion of their last pregnancy; Group B - patients with history of recurrent pregnancy loss but < 20 weeks of gestation in their present pregnancy at the time of inclusion in study; Group C - patients with history of recurrent pregnancy loss but more than 20weeks gestation in their present pregnancy at the time of inclusion in the study. A detailed clinical history , thorough clinical examination and investigated with a certain group of pre-decided laboratory tests and special tests wherever relevant and possible, were done. The causes of RPL were evaluated.

Results: Underlying causes were diagnosed in 35% cases ,while 65% cases remained unexplained. Anatomical causes were detected in 20% cases , wherein incompetent cervix was the most common cause while uterine malformations were present in 23.5% cases among which septate uterus was most common . 6% had Endocrine etiology ,comprising of hypothyroidism and diabetes mellitus . Infective cause in 6% and autoimmune causes in 3% patients.

Conclusion: From our study we conclude that , even after detailed evaluation majority of cases of RPL remain unexplained . Anatomical causes account for majority causes in RPL .

Introduction:

Recurrent Pregnancy Loss remains an enigma as the underlying cause mostly eludes the clinician , making diagnosis and treatment extremely difficult . Also, it is hugely distressing for a woman leading to anxiety, grief and psychological upset . Therefore, RPL is a highly important clinical entity for study , research and analysis . Despite numerous studies evaluating causes, investigations , management , and outcome , nothing can be carved into stone yet , as the results of the studies are conflicting or controversial . This

further increases the need for more research into this condition..

When recurrent pregnancy loss (RPL) is defined as 3 consecutive pregnancy losses prior to 20 weeks from the last menstrual period, 1% to 2% of women are affected. Because the risk of subsequent miscarriages is similar among women that have had 2 versus 3 miscarriages, and the probability of finding a treatable etiology is similar among the 2 groups, most experts evaluate after 2 losses.(1)Accepted etiologies for RPL include parental chromosomal abnormalities,

untreated hypothyroidism, uncontrolled diabetes mellitus, certain uterine anatomic abnormalities, and the antiphospholipid antibody syndrome (APS). Other probable or possible etiologies include additional endocrine disorders, heritable and/or acquired thrombophilias, immunologic abnormalities, and environmental causes. After evaluation for these causes, more than 33% of all cases remain unexplained.(1,2)

Materials and methods:

Study was carried out for a period of two year from- 1st Sept. 2012 to 31st Aug. 2014 in the Department of Obstetrics and Gynecology, Rural Medical College, Loni.

Study design : Observational Study

Study population: All patients seen in OPD/IPD of Obstetrical and Gynecological Dept. meeting the inclusion criteria

Sample size: 70 cases

Inclusion criteria : Women ages 18 to 44 years of age with history of at least two or more miscarriages less than 20 weeks gestation.

Data collection-

Sources: Indoor/outdoor case records and Hospital medical record department.

Data storage : On serially numbered structured proforma and master chart.

Methodology

All patients with history of two or more pregnancy loss evaluated in OPD/IPD in Pravara Hospital and meeting inclusion criteria were studied.

A detailed clinical history ,thorough clinical examination and investigations with a certain group of pre-decided laboratory tests and special tests wherever relevant and possible, were done through a pre-structured proforma.

Wherever a cause for RPL was determined, treatment was given as per standard protocols and patient was followed up in all cases to determine maternal and foetal outcome.

Observations and results

1) Incidence of RPL cases among all cases seen in OPD/IPD:

In the present study , 70 patients who were fulfilling the inclusion criteria of recurrent pregnancy loss were included. These patients had a history of two or more consecutive miscarriages in their previous pregnancies

Table 1 : Incidence of RPL cases among all cases seen in OPD/IPD:

	NUMBER	PERCENTAGE
RPL CASES	70	1.2
OTHER CASES	5930	98.8
TOTAL	6000	100

Patients seen the OPD/IPD of Rural Medical College who fulfilled the inclusion criteria of Recurrent Pregnancy Loss were enrolled. Out of 6000 pregnant patients seen during the study period 70 had RPL ,giving incidence of 1.2%

2) Primary and secondary RPL cases among patients enrolled in study:

In the present study, majority of the patients were in the Primary RPL group (71%) i.e. these patients did not have any successful previous pregnancy, while secondary RPL was present in 29% patients(i.e. those who had at least one successful past pregnancy).

Table No.2: Distribution of cases according to type of Recurrent Pregnancy Loss:

Type of RPL	No. of Cases	Percentage (%)
Primary	54	77.2%
Secondary	16	22.8%
Total	70	100%

3. Number of Abortions In RPL Patient Before Inclusion In Study

Majority of patient had 2 abortions and accounted for 57% of total cases, 30% patients had 3 abortions, 9% patients had 4 abortions . 2 patients had history of 5 abortions and 1.3% accounted each for 6 or more number of abortions.

Table No. 3: Number of Abortions Before Inclusion In Study

Number of Abortions	Number of RPL Patients	Percentage (%)
Two	40	57%
Three	20	28.6%
Four	6	9%
Five	2	2.8%
Six	1	1.3%
Seven And More	1	1.3%
Total	70	100%

4) First trimester VS second trimester abortions in patients with RPL:

In this study of RPL, most abortions, according to history occurred in the first trimester and accounted for 72%, remaining 28% occurred during the second trimester.

Table No 4.Percentage of First and Second Trimester Abortions:

Trimester	Number Of Abortions	Percentage (%)
First Trimester Abortions	126	72%
Second Trimester Abortions	48	28%
Total	174	100%

5) Age distribution of patients with RPL

In this study most of the patients (48.5%)were less than 25 Years of age , while 41.4% of patients were in the age group of 26-30years. This younger age group constituted majority as age of marriage and conception in India is less . 6 patients were between 31-34 years of age, while 2 patients were 35 years of age .

6) Obstetric status at the time of inclusion in study

At the time of inclusion in study, patients were divided into three groups - 34% patients had a history of 2 or more pregnancy losses and came with a recent abortion. Whereas 66% patients had history of 2 or more prior abortions, but were pregnant at the time of inclusion, of which, 19% were <20wks gestation and 47% were >20 wks gestation

7) Relevant History And Findings In Patients With RPL:

Detailed relevant history was taken from all patients with RPL, the observations of which have been shown in the above chart.14% patients had history of irregular menses , 7% had history of consanguinity , 5.5% gave history of secondary infertility for which treatment was taken. 28.5% gave history of dilatation

and curettage done in previous miscarriages , 9% patients had a bad obstetric history , 16% had history of preterm labor , while congenital anomalies were present in previous pregnancies of 3% patients . History of autoimmune illness and hypothyroidism was present in 2.8% each . History of diabetes in previous pregnancy was positive in 2.8%. History of gestational hypertension was found in 4%, history of genitourinary tract infection was present in 6% . BMI < 18.5 was present in 9% patients , BMI of > 25.5 was present in 14% , and a BMI > 30.5 was present in 6% patients .

8) Causes of RPL Found After Investigation and Evaluation

Among the various causes of RPL found in the undertaken study, Anatomical causes were found 20% of patients, endocrine and infective causes were seen in 6% each and autoimmune causes were seen in 3% patients. However in about 65% patients no definite cause was found and etiology was attributed as idiopathic.

Table 8: Causes of RPL Found After Investigation and Evaluation:

Causes	Number of Patients	Percentage (%)
Anatomical	14	20%
Endocrine Factors	4	6%
Autoimmune Disorders	2	3%
Infective Causes	4	6%
Idiopathic	46	65%
Total	70	100%

Discussion:

Recurrent pregnancy loss has been a Rubik’s puzzle in the field of obstetrics and gynecology since long. Extensive and varied studies in the past as well as

recent times have been successful in identifying certain factors which may be associated with RPL , but none of these studies has compared the prevalence of these factors in normal population. Moreover, a universal definition of recurrent pregnancy loss has not been used . Therefore , the incidence, causes, outcomes among various studies is variable, conflicting or controversial . The present study was aimed at identifying causes of recurrent pregnancy loss, its management and outcome in rural population. Total 70 patients with history of two or more consecutive pregnancy loss , in the reproductive age group , were included and studied for various causes of RM. As the study was done in rural population , majority of patients were in the low socioeconomic status .

Therefore GRADE A investigations , except karyotyping , were done in all whereas GRADE B investigations were restricted to positive findings in history and clinical examination . Karyotyping was done only in those couples who were cost affording and willing.

.Incidence-Patients seen at Rural Medical College, Loni , who fulfilled the inclusion criteria of Recurrent Pregnancy Loss defined as 2 or more consecutive pregnancy losses prior to 20 weeks of gestation ,were enrolled. Out of 6000 pregnant patients seen at OPD/IPD during the study period 70 had RPL giving incidence of 1.2% which is similar to study like Stirrat GM et al (3)

Primary And Secondary RPL Cases Among Patients Enrolled In Study:

In the present study, incidence of primary Recurrent pregnancy loss was 77.2% and that of secondary Recurrent pregnancy loss was 22.8%. It clearly indicates that primary RPL (i.e. patients with all

previous unsuccessful pregnancies), was more prevalent than secondary RPL which correlates with Coulam et al, who reported 71% Primary RPL cases and 29% secondary RPL. Studies done by Jivraj et al and TC Li et al, also reported higher rates of primary RPL over Secondary RPL. (4,5)

First Trimester Vs Second Trimester Abortions in Patients With RPL:

In the present study of recurrent pregnancy loss, 72% (126) abortions, according to patients history, occurred in the first trimester (pre-embryonic <6wks and embryonic miscarriage >6wks but <10wks). Rest 28% were fetal loss in second trimester. This was consistent with the studies done earlier. As 72% of these abortions had occurred at <10 weeks, it showed that this was the most perilous period for women with RPL. Findings were consistent with studies by Drakeley et al (6)

Number of Abortions in RPL Patient before Inclusion in Study

In the present study, majority of patients reported to tertiary centre after two abortions and accounted for 57% of the total cases. 30% had a history of three miscarriages, 9% had history of four abortions while 2.8% reported with history of five abortions. One patient had history of six consecutive abortions and one had twelve abortions with no previous successful pregnancy. The mean number of abortions was 2.7 in present study. This was comparable with study by Brigham et al. (7)

Age Distribution of Patients with RPL:

The mean age in present study, was 25.2 yrs, with only two patients being > 35 yrs of age. In the study done by Brigham et al mean age of patients with RPL was 32 yrs, whereas Bhattacharya et al reported the mean age as 27.5 yrs. Due to the younger age at marriage and conception, the mean age in women

with RPL, in our study is lower than study done by Brigham et al but similar to study done by Bhattacharya et al. (7,8)

Relevant History And Findings In Patients With RPL

A detailed history, of patients with recurrent pregnancy loss, was taken. According to the menstrual history, 1% had short cycles, 14% had irregular cycles. Of these 5.2% had history of irregular menses following D&C, 2.2% had BMI < 18.5 kg/m² and 4.6% had BMI < 25 kg/m². 85% had regular menstrual cycles. The mean BMI of 70 women included in the present study was 23.7 kg/m², which was found to be consistent with studies done by Bhattacharya et al (mean BMI 25.5 kg/m²) (8) and TC Li et al (mean BMI 24.1 kg/m²) (5). History of consanguinity was present in (7%) 5 patients. Among them, after follow up in present study (80%) 4, continued pregnancy beyond 20 wks gestation but with one patient having multiple congenital anomalies detected at 18 wks gestation. 20% (i.e. 1 in 5) re-aborted in present study. History of congenital anomalies in previous pregnancy was present in 3% patients.

5.5% patients gave a history of infertility and 28.5% patients had undergone D&C for previous miscarriages. 9% patients had bad obstetric history which included two or more consecutive abortions with IUD/ still birth. History of preterm labor was present in 16% women. None of the patients gave a positive family history of recurrent miscarriage. A history of PCOS or Thrombophilias was not present either. This may require further study.

History of autoimmune disease, hypothyroidism and diabetes was present in 2.8%, 2.8% and 2.8% respectively. A history of gestational hypertension in previous pregnancies was noted in 4% patients, it

was 1.1% in study by Bhattacharya et al (8) and 7.3% in the study by Jivraj et al (4). And 6% patients gave a history of infection in previous pregnancies.

Causes of Recurrent Pregnancy Loss

Among the various causes of RPL found in the undertaken study, anatomical causes were found 20% of patients. These included cervical insufficiency in 15 patients and uterine malformations in 4 patients, of which septate uterus was present in 2 patients (~50%), bicornuate uterus in one (~25%) and arcuate uterus in one patient (~25%). Saito et al (9) and Jivraj et al (4) reported the rate of anatomical causes as 9% and 7% respectively. Grimbizis GF et al (2001), (10) found the mean incidence of septate uterus ~35%, bicornuate uterus ~25% and arcuate uterus ~20%. Endocrinal etiology was diagnosed in 6% patients, of which, 2 patients had gestational diabetes mellitus and two were diagnosed with hypothyroidism. This was consistent with Saito et al who reported the rate of endocrinal causes in 6.9% cases of which 2.9% had hypothyroidism, 1.2% had diabetes and 2.8% had hyperthyroidism. In the study by Jivraj et al endocrine pathology was found in 13.5% cases.

Infective causes were seen in 6%. This was consistent with 5% rate of infective causes found in the study of Holly B Ford et al. In these patients high vaginal swab culture showed bacterial vaginosis and Chlamydia trachomatis. Autoimmune causes were seen in two patients i.e. 3% patients. This included systemic lupus erythematosus and antiphospholipid syndrome. Due to high cost of karyotyping, genetic causes could not be evaluated in our study. In about 65% patients no definite cause was found, also because some of them were pregnant at the time of inclusion in study and etiology was attributed as unexplained. This was consistent with study by Jivraj et al wherein rate of unexplained RPL was 66%. Holly B Ford reported 40% cases, while Saito et al found that 30% cases were unexplained.

Conclusion:

From our study we conclude that, even after detailed evaluation majority of cases of RPL remain unexplained. Anatomical factors account for majority causes in RPL.

Limitations of the study: As genetic causes could not be evaluated due to financial restraints, further studies are required in this aspect.

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