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Original Research Article

An evaluation of etiology of recurrent pregnancy loss: prospective observational study

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ABSTRACT

Background: Recurrent pregnancy loss (RPL) is a global issue, affecting 1-2% of fertile women. RPL can be explained as two or more pregnancy losses which are documented either by ultrasonography or histopathological examination. This study aimed to evaluate etiology of RPLs.
Methods: This prospective observational study was carried out in 40 women with history of RPL attending outpatient department (OPD) and inpatient department (IPD) of the department of obstetrics and gynaecology at the tertiary care centre of Dr. Vitthalrao Vikhe Patil Foundation's (DVVPF's) Medical College, Ahmednagar. The study was carried out from April 2020 to May 2021 in 40 women with history of RPL.
Results: RPL most commonly occurs due to unexplained causes, followed by endocrinal causes. It was found most commonly in 21-30 years age group.
Conclusions:

Keywords: Recurrent pregnancy loss, Miscarriages, Habitual abortion

INTRODUCTION

Recurrent pregnancy loss (RPL) is the most widespread problem that occurs in over two thirds of human conception.[1] According to Royal College of Obstetrics and Gynaecology, a miscarriage is defined as spontaneous loss of pregnancy before 20 weeks and RPL is defined as failure of three or more consecutive clinically documented conceptions before 20 weeks.[2] However according to American society of reproductive medicine (2012), RPL can be defined as two or more pregnancy losses which have been documented by either ultrasound or histopathological examination. It occurs in 1-2% of fertile women.[3]

The risk of miscarriage is high in early pregnancy, mostly in first trimester. The risk of subsequent pregnancy losses is 30% after two losses and 33% after 3 losses among patients without history of live birth. Hence, role of evaluation after just 2 losses is recommended.[4]

The causes of RPLs include parental chromosomal aberrations, uterine malformations, cervical incompetence, endocrine problems, infectious diseases, autoimmune diseases, thrombophilic disorders, anti-phospholipid antibody syndrome, alloimmune causes and idiopathic causes in approximately 50% of cases.[5] Adequate assessment of causes of RPL can aid in proper management of the cases.

Aims and objectives

The objective of this study was to evaluate etiology of RPLs through necessary investigations regarding history of RPL.

METHODS

This prospective observational study was carried out in 40 women with history of RPL attending outpatient department (OPD) and inpatient department (IPD) of the department of obstetrics and gynaecology at the tertiary care centre of Dr. Vitthalrao Vikhe Patil Foundation's (DVVPF's) Medical College, Ahmednagar. The study was carried out from April 2020 to May 2021.

Detailed clinical history, thorough clinical examination and relevant investigations were performed. Blood investigations like complete blood count (CBC), random blood sugar, thyroid profile, levels of hormones like thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, anti-phospholipid antibodies, and HbA1c in non-pregnant female with history of RPL were performed. Other laboratory investigations for infectious diseases like toxoplasmosis, rubella cytomegalovirus, herpes simplex, and HIV (TORCH), and syphilis, karyotyping of parents, radiological investigations like ultrasonography (USG) abdomen and pelvis were performed.

The data was compiled, tabulated, and analysed with the help of Microsoft-excel. Appropriate statistical techniques like Chi-square test and t-test were applied for evaluation. Prior approval from institutional ethical committee was taken.

Inclusion criteria

Non-pregnant women with history of RPL, and women who were willing to participate in the study and giving consent were included in the study.

Exclusion criteria

Women with history of single abortion, and women with history of induced abortion were excluded from the study.

RESULTS

Maximum number of cases with recurrent pregnancy losses belonged to the age group of 21-30 (Table 1).

Table 1: Association of pregnancy loss with age.

Age wise distribution (years)	No. of cases	%
21-30	21	52.5
31-40	17	42.5
>41	2	0.05

RPL was found to be more pronounced in urban women as compared to rural women (Figure 1).

Primary RPL was more eminent than secondary RPL (Table 2).

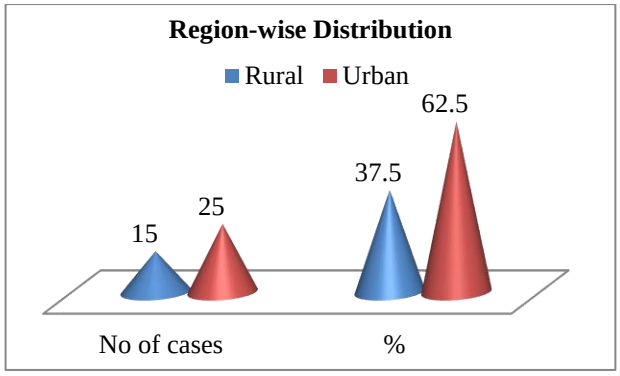

Figure 1: Association of pregnancy loss with region.

Table 2: Distribution according to type of RPL.

Type of RPL	No of cases	%
Primary	30	75
Secondary	10	25

Those women having three abortions comprised majority of the population having recurrent miscarriage, followed by those having number of 2, 4 and 5 abortions in the similar sequence (Table 3).

Table 3: Distribution according to frequency of RPL.

No. of abortion	No. of cases	%
2	15	37.5
3	17	42.5
4	5	12.5
>5	3	7.5

RPL most commonly occurred in 1st trimester, followed by 2nd trimester (Table 4).

Table 4: Association of RPL with trimester of pregnancy.

Trimester wise distribution	No of cases	%
1st trimester	16	40
2nd trimester	13	32.5
Both trimester	11	27.5

APLA syndrome was the most prominent immunological factor contributing to RPL (Table 5).

Table 5: Immunological causes of RPL.

Immunological causes	No of cases	%
APLA syndrome	6	85.71
SLE	1	14.28

Most common causes of RPL were thyroid disorders (54.54%) followed by diabetes mellitus (45.45%) (Figure 2).

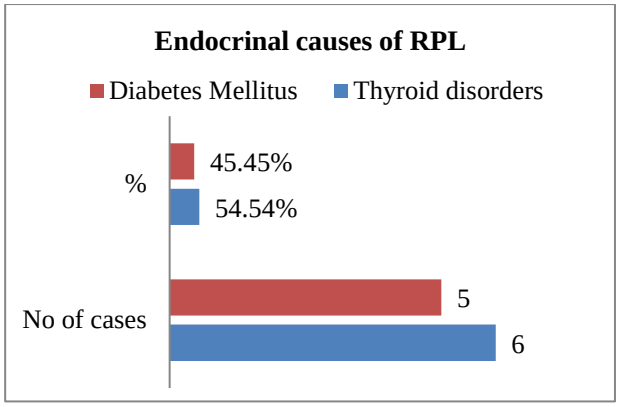

Figure 2: Endocrinal causes of RPL.

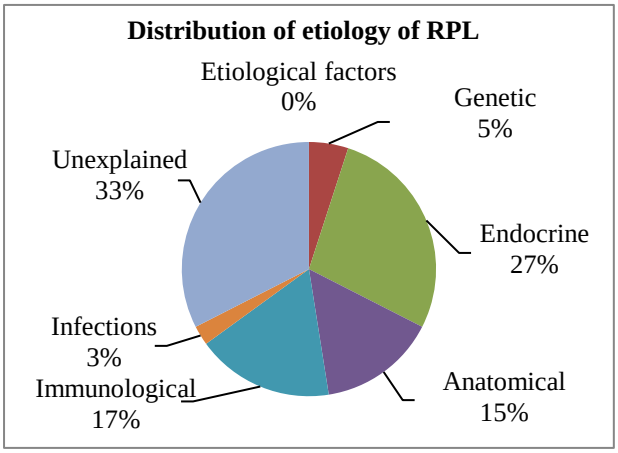

Figure 3: Distribution of etiology of RPL.

The majority cases of RPL were because of unexplained causes, followed by endocrinal, immunological, anatomical, genetic causes and infectious causes in the same order (Figure 3).

In our study, we detected 2 cases of RPL due to genetic causes. One case with trisomy 16 in the abortus, and one with parenteral chromosomal abnormality.

Among the 6 anatomical causes of RPL, 3 cases of RPL were due to cervical incompetence, 2 cases due to septate uterus and one case due to bicornuate uterus.

During evaluation of RPL, though there was no organic cause of stress established, we realised that women were experiencing stress and anxiety issues.

RPL was found most commonly in 21-30 years age group, most extensively occurring in urban population. Primary RPL cases were more pronounced than secondary RPL. Among the population having recurrent miscarriage, those women having three abortions comprised majority of the population of cases of RPL. In all the cases of RPL, 1st trimester was the period having majority recurrent miscarriage. Most common immunological disorder leading to RPL was APLA's syndrome, and most frequent endocrinal cause for RPL was thyroid disorders. Majority cases of RPL occurred due to unexplained causes, followed by endocrinal causes.

DISCUSSION

In the present study, we found that majority number of cases with RPL belonged to the age group of 21-30 years (52.5%). Similar findings were seen in the study of Singh and Shetty where the percentages of RPL were 53.84% and 67%, respectively.[4,5]

Our findings revealed a greater number of pregnancy losses in urban areas (62.5%) as compared to rural areas (37.5%). This finding was however contrast to the study conducted in China by Zheng, which showed 1.68 times increased risk of spontaneous abortion in rural areas than urban areas.[6]

In our research, we found that more women suffered from primary RPL (75%) as compared to secondary RPL (25%). This finding showed similarity to the analysis of Ali in research conducted at Srinagar, where most of the women suffered from primary RM (74.7%).[7]

Our studies showed that, the number of women having three abortions comprised majority of the population (42.5%), whereas those undergoing more than five abortions contributed least to the population (7.5%). Similarly, the data published by Imam showed that the risk of miscarriage is 30% after two previous spontaneous abortions and 35% after the third abortion.[8]

Occurrence of RPL was most common in 1st trimester (40%). This finding of ours showed contrast to the findings of Costa, whose research in Brazil revealed miscarriage prominently in mid-trimesters.[9]

APLA syndrome was the predominant immunological factor leading to RPL (85.71%) in immunological causes of RPL in our study. This is because our hospital gets many referrals from other health-care centres for evaluation of cases of RPL. Similar findings were obtained in the study carried out by Eltayeb, where APLA's syndrome was the most prevalent immunological disorder in their study population.[10]

In our study, 6 cases out of 11 revealed thyroid disorders as the etiology and remaining 5 cases showed the cause of RPL as diabetes mellitus. A study conducted in Italy by Pluchino also showed significantly increased risk of RPL in cases with thyroid diseases and diabetes mellitus.[11]

Two cases of RPL were due to genetic causes in our study. We detected trisomy 16 in the abortus of RPL in one case. The other case of RPL was due to parenteral chromosomal abnormality. Study conducted by Warren also showed that most common trisomy in abortus of RPL was trisomy 16.[12]

In our study, majority of anatomical causes of RPL were due to cervical incompetence, followed by septate uterus. Similar findings were found in the study conducted by Medrano-Uribe, where cervical weakness was the major anatomical cause of RPL.[13]

Overall, our study showed majority cases of RPL due to unexplained causes (33%), followed by endocrinal causes (27%) and infectious diseases (3%) were the factors that caused the least impact for RPL. However, findings of Lee suggest that infections are not a proven cause of RPL.[14] Also contrary to our findings, study of Singh show that majority cases of RPL (53%), had identifiable causes associated with it.[4]

CONCLUSION

RPLs though having unexplained etiology in many cases, identifiable causes are also revealed in the remaining major population. However, we concluded that further research in the evaluation of causative factors can help in understanding the proportion and distribution of etiologies in various populations. As there are multiple etiological factors associated with RPL, management becomes empirical. So, conducting further research and establishing guidelines will further help in implicating prevention, treatment and management of recurrent miscarriages. Psychological reassurance can help create a positive impact in women with RPL. Due to prevailing social and economic issues in rural population, there is need for clear systematic guidelines for their investigations and management taking into consideration rural population too.

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