

The Effect of Prednisone and Levothyroxine Sodium on Miscarriage Risk and Thyroid Function in Patients with High TPOAb Concentrations: A Retrospective Cohort Study

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Objective: The potential benefit of immunomodulatory therapy in women with high TPOAb concentrations and TSH levels exceeding 2.5 mIU/L remains unclear. This study aimed to evaluate the effects of prednisone combined with levothyroxine sodium (LT4) on miscarriage risk, thyroid function, LT4 dosage and adverse events in this population.

Methods: A retrospective cohort study was conducted, in which patients were divided into Group A (treated with levothyroxine sodium tablets alone) and Group B (treated with prednisone combined with levothyroxine sodium tablets). Statistical analyses included chi-square tests, independent sample t-tests, paired sample t-tests and repeated measures ANOVA.

Results: Compared with levothyroxine sodium alone, combined treatment significantly reduced miscarriage risk in Group B ($P=0.019$). TPOAb concentrations in Group B decreased significantly during treatment ($P<0.001$), while TSH levels showed less fluctuation and remained relatively stable during pregnancy. In addition, Group B required a lower total dose of levothyroxine sodium ($P<0.001$) and had a lower incidence of adverse reactions.

Conclusion: Prednisone combined with levothyroxine sodium was associated with a lower miscarriage rate, more stable thyroid function during pregnancy, and reduced LT4 requirements in patients with high TPOAb concentrations and TSH levels >2.5 mIU/L. These findings suggest that this combined regimen may be a useful option for improving early pregnancy management in this specific patient population.

Keywords: prednisone, levothyroxine, thyroid peroxidase antibodies, recurrent pregnancy loss, thyroid function tests

Introduction

Elevated levels of thyroid peroxidase antibody (TPOAb) levels have been associated with adverse pregnancy outcomes including recurrent spontaneous miscarriage and preterm birth.¹ Women with TPOAb positivity often exhibit altered thyroid function during the preconception period or early pregnancy, particularly higher thyroid-stimulating hormone (TSH) levels. Previous studies have shown that levothyroxine (LT4) alone does not significantly improve pregnancy outcomes in TPOAb-positive women when TSH is below 2.5 mIU/L.^{2,3} In clinical practice, LT4 treatment is commonly prescribed for TPOAb-positive patients with TSH levels exceeding 2.5 mIU/L to optimize thyroid function and reduce the risk of pregnancy complications.⁴ However, pregnancy outcomes remain unsatisfactory in some patients despite LT4 treatment, suggesting that factors beyond thyroid dysfunction may also contribute.

Existing studies suggest that elevated TPOAb may contribute to adverse pregnancy outcomes through immune dysfunction, which may partly explain the limited benefit of LT4 alone in these patients.^{5,6} Glucocorticoids, as

immunomodulatory agents, can reduce the production of autoantibodies and alleviate immune-mediated tissue injury.⁷ They have also been investigated in immune-related recurrent miscarriage.⁸ In our clinical practice, we further observed that poor pregnancy outcomes despite LT4 treatment appeared to be more common among women with high TPOAb concentrations, suggesting that this subgroup may represent a clinically important high-risk population.

It is noteworthy that previous studies have mostly evaluated TPOAb as a binary variable (positive/negative) in relation to recurrent miscarriage or pregnancy outcomes, whereas stratified analyses based on TPOAb levels have been limited.^{9,10} Although a few studies have begun to examine the association between different TPOAb levels and pregnancy outcomes, most have focused on differences in levothyroxine requirement across TPOAb strata, and data on immunomodulatory therapy remain scarce.¹¹ Evidence regarding the reproductive outcomes of prednisone plus LT4 in women with high TPOAb concentrations is therefore limited. To address this gap, we conducted a retrospective cohort study to evaluate the association of prednisone plus LT4 with reproductive outcomes in this population.

Materials and Methods

Data Source

This study was designed as a retrospective cohort study and included 78 non-pregnant patients with high TPOAb concentrations from the Reproductive Center and Women's Health Clinic of our hospital, between January 2022 and December 2023. All relevant data were retrospectively collected from the outpatient electronic medical record system. The study was approved by the Ethics Committee of Zigong Maternal and Child Health Hospital (2023) No.38 and was conducted in accordance with the Declaration of Helsinki and applicable ethical standards. Given the retrospective nature of the study, the requirement for individual informed consent was waived by the Ethics Committee. All patient data were anonymized prior to analysis.

Inclusion and Exclusion Criteria

Inclusion Criteria

① Age between 20 and 35 years; ② High TPO antibody levels (TPOAb concentration ≥ 500 mIU/mL); ③ Normal thyroid function ($2.5 \text{ mIU/L} < \text{TSH} \leq 4.0 \text{ mIU/L}$, with FT3 and FT4 within normal ranges); ④ History of recurrent miscarriage.

Exclusion Criteria

① Autoimmune diseases: Antiphospholipid syndrome, systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, systemic sclerosis; ② Polycystic ovary syndrome; hyperprolactinemia; ③ Bilateral tubal obstruction or significant hydrosalpinx; ④ Ultrasound before ovulation indicating endometrial thickness $< 7 \text{ mm}$; ⑤ Uterine abnormalities: intrauterine adhesions, uterine septum, endometrial polyps, etc; ⑥ Chromosomal abnormalities in either partner; ⑦ Positive antisperm antibody, anti-endometrial antibody, anticardiolipin antibody, or anti-ovarian antibody; ⑧ Coagulation disorders, hyperhomocysteinemia; ⑨ Hypertension, diabetes, kidney disease, and other systemic diseases; ⑩ Patients known to be allergic to study drugs such as prednisone acetate or levothyroxine sodium.

Diagnostic Criteria

- ① Recurrent Pregnancy Loss (RPL) is defined as experiencing two or more successive miscarriages. In 2016, the European Society of Human Reproduction and Embryology (ESHRE) suggested adopting the term RPL in place of RSA (Recurrent Spontaneous Abortion). This recommendation encompasses miscarriages that do not result in a detectable embryo, such as chemical pregnancies.¹²
- ② Hyperemesis Gravidarum (HG) is characterized by severe and persistent nausea and vomiting in early pregnancy, resulting in dehydration, ketonuria, and potentially acidosis, often requiring hospitalization. It is crucial to exclude other organic diseases.¹³
- ③ Subchorionic Hematoma: Described as a crescent-shaped, anechoic region located between the chorion and the uterine muscle layer.¹⁴

Intervention Measures

Our sample size calculation used miscarriage rate as the primary outcome, applying a two-sample proportion test. Using 2020 Chinese consensus and epidemiology with cohort features, we set rates: $\pi_1=11\%$ in never-miscarried; $\pi_2=40\%$ in patients with ≥ 2 -miscarriage. Because all participants had ≥ 2 miscarriages, we used the never-miscarried rate as the efficacy benchmark. With a two-sided $\alpha=0.05$ and 80% power ($1-\beta$), the required sample size per group was calculated as 35. Accordingly, seventy-eight patients were enrolled and analyzed according to the treatment they received in routine clinical practice rather than a predefined study protocol Group A, included 40 patients receiving levothyroxine and Group B included 38 patients receiving prednisone plus levothyroxine.

The specific contents of the intervention protocols are detailed as follows.

Prednisone (5mg per tablet, 100 tablets per bottle, Shanghai Jinbuhuan Lankao Pharmaceutical) is administered as follows: an initial daily dose of 10mg is taken orally. After four weeks of oral prednisone, the dose was adjusted to 5 mg once daily. If pregnancy occurs, the treatment is maintained until the 8th week of gestation before discontinuation. If pregnancy does not occur, the medication is continued until the 12th week of treatment after which it is discontinued. Upon conception, the medication is continued until the 8th week of gestation.

Levothyroxine sodium tablets (50 μg per tablet, 100 tablets per box, Merck Sharp & Dohme) are administered as follows: an initial daily dose of 50 μg is taken orally, with re-evaluation after one month of continuous use. The dosage is adjusted according to re-evaluated thyrotropin (TSH) levels: if TSH is > 2.5 mIU/L, the daily dose is increased by 12.5 μg ; if TSH is ≤ 0.35 mIU/L, the daily dose is decreased by 12.5 μg . Although the inclusion criterion for TSH was 2.5–4 mIU/L, LT4 dosage was adjusted during follow-up to maintain TSH within the target range of 0.35–2.5 mIU/L during treatment and early pregnancy.

Ovulation induction protocol: All patients begin taking oral letrozole tablets (5mg per tablet, 10 tablets per box, Jiangsu Hengrui Medicine) on the 5th day of menstruation, at a dose of 5mg daily for 5 days. After 4 weeks, a follow-up ultrasound is performed two days after stopping the medication. If the dominant follicle diameter is ≤ 1 cm, an injection of human menopausal gonadotropin (HMG, 75u per vial, Livzon Pharmaceutical Factory) at 75u per day is administered for 3 days. The HMG dosage is then adjusted based on follicle growth and development, continuing the ovulation induction for three cycles.

Dydrogesterone (10mg per tablet, 20 tablets per box, Abbott Laboratories) is administered as follows: 10mg daily, taken orally in two divided doses for 14 days. Starting on the day of ovulation or when progesterone (P) exceeds 3ng/mL, the medication is taken for 14 days. If serum HCG is below 6mIU/mL, the medication is discontinued; if serum HCG is 6mIU/mL or higher, the treatment continues until the 12th week of pregnancy, unless the pregnancy is terminated.

Outcome Measures

Primary Outcome Measures

The primary outcome measures assessed in this study are reproductive outcomes, including biochemical pregnancy, ectopic pregnancy, clinical pregnancy, and spontaneous miscarriage. Biochemical pregnancy is defined as a serum HCG level of 6 mIU/mL or higher. Clinical pregnancy is defined by the detection of a gestational sac in the uterine cavity via transvaginal ultrasound. Ectopic pregnancy is characterized by a serum HCG level of 3500 U/L or higher and the absence of a gestational sac or embryo within the uterus as detected by transvaginal ultrasound. Spontaneous miscarriage is defined as embryonic loss occurring before 10 weeks of gestation.

Secondary Outcome Measures

Secondary outcome measures include changes in TPOAb concentration and thyroid function parameters (FT3, FT4, TSH), monitored at 4, 8, and 12 weeks after treatment, and at the 5 weeks of gestation. Additionally, the total dose of LT4 used during the three-month treatment period was recorded. Adverse events, including hyperemesis gravidarum, subchorionic hematoma, and elevated blood glucose levels, were also recorded.

Data Collection

All data were sourced from the outpatient electronic medical record system and are retrospective. The indicators collected and analyzed in this study include female age, body mass index (BMI), anti-Müllerian hormone (AMH) levels. Previous fertility history, number of miscarriages, TSH levels and TPOAb concentrations.

Statistical Analyses

All data analyses in this study were performed using SPSS 22.0 statistical software. The Chi-square test assessed differences between categorical variables. For continuous variables with a normal distribution, an Independent Samples *t*-test compared differences between two groups, while a Paired Samples *t*-test was used for comparing continuous variables within the same sample at different time points. For continuous data not following a normal distribution, the Mann–Whitney *U*-test and other relevant non-parametric tests were employed. Repeated Measures ANOVA evaluated changes in variables over different time points. Between-group differences at each time point were assessed using Independent Samples *t*-tests. All statistical tests were two-tailed, with a *P*-value less than 0.05 indicating statistical significance.

Results

In this study, baseline comparisons between groups A and B showed no significant differences in age, BMI, AMH, or number of abortions. These findings indicate that the two groups were comparable at baseline. See [Table 1](#).

Reduction in Miscarriage Risk

The Chi-square test was used to evaluate the impact of combined treatment in Group B compared to single treatment in Group A on miscarriage risk. The statistical analysis revealed a significant decrease in miscarriage risk for Group

Table 1 Baseline Characteristics, Pregnancy Outcomes, and Adverse Reactions in Groups A and B

Variables	Total (n = 78)	Group A (n = 40)	Group B (n = 38)	Statistic	P
AMH, Mean ± SD	2.44 ± 0.59	2.42 ± 0.57	2.46 ± 0.63	t=-0.24	0.812
Age, M (Q ₁ , Q ₃)	31.00 (29.00, 33.00)	31.00 (29.00, 33.00)	31.00 (30.00, 32.00)	Z=-0.24	0.809
BMI, M (Q ₁ , Q ₃)	21.90 (19.50, 23.00)	21.70 (19.38, 23.00)	22.25 (20.02, 23.08)	Z=-0.55	0.582
Number of Abortions, M (Q ₁ , Q ₃)	3.00 (2.00, 3.00)	3.00 (2.00, 3.00)	3.00 (2.00, 3.00)	Z=-0.09	0.927
Biochemical Pregnancy, n (%)				χ ² =0.01	0.935
0	69 (88.46)	36 (90.00)	33 (86.84)		
1	9 (11.54)	4 (10.00)	5 (13.16)		
Ectopic Pregnancy, n (%)				χ ² =0.00	1.000
0	75 (96.15)	38 (95.00)	37 (97.37)		
1	3 (3.85)	2 (5.00)	1 (2.63)		
Clinical Pregnancy, n (%)				χ ² =0.21	0.651
0	39 (50.00)	21 (52.50)	18 (47.37)		
1	39 (50.00)	19 (47.50)	20 (52.63)		
Recurrent Miscarriage, n (%)				χ ² =5.52	0.019
0	61 (78.21)	27 (67.5)	34 (89.47)		
1	17 (21.79)	13 (32.5)	4 (10.53)		
Hyperemesis Gravidarum, n (%)				χ ² =8.78	0.003
0	68 (87.18)	30 (75.00)	38 (100.00)		
1	10 (12.82)	10 (25.00)	0 (0.00)		
Subchorionic Hematoma, n (%)				χ ² =4.11	0.043
0	60 (76.92)	27 (67.50)	33 (86.84)		
1	18 (23.08)	13 (32.50)	5 (13.16)		
Random Blood Sugar (after 3 months of treatment), Mean ± SD	7.51 ± 0.89	7.41 ± 0.68	7.61 ± 1.08	t=-0.98	0.332

Notes: In the tables, “0” indicates absence, and “1” indicates presence of the specified outcomes. Statistical analyses: *t*-test for continuous variables, Mann–Whitney *U*-test for non-normal variables, and Chi-square test for categorical variables.

B ($\chi^2= 5.52$, $P= 0.019$). However, there were no significant differences between the two groups in terms of biochemical pregnancy rate, ectopic pregnancy rate, and clinical pregnancy rate ($P>0.05$). This suggests that the combined treatment regimen in Group B may be advantageous in lowering the risk of miscarriage. See [Table 1](#).

Changes in TPOAb Concentration

By dynamically monitoring TPOAb concentrations and using Repeated Measures ANOVA, the impact of the two treatment methods on TPOAb levels was evaluated. The results showed that Group B, receiving combined treatment, experienced a significant decrease in TPOAb concentrations at 4, 8, and 12 weeks ($P<0.001$), with many patients' levels dropping below 500 IU/mL by the 12th week. In contrast, Group A, receiving single treatment, did not show significant changes in TPOAb concentrations at 4 and 8 weeks, and only exhibited a non-significant downward trend by the 12th week ($P>0.05$). The reduction in TPOAb concentration was greater in Group B than in Group A. See [Table 2](#).

Analysis of TSH Level Stability and Changes During Pregnancy

To evaluate the impact of the two treatment plans on TSH level stability, a Repeated Measures ANOVA was performed on TSH level data at 4, 8, and 12 weeks of treatment. The results showed that Group B, receiving combined treatment, had minor fluctuations in TSH levels, indicating good stability ($F=2.143$, $P>0.05$). In contrast, Group A, receiving single treatment, exhibited significant TSH level fluctuations ($F=15.95$, $P<0.05$). Between-group comparisons at individual time points showed no significant difference at baseline or at 4 weeks of treatment, whereas significant differences were observed at 8 weeks, 12 weeks, and 5 weeks of gestation. See [Table 3](#).

To evaluate TSH level changes during pregnancy, a Paired Sample *t*-test compared TSH levels between the combined treatment Group B and the single treatment Group A at 12 weeks of treatment and 5 weeks of gestation. The analysis showed no significant TSH level changes for Group B at these time points ($t=-2.498$, $P>0.05$), while Group A experienced a significant increase in TSH levels at 5 weeks of gestation ($t=-3.914$, $P<0.05$). No significant change was observed in Group B, whereas Group A showed a significant increase during early pregnancy. See [Table 4](#).

Total Dose of Levothyroxine Sodium Tablets

The total dosage of levothyroxine sodium tablets required by the two groups was compared using the Mann-Whitney *U*-test. The results showed that Group B, which received the combined treatment, required a significantly lower dosage of levothyroxine sodium tablets than Group A, which received single treatment ($Z = -6.60$, $P<0.001$). The total LT4 dose was significantly lower in Group B than in Group A. See [Table 5](#).

Incidence of Adverse Reactions

A Chi-square test was conducted to compare the incidence of adverse reactions between the combined treatment Group B and the single treatment Group A. The results showed that the incidence of hyperemesis gravidarum ($\chi^2=8.78$, $P=0.003$) and subchorionic hematoma ($\chi^2=4.11$, $P=0.043$) was significantly lower in Group B. These adverse events occurred less frequently in Group B than in Group A. See [Table 1](#).

Discussion

This study assessed whether prednisone acetate and levothyroxine sodium, alone or in combination, were associated with improved reproductive outcomes in patients with high TPOAb concentrations while maintaining an acceptable safety profile. The present findings showed that, compared with LT4 alone, the combination regimen was associated with a lower miscarriage rate, lower TPOAb concentrations, more stable TSH levels, a lower total LT4 dose, and fewer adverse events.

Table 2 Changes in TPOAb Concentration

Variables	Groups	Before Treatment	4 Weeks of Treatment	8 Weeks of Treatment	12 Weeks of Treatment	5 Weeks of Gestation	F Time	F Between-Group	F Interaction	F Within-Group	P Within-Group
TPOAb	A group	2696.01 ± 904.15	2644.63 ± 808.50	2565.19 ± 751.65	2372.38 ± 719.36	2378.18 ± 958.34	59.45	134.6	35.08	1.29	0.274
	B group	2749.47 ± 1194.32	1598.38 ± 613.06	1068.83 ± 411.87	629.20 ± 264.18	312.15 ± 225.18					
	t	-0.22	6.41	10.98	15.58	13.25					
	P	0.824	<0.001	<0.001	<0.001	<0.001					

Notes: Values are presented as mean±SD. Between-group comparisons at each time point were performed using independent-samples t tests. Changes over time were evaluated using repeated-measures ANOVA. F time, F between-group, and F interaction represent the effects of time, group, and time×group interaction, respectively. F within-group and P within-group indicate the within-group time effect for each treatment group.

Table 3 Changes in TSH Levels During Treatment and Early Pregnancy

Variables	Groups	Before Treatment	4 Weeks of Treatment	8 Weeks of Treatment	12 Weeks of Treatment	5 Weeks of Gestation	F Time	F Between-Group	F Interaction	Five-Group ANOVA	P Variance
TSH	A group	3.29 ± 0.41	2.38 ± 0.87	3.06± 0.41	1.95 ± 0.92	2.59 ± 1.23	87.70	68.36	10.94	15.95	<0.001
	B group	3.33 ± 0.43	2.16± 0.36	1.97 ± 0.23	1.27± 0.25	1.88 ± 0.46					
	Difference (A-B)	-0.04	0.22	1.09	0.68	0.71					
	t	-0.33	1.53	7.41	4.46	5.35					
	P	0.740	0.131	<0.001	<0.001	<0.001					
									2.143	0.153	

Notes: Values are presented as mean ± SD. Difference (A-B) indicates the mean between-group difference at each time point. Between-group comparisons used independent-samples t tests, and longitudinal changes were evaluated by repeated-measures ANOVA.

Table 4 Changes in TSH Levels During Pregnancy

Groups	12 Weeks of Treatment TSH	5 Weeks of Gestation TSH	t	P
A group	1.95±0.92	2.59±1.23	-3.914	<0.001
B group	1.27±0.25	1.88±0.46	-2.498	0.123

Notes: Values are presented as mean ± SD. Within-group comparisons between 12 weeks of treatment and 5 weeks of gestation were performed using paired-samples t tests.

Table 5 Total Dose of Levothyroxine Sodium During the 3-Month Treatment Period

Variables	Total (n = 78)	A (n = 40)	B (n = 38)	Statistic	P
LT4 total dose _{ug} , M (Q ₁ , Q ₃)	4500.00 (4500.00, 5250.00)	5250.00 (5062.50, 6000.00)	4500.00 (4500.00, 4500.00)	Z=-6.60	<0.001

Notes: Values are presented as median (Q₁, Q₃). The between-group comparison of total LT4 dose was performed using the Mann-Whitney U-test.

The Reduction in Miscarriage Rate in Combined Treatment Group B and Differences in Other Pregnancy Outcomes

In this study, the risk of miscarriage was significantly reduced in the combined treatment group. This finding is consistent with existing research results,^{15,16} which suggest that prednisone may reduce endometrial inflammation by inhibiting the release of inflammatory mediators, which could contribute to more favorable environment for embryo implantation. In addition, prednisone may improve the immune microenvironment of the endometrium by regulating T cell activity, which is crucial for successful embryo implantation and pregnancy maintenance.¹⁷ Although prednisone shows potential advantages in reducing the risk of miscarriage, our study did not observe a significant effect on reducing biochemical pregnancy rates, ectopic pregnancy rates. Previous studies suggest that the evidence supporting prednisone for implantation-related outcomes remains limited.¹⁸ Taken together, our findings indicate that the observed association was more apparent for miscarriage reduction than for implantation-related outcomes. Moreover, the occurrence of miscarriage is not only related to immune factors but may also be closely associated with other factors such as the genetic quality and developmental potential of the embryo.¹⁹ Our findings are generally consistent with the results of 16 randomized controlled trials conducted by Boomsma et al involving 2232 couples.²⁰ Given this, future research should explore these potential confounding factors in greater depth and apply more precise statistical analysis methods to adjust for them, in order to more accurately assess the true impact of prednisone on different pregnancy outcomes.

Changes in TPOAb Concentration and Stability of TSH Levels

In this study, patients receiving the combined treatment showed a significant reduction in TPOAb concentration, particularly after 12 weeks, with many patients' levels dropping below 500 IU/mL. This reduction may be related to prednisone's anti-inflammatory and immunomodulatory effects. Previous studies have also suggested that prednisone may reduce TPOAb levels by modulating T-cell activity and decreasing B-cell-mediated antibody production, thereby alleviating thyroid autoimmunity injury.^{21,22} This may be one possible explanation for the more stable TSH levels observed in the combined treatment group. Existing evidence indicates that reducing TPOAb levels could improve the environment for sustaining pregnancy and fetal development.²³

We also observed that TSH levels in the combined treatment group (Group B) were more stable and exhibited less fluctuation. This improved stability may be related to the synergistic effects of prednisone and levothyroxine sodium (LT4). Stable thyroid hormone levels are important for maintaining maternal thyroid function and supporting early fetal development.^{24,25} Therefore, better TSH stability during early pregnancy may be clinically relevant in this population. Although large RCTs have shown that LT4 monotherapy does not significantly improve the live birth rate in pregnant women with TSH ≤ 2.5 mIU/L, current guidelines still recommend intervention in women with TSH between 2.5 and 4.0 mIU/L under specific clinical conditions. In this study, we observed that TSH fluctuations were significantly suppressed within this range, suggesting that maintaining stable thyroid hormone levels in this window may help reduce pregnancy

complications. However, this interpretation should be made cautiously and requires further confirmation in larger prospective studies.

Total Dose of Levothyroxine Sodium Tablets and the Occurrence of Complications

In this study, the total dosage of levothyroxine sodium required in the combined treatment group B was significantly lower than in the monotherapy group A. This may be related to the potential synergistic effect of prednisone in inhibiting TPOAb production, which may reduce the need for LT4 dose adjustment by improving thyroid immune status.²⁶ This may partly explain the more stable thyroid-related indicators observed in the combined treatment group and the lower need for LT4 dose adjustment during follow-up. A lower dosage of levothyroxine sodium may help minimize the occurrence of drug-related side effects and complications.

Hyperemesis gravidarum is a common complication in early pregnancy, and its occurrence is associated with various factors, including hormonal changes. Previous studies have suggested that corticosteroids may be helpful in severe hyperemesis gravidarum.^{27,28} This may be relevant to the lower incidence of hyperemesis gravidarum observed in the combined treatment group in our study. Although the exact etiology of subchorionic hematoma (SCH) has not been fully elucidated, existing studies suggest that its occurrence may be related to superficial trophoblast invasion and insufficient angiogenesis, leading to fragile villous blood vessel structures that are prone to rupture and bleeding.²⁹ In addition, previous studies have suggested that prednisone may reduce the risk of SCH by modulating vascular permeability and coagulation factor activity.³⁰ This may be relevant to the lower incidence of SCH observed in the combined treatment group in our study.

This retrospective cohort study may be subject to selection and information biases. Additionally, the relatively small sample size could affect the generalizability of the results. Without long-term follow-up, the enduring effects of the treatment on patients' quality of life remain unknown. Moreover, because mechanistic endpoints were not included, the biological basis of the observed associations remains to be clarified.

Conclusion

In conclusion, prednisone combined with LT4 was associated with lower miscarriage risk, more favorable thyroid-related indicators, a lower LT4 dosage, and fewer adverse reactions than LT4 monotherapy in patients with high TPOAb concentrations. These findings suggest that this combined regimen may be a potentially useful option for early pregnancy management in this selected population, although confirmation in larger prospective studies is still needed.

Data Sharing Statement

The data that support the findings of this study are not publicly available due to privacy concerns and their intended use in future research projects. However, these data may be made available upon reasonable request to the corresponding author, subject to approval by the Institutional Review Board and provided that the request aligns with ethical guidelines and does not interfere with ongoing or planned research activities.

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Disclosure

The authors report no conflicts of interest in this work.

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