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Original Research Article

Recurrent pregnancy loss and thyroid abnormalities: a case control study from a tertiary care hospital in Delhi

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ABSTRACT

Background: To evaluate the association of thyroid dysfunction and thyroid autoimmunity with recurrent pregnancy loss (RPL) and to assess their impact on pregnancy outcomes.
Methods: This hospital-based case–control study was conducted at a tertiary care centre. Fifty-nine pregnant women with a history of two or more consecutive pregnancy losses were enrolled as cases and compared with 59 age-matched pregnant women with no prior pregnancy loss. Thyroid function tests and anti–thyroid peroxidase (anti-TPO) antibodies were assessed in all participants. Pregnancy outcomes were followed until delivery.
Results: Thyroid dysfunction was significantly more prevalent among women with RPL compared to controls (35.6% vs. 18.6%, p=0.03). Subclinical hypothyroidism was the most common abnormality, observed in 25.4% of cases and 13.6% of controls. Anti-TPO antibody positivity was higher among cases than controls (20.3% vs. 13.6%), though this difference was not statistically significant. Increasing severity of thyroid dysfunction was significantly associated with a higher number of pregnancy losses (p=0.004). Among women with RPL, those with thyroid dysfunction had lower live birth rates compared to euthyroid women (61.9% vs. 81.6%, p=0.04), along with higher rates of miscarriage and neonatal intensive care unit admission.
Conclusions: Thyroid dysfunction, particularly subclinical hypothyroidism, is more common in women with recurrent pregnancy loss and is associated with adverse pregnancy outcomes. Routine screening for thyroid dysfunction and thyroid autoimmunity should be considered in the evaluation of women with RPL.

Keywords: Pregnancy outcome, Recurrent pregnancy loss, Subclinical hypothyroidism, Thyroid dysfunction, Thyroid autoimmunity

INTRODUCTION

RPL defined as two or more consecutive pregnancy losses, affects approximately 1–2% of women of reproductive age and continues to pose a significant clinical challenge.[1] Despite advances in diagnostic evaluation, a considerable proportion of cases remain unexplained, underscoring the need to identify potentially modifiable risk factors. Endocrine disorders account for approximately 8% to 12% of all cases of RPL.[2] Thyroid disorders are a leading endocrine cause of recurrent pregnancy. Thyroid hormones play a crucial role in implantation, placental development and early foetal growth.[3] Hypothyroidism is more commonly encountered during pregnancy and affects about 7% of women.[4] Hyperthyroidism affects approximately 0.1% to 0.4% of pregnancies.[5] Both overt and subclinical hypothyroidism have been associated with adverse reproductive outcomes, including miscarriage and preterm birth.[6] Notably, even mild thyroid dysfunction may negatively influence pregnancy outcomes. Thyroid autoimmunity, most commonly identified by the presence of anti-thyroid peroxidase (anti-TPO) antibodies, has also been implicated in recurrent pregnancy loss, even among euthyroid women. The prevalence of thyroid autoantibodies ranges from 3% to 18% in pregnant women.[7] Proposed mechanisms include immune-mediated

disruption of trophoblastic invasion and placental function. Although several studies have explored thyroid disorders in pregnancy, data specifically addressing thyroid dysfunction and autoimmunity in women with RPL and their subsequent pregnancy outcomes remain limited, particularly within the Indian population. The present study was therefore undertaken to evaluate the association between thyroid dysfunction, thyroid autoimmunity and recurrent pregnancy loss and to assess their impact on pregnancy outcomes in a tertiary care setting.

METHODS

This hospital-based case–control study was conducted in the Department of Obstetrics and Gynaecology, Kasturba Hospital, Delhi, from September 2023 to October 2024, following approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrolment.

Pregnant women aged 18–45 years with a history of two or more consecutive spontaneous pregnancy losses were included as cases. Age-matched pregnant women with no history of pregnancy loss and at least one ongoing viable pregnancy were recruited as controls. Women with known uterine anomalies, chromosomal abnormalities, autoimmune disorders other than thyroid disease or chronic medical illnesses such as diabetes mellitus, hypertension or renal disease were excluded.

All participants underwent biochemical evaluation of thyroid function, including serum thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4) and anti–thyroid peroxidase (anti-TPO) antibodies. Thyroid dysfunction was classified in accordance with the Federation of Obstetric and Gynaecological Societies of India (FOGSI) guidelines. Participants were prospectively followed until delivery and pregnancy outcomes including live birth, miscarriage, preterm birth and neonatal intensive care unit (NICU) admission were documented.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20. Categorical variables were analysed using the Chi-square test, while continuous variables were compared using Student's t-test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Women with RPL and controls were comparable with respect to demographic characteristics, including age, religion and socio-economic status. However, the mean body mass index (BMI) was significantly higher among cases compared to controls (25.88±3.56 vs. 23.59±2.96, p=0.001) (Table 1).

A significantly higher prevalence of thyroid dysfunction was seen among women with recurrent pregnancy loss as compared to controls (35.6% vs 18.6%, p=0.03) (Table 2). Thyroid dysfunction was observed more frequently in women with three or more pregnancy losses compared to those with two losses with results reaching statistical significance (61.3% vs. 7.14%, p<0.001), demonstrating a strong association between thyroid dysfunction and increasing severity of recurrent pregnancy loss (Table 3). Although anti-thyroid peroxidase (anti-TPO) antibody positivity was higher among women with RPL compared to controls (20.3% vs. 13.6%), the difference was not statistically significant (p=0.462). Mean anti-TPO antibody levels were also comparable between the two groups (p=0.326) (Table 2). Among women with RPL, those with thyroid dysfunction showed a higher incidence of adverse pregnancy outcomes, including miscarriage (28.6% vs. 13.2%), preterm birth (9.5% vs. 5.3%) and NICU admission (14.3% vs. 5.3%) compared to euthyroid women; however, these differences did not reach statistical significance (Table 4).

Table 1: Demographic profile of cases and controls.

Parameters	Cases (RPL) (n=59)	Controls (n=59)	P value
Mean age	25.95±4.297	24.39±4.02	0.45
BMI (kg/m^2)	25.88±3.56	23.59±2.96	0.001
Religion	19	19	1
Hindu	19	19	1
Muslim	40	40	
SES			
Upper	4 (6.8%)	6 (10.2%)	0.936
Middle	31 (52.5%)	27 (45.76%)	
Lower	21 (35.6%)	26 (44.07)	

Table 2: Thyroid status and autoimmunity in cases and controls.

Thyroid status	Cases (RPL) (n=59)	Controls (n=59)	P value
Euthyroid	38 (64.4%)	48 (81.4%)	0.03
Thyroid dysfunction	21 (35.6%)	11 (18.6%)	

Continued.

Thyroid status	Cases (RPL) (n=59)	Controls (n=59)	P value
Types of thyroid dysfunction			
Subclinical hypothyroidism	15 (25.4%)	8 (13.6%)	0.188
Overt hypothyroidism	5 (8.5%)	3 (5.1%)	
Hyperthyroidism	1 (1.7%)	0	
Anti-TPO antibody			
Anti-TPO antibody positive	12 (20.3%)	8 (13.6%)	0.326
Mean Anti-TPO	28.47±24.43	26.75±21.79	

Table 3: Association of thyroid status and number of pregnancy losses in RPL group.

Thyroid status	Two pregnancy losses (n=28)	≥Three pregnancy losses (n=31)	P value
Euthyroid	26 (92.85%)	12 (38.7%)	0.00026
Subclinical hypothyroidism	2 (7.14%)	13 (41.9%)	
Overt hypothyroidism	0	5 (16.1%)	
Hyperthyroid	0	1 (3.22%)	

Table 4: Pregnancy outcomes in women with RPL based on thyroid status.

Outcome	Thyroid dysfunction (n=21)	Euthyroid (n=38)	P value
Live birth	13 (61.9%)	31 (81.6%)	0.482
Miscarriage	6 (28.6%)	5 (13.2%)	0.269
Preterm birth	2 (9.5%)	2 (5.3%)	0.934
NICU admission	3 (14.3%)	2 (5.3%)	0.482

DISCUSSION

The present study demonstrates a significantly higher prevalence of thyroid dysfunction among women with RPL with subclinical hypothyroidism emerging as the most common abnormality. This finding is in agreement with earlier studies by Rao et al and Sahu et al, which reported an increased burden of mild thyroid dysfunction in women with recurrent miscarriage, highlighting the potential role of subtle thyroid abnormalities in recurrent pregnancy loss.[8,9]

Elevated serum TSH levels in the presence of normal circulating thyroid hormone levels were more frequently observed among cases, suggesting that minor perturbations in thyroid function may adversely affect implantation and early placental development. Previous studies by Negro et al and Casey et al, have similarly demonstrated an increased risk of miscarriage and adverse obstetric outcomes in women with subclinical hypothyroidism, supporting the biological plausibility of these observations.[10,11] Although the difference in anti-TPO antibody positivity between cases and controls did not reach statistical significance, a higher prevalence was noted among women with RPL. Thyroid autoimmunity has been postulated to contribute to pregnancy loss through immune-mediated mechanisms, including impaired trophoblastic invasion and placental dysfunction. Studies by Stagnaro-Green et al and Poppe et al have highlighted the role of thyroid autoimmunity in adverse pregnancy outcomes, while Kutteh et al identified thyroid autoimmunity as an independent risk factor for recurrent miscarriage even in euthyroid women.[12-14] A significant association was also observed between the severity of thyroid dysfunction and the number of pregnancy losses, with women diagnosed with subclinical or overt hypothyroidism more likely to experience three or more miscarriages. Comparable trends have been reported by Thangaratinam et al and Toulis et al suggesting a dose–response relationship between thyroid dysfunction and reproductive failure.[15,16]

Furthermore, women with thyroid dysfunction in the present study experienced poorer subsequent pregnancy outcomes, including higher rates of miscarriage, preterm birth and NICU admission. These findings are consistent with existing literature and underscore the importance of routine screening, early diagnosis and appropriate management of thyroid dysfunction in women with recurrent pregnancy loss, particularly in resource-limited settings where preventable causes may otherwise go unrecognized.

The strengths of this study include its prospective case–control design, use of standardized biochemical assessment of thyroid function and autoimmunity and follow-up of participants to document pregnancy outcomes, enhancing clinical relevance. Inclusion of age-matched controls further strengthens internal validity. However, the single-centre, hospital-based nature of the study may limit generalizability. The relatively small sample size may have reduced power to detect significant differences in anti-TPO antibody positivity. Unmeasured confounders such as iodine status and treatment adherence

were not evaluated, warranting further multicentric studies.

CONCLUSION

Thyroid dysfunction, particularly subclinical hypothyroidism, is significantly more prevalent among women with recurrent pregnancy loss and is associated with poorer pregnancy outcomes. These findings underscore the importance of incorporating routine screening for thyroid dysfunction and thyroid autoimmunity into the evaluation of women with recurrent pregnancy loss, as early identification and appropriate management may improve subsequent pregnancy outcomes.

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