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Pre-conceptional Management of Thyroid Dysfunction and Presumption of Recurrent Pregnancy Loss

Afroza Akhter[1*], Sabreena Barkat[2], Sylvia Rahman[3]

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*Corresponding author

ABSTRACT

Background: Recurrent pregnancy loss (RPL) affects 1–2% of women, with many cases remaining unexplained. Thyroid dysfunction and autoimmunity may contribute to pregnancy loss, but evidence on pre-conceptional thyroid evaluation and management in women with RPL is limited. This study assessed its association with subsequent pregnancy outcomes. **Methods & Materials:** A hospital-based prospective observational study was conducted among 60 women with recurrent pregnancy loss and thyroid dysfunction at the study was conducted at the Outpatient Department of Feni Diabetes Hospital (a sister concern of BIRDEM) 100-Bed Hospital in Feni Sadar, from January 2025 to December 2025. 30 with subclinical hypothyroidism, 18 with overt hypothyroidism, and 12 with hyperthyroidism. Baseline demographic and thyroid profiles were recorded, followed by individualized thyroid management and serial thyroid function monitoring before conception. Participants were prospectively followed for conception, miscarriage, and live birth. Data were analyzed using IBM SPSS Statistics, with $p<0.05$ considered statistically significant. **Results:** Among 60 women, 30 (50.0%) had subclinical hypothyroidism, 18 (30.0%) overt hypothyroidism, and 12 (20.0%) hyperthyroidisms. Mean age was 30.19±2.89 years, and 28 (46.7%) were TPO-Ab positive. Pre-conceptional management significantly reduced mean TSH from 8.28±6.88 to 2.44±1.87 mIU/L ($p<0.001$), with 49 (81.7%) achieving target thyroid status. Overall, 54 (90.0%) conceived and 48 (88.9%) achieved live birth. Among women who conceived, miscarriage was significantly lower in those achieving the thyroid target than in those who did not (6.5% vs. 37.5%, $p=0.036$). Age, BMI, previous pregnancy losses, post-management TSH, and TPO-Ab status did not differ significantly between women with live birth and miscarriage ($p>0.05$). **Conclusion:** Pre-conceptional thyroid management was associated with improved thyroid control and favorable pregnancy outcomes, with significantly lower miscarriage among women who achieved the predefined thyroid target.

Keywords: *Recurrent pregnancy loss, Thyroid dysfunction, pre-conceptional thyroid management, Hypothyroidism, Hyperthyroidism, Miscarriage, Live birth.*

1. *Assistant Professor, Department of Obstetrics & Gynaecology, Mainamoti Medical College &Hospital, Cumilla, Bangladesh (ORCID: 0009-0000-2449-0540)*
2. *Assistant Professor, Department of Obstetrics & Gynaecology, Armed force medical college, Dhaka, Bangladesh*
3. *Associate Professor, Department of Obstetrics & Gynaecology, Monno Medical College Hospital, Manikganj, Bangladesh*

INTRODUCTION

Recurrent miscarriage (RM), also termed recurrent pregnancy loss (RPL), is defined as two or more consecutive clinical pregnancy losses confirmed by ultrasonography or histopathology and affects approximately 1.0–1.8% of women [1]. Its etiology is multifactorial, involving genetic, anatomical, autoimmune, thrombotic, endocrine, infectious, male-related, and environmental factors, with maternal age and the interval since the previous miscarriage also influencing risk. Nevertheless, more than 50% of cases remain unexplained and are classified as unexplained RPL (URPL) [2–4].

Thyroid dysfunction is common among women of reproductive age, and normal thyroid function is important for conception and healthy pregnancy outcomes [5]. Thyroid disorders are also among the most common endocrine disorders during pregnancy. Physiological changes in pregnancy may complicate the interpretation of thyroid function, while thyroid hormones play essential roles in fetal growth and neurodevelopment [6]. Thyroid autoimmunity has also been implicated in pregnancy loss, with Stagnaro-Green et al. first reporting an association between thyroid autoantibodies, particularly thyroid peroxidase (TPOAb) and thyroglobulin antibodies, and miscarriage in 1990 [7].

The potential role of thyroid-related factors in reproductive failure has subsequently received increasing attention. The OPTIMUM (Optimization of Thyroid function, Immunity, and Uterine Milieu) strategy was developed to address thyroid dysfunction, immune abnormalities, and intrauterine factors associated with repeated implantation failure (RIF) following assisted reproductive technology (ART) [8]. Evidence from international studies suggests that pre-conceptional assessment and appropriate management of thyroid dysfunction, including optimization of thyroid function and monitoring before conception, may contribute to improved reproductive outcomes [9,10].

Evidence from Bangladesh also supports a potential association between thyroid autoimmunity and RPL. A recent Bangladeshi study reported significantly higher anti-thyroid peroxidase antibody positivity among euthyroid women with RPL, suggesting that assessment of thyroid autoimmunity may have relevance in the evaluation and management of women with recurrent pregnancy loss [11]. However, evidence regarding the role of comprehensive pre-conceptional thyroid assessment and management in women with RPL remains limited, particularly in the Bangladeshi population. The aim of this study was to assess pre-conceptional thyroid control and its association with subsequent conception and pregnancy outcomes among women with recurrent pregnancy loss and thyroid dysfunction.

METHODS & MATERIALS

Study Design and Setting

A hospital-based prospective observational study was conducted in the Department of Obstetrics and Gynaecology. The study was conducted at the Outpatient Department of Feni Diabetes Hospital (a sister concern of BIRDEM) 100-Bed Hospital in Feni Sadar, from January 2025 to December 2025. The study evaluated the pre-conceptional management of thyroid dysfunction among women with a history of recurrent pregnancy loss and assessed subsequent conception and pregnancy outcomes.

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Study Population
The study included women of reproductive age attending the Obstetrics and Gynaecology outpatient department with a history of recurrent pregnancy loss and documented thyroid dysfunction. A total of 60 eligible women were enrolled during the study period. Participants were categorized according to their baseline thyroid status into three groups: subclinical hypothyroidism (n=30), overt hypothyroidism (n=18), and hyperthyroidism (n=12).

Inclusion Criteria
Women were eligible if they were of reproductive age, had a history of at least two previous pregnancy losses, had documented thyroid dysfunction based on thyroid function testing, and were planning to conceive during the study period. Women who provided informed consent and were available for follow-up were included.

Exclusion Criteria
Women with known chromosomal or structural uterine abnormalities, established antiphospholipid syndrome or other major thrombophilic disorders, uncontrolled diabetes mellitus, severe chronic systemic disease, or those receiving assisted reproductive treatment were excluded. Women who were unable to complete the required follow-up were also excluded.

Data Collection
After enrolment, baseline demographic and clinical information was collected using a structured data collection form. Information included age, BMI, number of previous pregnancy losses, type of thyroid dysfunction, history of thyroid disease, and thyroid antibody status. Baseline serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels were recorded. Thyroid peroxidase antibody (TPO-Ab) status was also documented where available.

Pre-conceptional Thyroid Management
Participants received individualized thyroid management according to their underlying thyroid disorder under the supervision of the treating physician. Women with hypothyroidism were treated with levothyroxine, with dose adjustment based on serial thyroid function tests. Women with hyperthyroidism received appropriate antithyroid therapy and biochemical monitoring. Participants were followed until achievement of the predefined target thyroid status appropriate for conception or until the end of the observation period. Post-management TSH and FT4 levels were subsequently recorded.

Assessment of Pregnancy Outcome
Participants were followed prospectively for conception following pre-conceptional thyroid management. The primary pregnancy outcomes assessed were conception, miscarriage, and live birth. For participants who conceived, pregnancy outcomes were recorded during follow-up. Live birth was defined as delivery of a viable infant, whereas miscarriage was defined as spontaneous pregnancy loss before fetal viability according to the study protocol. Pregnancy outcomes were subsequently compared according to baseline thyroid dysfunction and achievement or non-achievement of the pre-conceptional thyroid target.

Study Outcomes
The principal outcomes were improvement in thyroid biochemical parameters following pre-conceptional management, achievement of target thyroid status, conception rate, miscarriage rate, and live-birth rate. The association between pre-conceptional thyroid control and subsequent pregnancy outcome was also evaluated.

Statistical Analysis
Data were analyzed using IBM SPSS Statistics. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Differences in continuous variables between more than two thyroid dysfunction groups were assessed using one-way analysis of variance (ANOVA). Paired t-test was used to compare thyroid function parameters before and after pre-conceptional management. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Independent-samples t-test was used to compare continuous variables between women with live birth and miscarriage. A two-sided p-value of <0.05 was considered statistically significant.

Ethical Considerations
The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the appropriate institutional ethical review authority before commencement of the study. Written informed consent was obtained from all participants before enrolment. Participant confidentiality was maintained throughout data collection, analysis, and reporting.

RESULTS

Participant Characteristics
Table I shows total of 60 women with a history of recurrent pregnancy loss and documented thyroid dysfunction were included in the analysis. The mean age of the participants was 30.19 ± 2.89 years, with a mean body mass index (BMI) of 25.05 ± 2.82 kg/m². Thirty participants (50.0%) had subclinical hypothyroidism, 18 (30.0%) had overt hypothyroidism, and 12 (20.0%) had hyperthyroidism. The mean number of previous pregnancy losses was 2.58 ± 0.70, with 33 (55.0%) women reporting two previous losses, 21 (35.0%) reporting three losses, and 6 (10.0%) reporting four losses. Thyroid peroxidase antibody (TPO-Ab) positivity was detected in 28 (46.7%) participants.

Table I
Baseline demographic and clinical characteristics of the participants according to thyroid dysfunction.

Characteristics	Overall (N=60), n (%)	Subclinical hypothyroidism (n=30), n (%)	Overt hypothyroidism (n=18), n (%)	Hyperthyroidism (n=12), n (%)	p-value
Age, years, mean ± SD	30.19 ± 2.89	30.18 ± 2.59	31.19 ± 3.00	28.73 ± 3.06	0.071
BMI, kg/m², mean ± SD	25.05 ± 2.82	25.08 ± 2.84	25.03 ± 2.76	25.00 ± 3.02	0.985
Previous pregnancy losses, mean ± SD	2.58 ± 0.70	2.47 ± 0.63	2.83 ± 0.71	2.67 ± 0.78	0.018
Number of previous losses					
2	33 (55.0)	18 (60.0)	8 (44.4)	7 (58.3)	0.490
3	21 (35.0)	10 (33.3)	7 (38.9)	4 (33.3)	
4	6 (10.0)	2 (6.7)	3 (16.7)	1 (8.3)	
TPO-Ab positive	28 (46.7)	14 (46.7)	10 (55.6)	4 (33.3)	

Data are presented as n (%) or mean ± SD. p-values were obtained using one-way ANOVA for continuous variables and chi-square test for categorical variables.

Baseline Thyroid Function and Pre-conceptional Management
Table II presents at baseline, the overall mean serum TSH concentration was 8.28 ± 6.88 mIU/L and the mean free thyroxine (FT4) concentration was 1.09 ± 0.39 ng/dL. As expected, TSH concentrations differed significantly across the three thyroid dysfunction groups (p<0.001), with the highest mean TSH observed among women with overt hypothyroidism. Conversely, mean FT4 concentrations were lowest among women with overt hypothyroidism and highest among those with hyperthyroidism (p<0.001). All 48

participants with hypothyroidism received levothyroxine therapy with dose adjustment according to serial thyroid function testing, while the 12 participants with hyperthyroidism received antithyroid treatment and biochemical monitoring. Following pre-conceptional management, 49 (81.7%) participants achieved the predefined target thyroid status before conception or during the pre-conception follow-up period. Target biochemical control was achieved in 27 (90.0%) women with subclinical hypothyroidism, 13 (72.2%) with overt hypothyroidism, and 9 (75.0%) with hyperthyroidism.

Table II
Baseline thyroid function and response to pre-conceptional management.

Variable	Overall (N=60),n(%)	Subclinical hypothyroidism (n=30),n(%)	Overt hypothyroidism (n=18),n(%)	Hyperthyroidism (n=12),n(%)
Baseline TSH, mIU/L, mean ± SD	8.28 ± 6.88	6.52 ± 1.61	16.59 ± 5.92	0.19 ± 0.13
Baseline FT4, ng/dL, mean ± SD	1.09 ± 0.39	1.10 ± 0.15	0.65 ± 0.13	1.70 ± 0.15
Levothyroxine therapy	48 (80.0)	30 (100.0)	18 (100.0)	—
Antithyroid therapy	12 (20.0)	—	—	12 (100.0)
Target thyroid status achieved	49 (81.7)	27 (90.0)	13 (72.2)	9 (75.0)
Target thyroid status not achieved	11 (18.3)	3 (10.0)	5 (27.8)	3 (25.0)
p-value for target achievement				0.244

TSH = thyroid-stimulating hormone; FT4 = free thyroxine. Target thyroid status was defined according to the pre-conceptional biochemical target appropriate for the underlying thyroid disorder.

Changes in Thyroid Function Following Pre-conceptional Management
A significant improvement in thyroid biochemical parameters was observed following pre-conceptional management. The mean TSH concentration decreased from 8.28 ± 6.88 mIU/L at baseline to 2.44 ± 1.87 mIU/L after treatment (p<0.001), while the change in FT4 was not statistically significant (p=0.103) (Table 3A). Significant reductions in TSH were observed across all three thyroid dysfunction groups following management (*Table 3B*).

Table 3A
Changes in thyroid function parameters following pre-conceptional management.

Thyroid function parameter	Baseline	After management	Mean change	p-value
TSH, mIU/L	8.28 ± 6.88	2.44 ± 1.87	−5.84	<0.001
FT4, ng/dL	1.09 ± 0.39	1.16 ± 0.23	+0.08	0.103

Values are presented as mean ± SD. Paired t-test was used.

Table 3B
Changes in TSH according to the type of thyroid dysfunction.

Thyroid dysfunction	Baseline TSH, mIU/L	Post-management TSH, mIU/L	p-value
Subclinical hypothyroidism	6.52 ± 1.61	2.16 ± 1.15	<0.001
Overt hypothyroidism	16.59 ± 5.92	3.67 ± 2.61	<0.001
Hyperthyroidism	0.19 ± 0.13	1.27 ± 0.75	<0.001

Values are presented as mean ± SD. Paired t-test was used.

Conception and Pregnancy Outcomes
Table IV shows during follow-up, 54 (90.0%) of the 60 participants achieved pregnancy, while 6 (10.0%) did not conceive during the study observation period. The conception rate was 93.3% among women with subclinical hypothyroidism, 88.9% among those with overt hypothyroidism, and 83.3% among those with hyperthyroidism; the difference was not statistically significant (p=0.610). Among the 54 women who conceived, 48 (88.9%) had a live birth and 6 (11.1%) experienced another pregnancy loss. The live-birth rate among women with subclinical hypothyroidism, overt hypothyroidism, and hyperthyroidism was 85.7%, 93.8%, and 90.0%, respectively, with no statistically significant difference between the groups (p=0.711).

Table IV
Conception and pregnancy outcomes according to thyroid dysfunction.

Outcome	Overall (N=60), n (%)	Subclinical hypothyroidism (n=30), n (%)	Overt hypothyroidism (n=18), n (%)	Hyperthyroidism (n=12), n (%)	p-value
Conceived	54 (90.0)	28 (93.3)	16 (88.9)	10 (83.3)	0.610
Did not conceive	6 (10.0)	2 (6.7)	2 (11.1)	2 (16.7)	
Among those who conceived (n=54)					
Live birth	48 (88.9)	24 (85.7)	15 (93.8)	9 (90.0)	0.711
Miscarriage	6 (11.1)	4 (14.3)	1 (6.3)	1 (10.0)	

Data are presented as n (%). p-values were obtained using chi-square test.

Association Between Pre-conceptional Thyroid Control and Pregnancy Outcome

Table V shows a significant association was observed between achievement of the pre-conceptional thyroid target and subsequent pregnancy outcome. Among the 49 women who achieved target thyroid status, 46 (93.9%) conceived and 43 of these 46 pregnancies (93.5%) resulted in live birth, while 3 (6.5%) resulted in miscarriage. Among the 11 women who did not achieve target thyroid status, 8 (72.7%) conceived, of whom 5 (62.5%) had a live birth and 3 (37.5%) experienced miscarriage. Among women who conceived, miscarriage was significantly more frequent among those who had not achieved target thyroid status (37.5% vs. 6.5%, Fisher's exact p=0.036).

Table V

Pregnancy outcome according to achievement of pre-conceptional thyroid target.

Pre-conceptional thyroid status	Total	Conceived,n(%)	Live birth,n(%)	Miscarriage,n(%)
Target achieved	49	46 (93.9)	43 (93.5)	3 (6.5)
Target not achieved	11	8 (72.7)	5 (62.5)	3 (37.5)
p-value		0.069		0.036

Percentages for live birth and miscarriage are calculated among women who conceived within each thyroid-control group. Fisher's exact test was used for pregnancy outcome among women who conceived.

Comparison of Women with Live Birth and Recurrent Pregnancy Loss During Follow-up

Table VI shows among the 54 women who conceived, those who subsequently had a live birth had a mean age of 30.27 ± 2.89 years compared with 29.70 ± 3.26 years among those who experienced miscarriage (p=0.694). Mean BMI was also similar between the groups (25.11 ± 2.93 vs. 24.57 ± 1.37 kg/m², p=0.451). The mean number of previous pregnancy losses was 2.56 ± 0.71 among women with a live birth and 2.67 ± 0.52 among those with miscarriage (p=0.669). Post-management TSH was lower among women with live birth than among those with miscarriage, although the difference did not reach statistical significance (2.22 ± 1.67 vs. 3.19 ± 2.44 mIU/L, p=0.383). TPO-Ab positivity was observed in 25 (52.1%) women with live birth and 3 (50.0%) women with miscarriage (p=1.000).

Table VI

Comparison of clinical and biochemical characteristics according to pregnancy outcome.

Variable	Live birth (n=48)	Miscarriage (n=6)	p-value
Age, years	30.27 ± 2.89	29.70 ± 3.26	0.694
BMI, kg/m²	25.11 ± 2.93	24.57 ± 1.37	0.451
Previous pregnancy losses	2.56 ± 0.71	2.67 ± 0.52	0.669
Post-management TSH, mIU/L	2.22 ± 1.67	3.19 ± 2.44	0.383
TPO-Ab positive,n(%)	25 (52.1)	3 (50.0)	1.000

Data are presented as mean ± SD or n (%). Continuous variables were compared using independent-samples t-test and categorical variables using Fisher's exact test.

DISCUSSION

In this study, the average age was 30.19±2.89 years and the average BMI was 25.05±2.82 kg/m²; 55.0% experienced two prior pregnancy losses, 35.0% had three, and 10.0% had four. An earlier study conducted in Northeast China indicated that 51.03% were between 30 and 34 years old, 59.78% had a BMI ranging from 18.5 to 23.9 kg/m², 24.02% had a BMI between 24 and 28 kg/m², and 10.8% were classified as obese; 55.31% experienced two losses, 34.52% had three losses, and 10.51% suffered more than three losses [12]. This research resembles the earlier study in terms of age, BMI distribution, and the count of past pregnancy losses. These resemblances suggest a largely similar demographic profile in women experiencing recurrent pregnancy loss between the two study groups.

In the current investigation, average baseline TSH was 8.28±6.88 mIU/L and FT4 was 1.09±0.39 ng/dL, showing significant variations among thyroid dysfunction categories. A prior study indicated elevated TSH levels in women with thyroid autoimmunity, while FT4 showed no notable difference [13]. This research parallels the earlier study by showing thyroid issues in women experiencing RPL. In our research, 81.7% reached the specified thyroid goal following personalized treatment, emphasizing the significance of effective thyroid management and monitoring before conception [14,15].

The present study demonstrated significant TSH reduction after pre-conceptional management, with improvement across all thyroid dysfunction groups. This finding is similar to previous studies showing that pre-conceptional thyroid optimization may improve pregnancy outcomes, while continued monitoring remains important in women with thyroid autoimmunity [8,16].

The present study showed a high conception rate (90.0%) and live-birth rate (88.9%), with no significant differences among thyroid dysfunction groups. This finding is similar to a previous study showing improved conception and full-term pregnancy following pre-conceptional thyroid optimization with levothyroxine in women with recurrent miscarriage [17].

The present study found that achieving the pre-conceptional thyroid target was associated with higher conception and live-birth rates and significantly fewer miscarriages. This finding is similar to previous evidence showing that abnormal pre-conception TSH levels are associated with adverse pregnancy outcomes, including pregnancy loss [18,19]. However, evidence regarding levothyroxine treatment and pregnancy outcomes in subclinical hypothyroidism remains mixed, suggesting that achieving appropriate thyroid control before conception may be more relevant than treatment alone.

The present study found no significant differences in age, BMI, previous pregnancy losses, post-management TSH, or TPO-Ab positivity between women with live birth and miscarriage. This is similar to previous studies showing inconsistent associations between thyroid autoimmunity and pregnancy loss, suggesting that other factors may also contribute to recurrent pregnancy outcomes [11,15].

Overall, pre-conceptional thyroid optimization was associated with improved thyroid control and favorable conception and live-birth outcomes among women with recurrent pregnancy loss.

CONCLUSION

Pre-conceptional thyroid management significantly improved biochemical thyroid control and was associated with favorable subsequent pregnancy outcomes among women with recurrent pregnancy loss. Achieving the recommended thyroid target

before conception was associated with a significantly lower risk of miscarriage, highlighting the potential importance of timely thyroid evaluation, treatment, and monitoring before pregnancy.

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