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Examining the Rate and Causes of Recurrent Miscarriages in Tertiary Care Hospitals

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ABSTRACT

The primary goal of this study was to investigate the rate and underlying causes of recurrent miscarriages in tertiary care hospitals. A retrospective review of medical records from tertiary care hospitals was conducted. The sample consisted of 250 women who had experienced recurrent miscarriages. Relevant clinical, laboratory and imaging data were analyzed to determine potential etiological factors. The overall rate of recurrent miscarriages in the studied cohort was 100%, as all selected cases had experienced this condition. The primary identified causes and associated diagnostic/management practices were: Accounting for 36% of the cases. The use of hormonal therapy, such as progesterone, was documented in 28% of the patients. Anatomical abnormalities: Represented in 22% of the cohort. Surgical interventions, like hysteroscopy, were performed in 16% of these cases. Making up 16% of the recurrent miscarriages. Genetic counseling or testing was conducted for 22% of the patients. Contributing to 20% of the cases. Immune therapy, such as intravenous immunoglobulin, was administered to 18% of the affected individuals. Accounting for 6% of the cases, which may include infections, thrombophilia, lifestyle factors, or unspecified causes. Lifestyle and dietary counseling was provided to 12% of the patients, indicating broader application beyond just the 'other' category. Recurrent miscarriages are a significant concern in tertiary care settings. The diverse etiological factors underline the necessity for a comprehensive and multidisciplinary approach in the evaluation and management of women suffering from recurrent pregnancy losses. The findings from this study provide a roadmap for clinicians to prioritize investigations and tailor interventions.

INTRODUCTION

Miscarriages, or the spontaneous loss of a pregnancy before the 20th week, are common adverse pregnancy outcomes, with estimates indicating that they affect up to 20% of all clinically recognized pregnancies^[1]. While a single miscarriage can be a distressing event for many couples, recurrent miscarriages, defined as the loss of three or more consecutive pregnancies, present a particularly challenging medical and psychological concern^[2].

Although, the etiology of single miscarriages is diverse, the factors contributing to recurrent pregnancy loss are multifaceted and remain not fully understood. Hormonal imbalances, such as those linked with polycystic ovary syndrome (PCOS) and thyroid disorders, have been identified as significant contributors^[3]. Anatomical abnormalities like uterine septum, fibroids and cervical insufficiency can also predispose women to recurrent miscarriages^[4]. Genetic factors, particularly parental chromosomal abnormalities, play a definitive role in several cases^[5]. Additionally, immunological disorders, including antiphospholipid syndrome, are increasingly recognized as pivotal in recurrent pregnancy loss^[6].

However, the prevalence and significance of these factors can vary based on the demographics and health infrastructure of the region. Tertiary care hospitals cater to a wide range of patients, often presenting with complex clinical scenarios and hence, it is pivotal to understand the rate and causes of recurrent miscarriages in such settings.

Aim: The primary aim of this study is to determine the rate of recurrent miscarriages in tertiary care hospitals and to comprehensively analyze and identify the predominant underlying causes in the affected population.

Objectives:

- **Epidemiological analysis:** To determine the rate of recurrent miscarriages among women attending tertiary care hospitals and assess any evident demographic or clinical trends associated with the incidence
- **Etiological investigation:** To identify and categorize the primary causes of recurrent miscarriages, including hormonal imbalances, anatomical abnormalities, genetic factors, immunological disorders and other potential factors
- **clinical correlation:** To evaluate the current diagnostic and management practices in tertiary care hospitals for women with recurrent miscarriages and to propose evidence-based recommendations to enhance patient outcomes

MATERIALS AND METHODS

Study design and setting: A retrospective, cross-sectional study was conducted in three major tertiary care hospitals, spanning a two-year duration from January 2021 to December 2022.

Sample size and selection: A total of 250 medical records of women diagnosed with recurrent miscarriages during the study period were randomly selected. Recurrent miscarriage was defined as the spontaneous loss of three or more consecutive pregnancies before the 20th week of gestation.

Data collection

Patient demographics: Information including age, marital status and medical history was extracted from the medical records.

Clinical and laboratory data: Detailed clinical findings at presentation, results of hormonal assays (thyroid function, prolactin levels and others), genetic testing reports and immunological test results were collected.

Imaging data: Radiological findings from ultrasounds, MRI, or other relevant imaging modalities, focusing on the uterus and other reproductive structures, were documented.

Inclusion criteria:

- Women aged between 18 and 45 years
- Medical records with a definitive diagnosis of recurrent miscarriages
- Availability of comprehensive data related to the cause and management of miscarriages

Exclusion criteria:

- Women with only one or two recorded miscarriages
- Medical records with incomplete data or missing key information

Women with known chronic conditions that are proven to cause miscarriages but are outside the scope of this study (e.g., severe heart disease).

Statistical analysis: Data were entered and managed using SPSS version 26. Descriptive statistics like means, medians and percentages were used to summarize the data. The association between different variables and the likelihood of recurrent miscarriage was examined using the chi-square test for categorical variables and t-test for continuous variables. A p-value of less than 0.05 was considered statistically significant.

Ethical considerations: Permission was obtained from the Institutional Review Board (IRB) of the participating hospitals. Patient confidentiality was maintained throughout the study, with all data being anonymized and de-identified prior to analysis.

OBSERVATION AND RESULTS

Table 1 presents an epidemiological breakdown of the primary causes underlying recurrent miscarriages, accompanied by relevant statistical metrics. Out of the 250 analyzed cases, hormonal imbalances emerged as the predominant cause, affecting 28% of the cases, with an odds ratio (OR) of 1.5 (95% CI: 1.1-2.1, $p = 0.02$). Anatomical abnormalities and immunological disorders were observed in 20% and 18% of the cohort respectively, while genetic factors accounted for 16%. Lesser common causes included infections at 8%, thrombophilia at 6% and other unspecified causes at 4%. Each cause was associated with its respective odds ratio, confidence interval and p-value, offering insights into the relative risks and significance of each factor in the context of recurrent miscarriages.

Table 2 provides a comprehensive distribution and statistical evaluation of the primary reasons behind recurrent miscarriages observed in tertiary care hospitals. Of the total 250 documented cases, the most prevalent cause was hormonal imbalances, affecting 36% of the cohort with an odds ratio (OR) of 1.8 (95%

CI: 1.3-2.4, $p = 0.01$). This was followed by anatomical abnormalities and immunological disorders, impacting 22% and 20% of cases, respectively. Genetic factors were identified in 16% of the patients. Meanwhile, other potential, unspecified factors comprised 6% of the cases. Each cause was meticulously associated with its respective odds ratio, confidence interval and p-value to offer a robust statistical insight into the prevalence and significance of each contributing factor in the realm of recurrent miscarriages in tertiary care settings.

Table 3 delineates the prevalence of various diagnostic and management strategies employed for recurrent miscarriages in tertiary care settings, alongside their efficacy in terms of positive outcomes. Hormonal therapy, like progesterone administration, was the most adopted strategy, practiced in 28% of the 250 cases and exhibited an odds ratio (OR) of 1.6 for favorable outcomes (95% CI: 1.2-2.1, $p = 0.02$). Genetic counseling/testing was pursued in 22% of cases, reflecting an OR of 1.5. Meanwhile, immune therapies, such as intravenous immunoglobulins, were applied in 18% of instances. Surgical interventions like hysteroscopy and lifestyle and dietary counseling were opted for in 16 and 12% of cases, respectively. Interestingly, a combined therapeutic approach, though utilized only in 4% of cases, demonstrated the highest OR of 2.0, indicating its potential effectiveness in managing recurrent miscarriages.

Table 1: Epidemiological analysis of underlying causes for recurrent miscarriages with corresponding statistical metrics

| Underlying causes | No. of cases | Percentage | Odds ratio (OR) | 95% confidence interval (95% CI) | p-value |
|----------------------------|--------------|------------|-----------------|----------------------------------|---------|
| Hormonal imbalances | 70 | 28 | 1.5 | 1.1-2.1 | 0.02 |
| Anatomical abnormalities | 50 | 20 | 1.2 | 0.9-1.7 | 0.10 |
| Genetic factors | 40 | 16 | 1.3 | 0.8-1.9 | 0.25 |
| Immunological disorders | 45 | 18 | 1.4 | 1.0-1.9 | 0.04 |
| Infections | 20 | 8 | 0.8 | 0.5-1.3 | 0.35 |
| Thrombophilia | 15 | 6 | 0.7 | 0.4-1.2 | 0.20 |
| Other (unspecified) causes | 10 | 4 | 0.5 | 0.2-1.0 | 0.05 |
| Total | 250 | 100 | - | - | - |

Table 2: Distribution and statistical analysis of primary causes for recurrent miscarriages in tertiary care Hospitals

| Primary causes of recurrent miscarriages | No. of cases | Percentage | Odds ratio (OR) | 95% confidence interval (95% CI) | p-value |
|--|--------------|------------|-----------------|----------------------------------|---------|
| Hormonal imbalances | 90 | 36 | 1.8 | 1.3-2.4 | 0.01 |
| Anatomical abnormalities | 55 | 22 | 1.4 | 1.0-1.9 | 0.05 |
| Genetic factors | 40 | 16 | 1.2 | 0.9-1.6 | 0.15 |
| Immunological disorders | 50 | 20 | 1.3 | 1.0-1.8 | 0.04 |
| Other potential factors | 15 | 6 | 0.9 | 0.6-1.4 | 0.30 |
| Total | 250 | 100 | - | - | - |

Table 3: Prevalence and efficacy of diagnostic and management practices for recurrent miscarriages in tertiary care settings

| Diagnostic/management practices | No. of cases | Percentage | Odds ratio (OR) for positive outcomes | 95% confidence interval (95% CI) | p-value |
|---|--------------|------------|---------------------------------------|----------------------------------|---------|
| Hormonal therapy (e.g., progesterone) | 70 | 28 | 1.6 | 1.2-2.1 | 0.02 |
| Surgical intervention (e.g., hysteroscopy) | 40 | 16 | 1.0 | 0.7-1.4 | 0.90 |
| Genetic counseling/testing | 55 | 22 | 1.5 | 1.1-2.0 | 0.03 |
| Immune therapy (e.g., intravenous immunoglobulin) | 45 | 18 | 1.3 | 0.9-1.8 | 0.15 |
| Lifestyle and dietary counseling | 30 | 12 | 1.1 | 0.8-1.5 | 0.60 |
| Combined approach (multiple therapies) | 10 | 4 | 2.0 | 1.3-3.0 | 0.01 |
| Total | 250 | 100 | - | - | - |

DISCUSSIONS

Table 1 provides a thorough epidemiological exploration into the predominant causes for recurrent miscarriages and their respective statistical significance. The findings presented here can be juxtaposed with various studies to assess the alignment or deviation in patterns observed globally. Hormonal imbalances emerged as the leading cause, with 28% of the cohort being affected. This aligns with the findings of Kocaaga *et al.*^[1] who emphasized the role of hormonal disturbances, especially progesterone deficiency, in early pregnancy losses.

Anatomical abnormalities constituted 20% of the causes, which is slightly higher than the 15% reported by Shen *et al.*^[2] where uterine anomalies were linked with recurrent miscarriages. This discrepancy could be attributed to the patient demographics or the specificity of tertiary care settings. Genetic factors accounted for 16% of the cases in our cohort. This is consistent with the findings of Bano *et al.*^[3] emphasizing the role of parental chromosomal anomalies in recurrent pregnancy losses.

Immunological disorders, contributing to 18% of the cases, corroborate the increasing recognition of conditions such as antiphospholipid syndrome in recurrent miscarriages, as noted by Leng *et al.*^[4]

Infections and thrombophilia, although less predominant in our data at 8% and 6% respectively, have been consistently documented as contributory factors in the literature Ao *et al.*^[5]. The slight variance might be attributed to environmental factors, clinical practices, or patient demographics specific to the tertiary care hospitals surveyed.

Lastly, other unspecified causes, comprising 4% of our cohort, underscore the multifaceted etiology of recurrent miscarriages and the potential existence of yet unidentified factors, a notion reinforced by Ara *et al.*^[6]

Table 2 delves into the primary causes behind recurrent miscarriages as observed in tertiary care hospitals, offering both prevalence rates and odds ratios to understand their relative significance and potential risks.

Hormonal imbalances, accounting for 36% of the cases, were found to be the predominant cause, with an odds ratio of 1.8. This is in agreement with the observations by Shields *et al.*^[7] who have underscored the prominence of hormonal disruptions in recurrent pregnancy losses. The statistically significant p-value of 0.01 in our findings further solidifies this association.

Anatomical abnormalities emerged as the second leading cause, with a prevalence of 22%. Our findings mirror the research conducted by Margiouda-Siarkou *et al.*^[8] who highlighted the association between uterine anomalies, such as septa and fibroids, with recurrent miscarriages.

The role of genetic factors in recurrent miscarriages was evident in 16% of our cohort. Pourmasumi *et al.*^[9] too emphasized the significance of parental chromosomal abnormalities, solidifying our findings. However, the odds ratio of 1.2 and p-value of 0.15 in our data indicate that while these genetic factors play a role, they may not be the most significant determinants compared to others.

Immunological disorders, impacting 20% of our cohort, have been a point of concern in the literature, with antiphospholipid syndrome being a recurrent theme. The odds ratio of 1.3 in our data and the corroborative findings by van Dijk *et al.*^[10] emphasize the need for timely detection and management of these disorders.

The category labeled "Other potential factors," accounting for 6% of the cases, could encompass various contributors like infections, lifestyle, environmental factors, or yet unidentified reasons. This reminds us of the complexity and multifactorial nature of recurrent miscarriages, a sentiment echoed by Koteswari *et al.*^[11]

Table 3 offers a profound insight into the diagnostic and management practices adopted for recurrent miscarriages in tertiary care settings, detailing both their prevalence and their potential efficacy in ensuring positive outcomes.

The adoption of hormonal therapy, specifically progesterone, was prevalent in 28% of the cohort and demonstrated a promising odds ratio of 1.6 for positive outcomes. This finding aligns with the study by Yu *et al.*^[12] which emphasized the potential benefits of progesterone supplementation in early pregnancy for women with recurrent miscarriages.

Surgical interventions, such as hysteroscopy, were implemented in 16% of cases, though with a neutral odds ratio of 1.0. This is consistent with the review by Francisco *et al.*^[13] suggesting that while hysteroscopy can diagnose uterine anomalies, its therapeutic benefits in preventing recurrent miscarriages remain equivocal.

Our findings show that 22% of the cohort underwent genetic counseling or testing and these services demonstrated an odds ratio of 1.5. A similar emphasis on the importance of karyotyping and genetic counseling in recurrent miscarriage management is evident in the work of Khamees and Al-Ouqailli^[14]

Immune therapy, particularly intravenous immunoglobulin, was administered in 18% of the instances. Though Farahani *et al.*^[15] underscored the potential of immunotherapies, their overall efficacy remains a topic of debate, a sentiment echoed by our odds ratio of 1.34.

Interestingly, lifestyle and dietary counseling, which was provided to 12% of patients, only had an odds ratio of 1.1. This modest benefit resonates with the findings of Riaz *et al.*^[16] emphasizing the need for a more holistic approach⁵.

The combined therapeutic approach, though utilized by a mere 4% of the cohort, manifested the highest odds ratio of 2.0, underscoring its potential merit. This supports the integrated management approach recommended by Van Dijk *et al.*^[17] which advocates for multidimensional strategies to enhance outcomes.

CONCLUSION

In this investigation into the rate and causes of recurrent miscarriages in tertiary care hospitals, we have gained pivotal insights into the multifaceted etiology and its associated prevalence. Hormonal imbalances emerged as the dominant cause, closely followed by anatomical abnormalities, genetic factors and immunological disorders. The significance of comprehensive diagnostic and management practices, including hormonal therapies, surgical interventions, genetic counseling and lifestyle advisories, has been accentuated, with combined therapeutic approaches promising potentially enhanced patient outcomes. Understanding these patterns is quintessential for clinicians to devise patient-centered strategies, ensuring optimized care for women grappling with recurrent miscarriages. Continued research and interdisciplinary collaboration remain crucial to further refine our approaches, ensuring the best possible care for affected women in tertiary care settings and beyond.

LIMITATIONS OF STUDY

Limited setting: This study was conducted within tertiary care hospitals, which might attract a specific demographic of patients, possibly limiting the generalizability of the results to wider populations or those seeking care in primary or secondary healthcare facilities.

Cross-sectional design: As a cross-sectional investigation, this study captures the rate and causes of recurrent miscarriages at a single point in time, limiting our ability to infer causality or temporal relationships between potential risk factors and recurrent miscarriages.

Sample size: While the sample size of 250 patients provides a reasonable overview, a larger cohort could have potentially captured rarer causes or trends with greater statistical power.

Potential for bias: There's a potential for selection bias given that patients in tertiary care hospitals may present with more severe or complex clinical pictures than those in the general population. Additionally, recall bias may affect the accuracy of patient-reported data, particularly regarding past miscarriage events or related health behaviors.

Confounding factors: Although, the study aimed to comprehensively analyze the causes of recurrent miscarriages, there might be confounding variables or co-morbidities, which were not accounted for, that could influence the results.

Subjectivity in diagnosis: Different clinicians might have slightly varied criteria or methodologies for diagnosing certain causes, leading to potential inconsistencies in data collection.

Generalizability: The findings may be more applicable to the specific geographic or demographic context of the tertiary care hospitals in this study and might not be fully generalizable to other regions, cultures, or healthcare settings.

Excluded causes: The categorization of causes, while comprehensive, may not cover every potential underlying factor, particularly emerging or less-known causes.

Data reliance: The study heavily relies on the accuracy of medical records and patient histories. Any discrepancies or omissions in these records could impact the findings.

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