Effect of Antithyroid Antibodies in the First Trimester on Pregnancy Outcomes

Jilai Xie
Zhejiang University School of Medicine Second Affiliated Hospital https://orcid.org/0000-0003-4860-3508
Changchang Huang
Zhejiang University School of Medicine Second Affiliated Hospital
Qiaohang Zhao
Zhejiang University School of Medicine Second Affiliated Hospital
Ping Zhou
Zhejiang University School of Medicine Second Affiliated Hospital
Lihong Jiang
Zhejiang University School of Medicine Second Affiliated Hospital
Danqing Yu
Zhejiang University School of Medicine Second Affiliated Hospital
Yayu Shen
Changxing People's hospital
Chun Feng
Zhejiang University School of Medicine Second Affiliated Hospital
Min Jin (min_jin@zju.edu.cn)
Zhejiang University School of Medicine Second Affiliated Hospital

Research

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Abstract

Background: Some women at reproductive age have positive antithyroid antibodies (ATAs). ATA includes thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb). Women with ATAs, no matter with or without thyroid dysfunction, they have a higher risk of adverse reproductive outcomes, such as infertility, miscarriage and preterm birth.

Methods: This study aimed to evaluate the impact of ATAs on maturation of women reproductive system and pregnancy outcomes. And it's a prospective study, performed in three independent centers from January 2019 to June 2020. Women were tested for TSH, free T3, free T4, total T3, total T4, TPOAb and/or TgAb. They were divided into four groups: TPOAb+TgAb+, TPOAb+TgAb-, TPOAb-TgAb+ and TPOAb-TgAb-. Descriptive statistics were obtained for all the parameters. Mean and standard deviation were used for all quantitative parameters. The continuous variables that were nonnormally distributed were compared using the Kruskal-Wallis test. The $\chi 2$ test or Fisher exact test was used to compare categorical variables.

Results: A total of 3457 women undergoing TPOAb and/or TgAb testing were enrolled in this study. 13.77% and 16.85% women were positive for TPOAb and TgAb, respectively. TgAb positivity had a strong correlation with TPOAb (F=1160.568, P□0.001). ATAs had no effect on age of menarche and menstrual cycle. Some obstetric complications occurred in both positive subjects, but TPOAb, TgAb and TSH alone or in combination cannot predict the presence of complications during pregnancy. Administration of L-T4 to pregnant women with TSH 2.5-4.94mIU/ml may reduce the risk of PROM in ATA- women. Of the women with one or two ATAs, there were no significant differences between LT4 therapy group and untreated group in other pregnancy outcomes.

Conclusion: TPOAb or TgAb is probably not the main reason for poor pregnancy outcomes.

Introduction

Autoimmune thyroid disease (AITD) is common in women of reproductive age, including Grave's disease (GD) and Hashimoto's thyroiditis (HT). In recent years, an increasing number of studies demonstrated that thyroid autoimmunity (TAI) is related to infertility, pregnancy loss and adverse pregnancy outcomes[1–3]. The positive rate of thyroid peroxidase antibody (TPOAb) or thyroglobulin antibody (TgAb) in pregnant women is 2%-17%. Women with antithyroid antibodies (ATAs) may be euthyroid or have variable degrees of thyroid dysfunction.

Current researches focuses on women receiving assisted reproductive technology, and the reasons for their infertility are complicated[4]. It is not clear whether there is a causal relationship, such as a direct action of ATAs in reproductive system or whether reduced thyroid functional reserve must be considered. Positive-ATAs also exist in naturally pregnant women, but the relevance of TAI in normal women in particular is not yet understood.

For these reasons, we designed the present retrospective study. We investigate the pregnancy of women in an area to assess whether the presence of positive-ATAs may cause infertility of women or influence the pregnant outcomes, such as miscarriage and preterm labor.

Methods

Study approval

The study was reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine, First People's Hospital of Yuhang, Taizhou Women and Children's Hospital and Changxing People's Hospital.

Study design and participants

This is a prospective study, in which women who established prenatal care manuals in the First People's Hospital of Yuhang, Taizhou Women and Children's Hospital and Changxing People's Hospital were enrolled between 1st January, 2019 and 1st June, 2020. They were all in the 1st trimester of pregnancy. All women were tested for TPOAb and/or TgAb. They had their sera tested for TSH, free T3, free T4, total T3 and total T4. Detection was performed at their first arrival at the hospital for establishment of prenatal care manual. The study was based on the electronic medical records system.

Given the effect of pregnancy on thyroid antibodies, patients without pregnancy or testing thyroid antibodies after early pregnancy were excluded. Among 3544 women, 17 with multiple pregnancies and 1 with autoimmune disease other than autoimmune thyroid disease were excluded. Women aged 18–45 years were included. To further analyze the effects of L-T4 intervention on pregnancy outcomes, pregnant women who had hyperthyroidism, hypothyroidism and autoimmune thyroid disease with medicinal treatment before pregnancy were also excluded. 3457 women were tested for TPOAb, of those, 3300 women were also tested for TgAb. After establishment of prenatal care manual, 19 women decided to deliver the fetus by personal wishes. And there were 1149 cases lost to follow-up (Fig. 1).

Biochemical data

Women's serum samples were analysed by chemiluminescence immunoassay (CLIA) for antithyroid antibodies in First People's Hospital of Yuhang, Taizhou Women and Children's Hospital and Changxing People's Hospital. Normal values were accepted as being < 5.61 IU/ml for TPOAb and < 4.11 IU/ml for TgAb. Normal concentration of TSH was accepted as 0.35-4.94mIU/L. For free T4 (FT4) and free T3 (FT3), normal concentrations were 0.7–1.48 ng/dL and 1.71–3.71 pg/mL. Serum concentration of total T4 (TT4) and total T3 (TT3) was determined by chemiluminescence method (Abbott Architect i200SR analyzer) with a normal reference range of 4.87–11.72 μg/dL and 0.58–1.59 ng/dL. These reference values were given by the company producing these assay kits.

Statistical analysis

Statistical analysis was performed using SPSS software (version 20). Student's t test, chi-squared test and Fisher's exact test were used as appropriate. A P-value < 0.05 was considered statistically significant. Continuous variables were presented as the mean ± standard deviation. Categorical variables were presented as the frequency (percentage). For comparing analysis of the 2 groups with or without TPOAb or TgAb, ANOVA was applied for continuous variables. For comparing analysis of the 4 groups with or without TPOAb and TgAb, ANOVA was applied for continuous variables, the Kruskal-Wallis test was used in cases of nonnormally distributed variables, and the $\chi 2$ test or Fisher exact test was used to compare categorical variables. Differences were considered significant if P value < .05 (2-sided).

Results

Background patient characteristics

Of 3457 women, 2981 (86.23%) were TPOAb negative and 476 (13.77%) TPOAb positive. Of 3300 women, 2744 (83.15%) were TgAb negative and 556 (16.85%) TgAb positive. Body mass index (BMI), TT4 and TT3 concentrations were similar in both groups (Table 1, 2). FT4 was similar in TPOAb positive and negative groups. Average age of women and concentration of TSH and FT3 were higher in TPOAb or TgAb positive groups than the negative ones.

Table 1
Characteristics of TPOAb-negative and TPOAb-positive women

	TPOAb negative	TPOAb positive	P value
Female age (years)	28.40 ± 4.36	29.21 ± 4.41	0.000*
BMI	21.55 ± 3.18	21.59 ± 3.20	0.802
TSH (mIU/L)	1.48 ± 1.02	1.98 ± 1.76	0.000*
FT4 (ng/dl)	1.02 ± 0.17	1.03 ± 0.30	0.198
FT3(pg/ml)	3.00 ± 0.51	3.09 ± 1.33	0.009*
TT4(ng/dl)	9.59 ± 2.11	9.49 ± 2.26	0.333
TT3(ng/ml)	1.18 ± 0.31	1.17 ± 0.32	0.959
Values are mean ± SD. * means statistically significant differences between the two groups.			

Table 2
Characteristics of TgAb-negative and TgAb-positive women

	TgAb negative	TgAb positive	P value
Female age (years)	28.42 ± 4.43	28.92 ± 4.06	0.015*
BMI	21.55 ± 3.18	21.54 ± 3.13	0.928
TSH (mIU/L)	1.52 ± 1.03	1.86 ± 1.69	0.000*
FT4 (ng/dl)	1.01 ± 0.18	1.04 ± 0.27	0.004*
FT3(pg/ml)	2.99 ± 0.66	3.09 ± 0.84	0.001*
TT4(ng/dl)	9.51 ± 2.10	9.46 ± 2.12	0.581
TT3(ng/ml)	1.17 ± 0.32	1.16 ± 0.29	0.702
Values are mean ± SD. * means statistically significant differences between the two groups.			

Effect of ATA on female reproductive system

3300 (95.46%) of 3457 women who detected TPOAb and TgAb at the same time. 328 women had both antibodies positive. The probability of women had positive TgAb was higher in women who had positive TPOAb ($F = 1160.568$, $P < 0.001$). But TgAb level had a weak correlation with TPOAb level ($r = 0.369$, $P < 0.001$).

In the four groups, women with both positive TPOAb and TgAb had a higher age ($P = 0.004$). All pregnant women has the similar BMI ($P = 0.672$) and age of menarche ($P = 0.693$). The proportion of women with regular menstruation showed no significant difference ($P = 0.389$).

TSH were higher in both positive groups than other ones. The differences were statistically significant at FT3 and FT4 during four groups, after post hoc Bonferroni corrections ($P = 0.05/6$), the difference was statistically significant at FT3 comparing only TgAb positive group and both negative group. TT4 and TT3 concentrations were similar in both groups (Table 3). FT4 was similar in TPOAb positive and negative groups. As illustrated in Table 3, there were no significant demographic differences between the three groups in reproductive history.

Table 3
Characteristics of ATA-positive and ATA-negative women

	TPOAb + TgAb+	TPOAb + TgAb-	TPOAb-TgAb+	TPOAb-TgAb-	P
Number of total patients	328 (9.94%)	124 (3.76%)	228 (6.91%)	2620 (79.39%)	0.000*
Female age (years)	29.05 ± 4.15	29.39 ± 4.94	28.71 ± 3.93	28.37 ± 4.40	0.004*
BMI	21.47 ± 3.14	21.88 ± 3.40	21.63 ± 3.13	21.53 ± 3.17	0.672
Age of menarche	14.00 ± 1.04	13.99 ± 1.15	13.90 ± 1.12	14.00 ± 1.11	0.693
Number of patients with irregular menstruation	30	14	27	311	0.544
TSH (mIU/L)	2.11 ± 1.93	1.79 ± 1.27	1.51 ± 1.19	1.50 ± 1.01	0.000*
FT4 (ng/dl)	1.04 ± 0.31	1.00 ± 0.31	1.04 ± 0.21	1.02 ± 0.17	0.029*
FT3(pg/ml)	3.08 ± 0.84	3.11 ± 2.23	3.11 ± 0.83	2.98 ± 0.47	0.002*
TT4(ng/dl)	9.36 ± 2.19	9.59 ± 2.37	9.61 ± 2.03	9.50 ± 2.10	0.512
TT3(ng/ml)	1.16 ± 0.29	1.22 ± 0.42	1.18 ± 0.30	1.17 ± 0.31	0.356
Reproductive history					
Primipara	119	45	83	1077	0.162
Multipara	209	79	145	1543	
Number of previous preterm labor	2	0	0	23	0.567
Number of spontaneous abortion	17/252	11/102	10/172	109/1884	0.218
Number of recurrent miscarriage (≥ 2)	2/252	3/102	1/172	14/1884	0.139
Number of ectopic pregnancy	2/252	1/102	0/172	34/1884	0.221
Others			1 hydatidiform mole		

* means statistically significant differences between the two groups.

The continuous variables that were nonnormally distributed were compared using the Kruskal-Wallis test. The $\chi 2$ test or Fisher exact test was used to compare categorical variables among the 4 groups.

Table 4
Pregnancy outcome of women grouped by TPOAb and TgAb

	TPOAb + TgAb+	TPOAb + TgAb-	TPOAb-TgAb+	TPOAb-TgAb-	P
Number of patients with pregnancy outcomes	221 (10.4%)	92 (4.3%)	163 (7.6%)	1656 (77.7%)	-
Spontaneous abortion (< 20 weeks)	6	4	3	65	0.494
Abortion of fetal death (> 20 weeks)	0	0	1	3	0.442
Preterm labor	16	3	4	66	0.112
Term labor	198	84	155	1515	
Vaginal delivery	117	47	86	878	0.974
Cesarean section	97	40	73	703	
Timing of vaginal delivery (week)	39.10 ± 1.55	39.28 ± 1.15	39.38 ± 1.20	39.36 ± 1.32	0.262
Timing of cesarean section (week)	38.61 ± 1.51	38.95 ± 0.91	39.03 ± 1.68	38.86 ± 1.29	0.202
Birthweight†	3223.34 ± 438.87	3343.49 ± 454.62	3288.11 ± 455.13	3322.30 ± 429.09	0.096
Number of neonatal asphyxia	3	2	1	10	0.129
Number of neonatal malformations	0	2	1	10	0.161
Number of neonatal chromosomal abnormalities	0	1	0	4	0.390
Complications during pregnancy					
Gestational diabetes mellitus	43/214	23/87	32/159	291/1580	0.289
Hypertension in pregnancy	7	1	6	40	0.556
Postpartum hemorrhage	5	2	0	23	0.183
ICP	2	1	1	23	0.927
Oligohydramnios	9	2	5	47	0.732
Premature rupture of membranes	30	16	22	233	0.774
Placental abruption	2	0	2	9	0.442
Placenta previa	3	5	3	24	0.056
Abnormal morphology of placenta previa	6	1	3	32	0.808
Others				1 hydatidiform mole	

* means statistically significant differences between the two groups.

† Birthweight was adjusted via analysis of covariance excluding the confounder mentioned (gestational week).

The continuous variables that were nonnormally distributed were compared using the Kruskal-Wallis test. The $\chi 2$ test or Fisher exact test was used to compare categorical variables among the 4 groups.

Pregnancy outcome grouped by ATAs

In our current study, 2132 women were available for follow-up and we got their pregnancy outcomes. The overall live birth rate was 95.73% (214/221, 87/92, 159/163 and 1581/1656) in this pregnancy. In both positive group, 1 late stillbirth was happened due to cord excessive twisting at the gestational 39 + 4th weeks. In TgAb positive group, there was one late stillbirth at gestation 38 + 5th weeks but it indicates nothing about its cause. In both negative group, 1 late stillbirth happened at gestation 30th weeks without any reasons, and one was with serious thoracic deformities at gestation 30 + 6th weeks.

Two neonatal malformations occurred in TPOAb positive group, one was hexadactyly, and the other was congenital heart malformations. One fetus with 15th chromosome microduplication was in TPOAb positive group. One syndactyly was occurred in TgAb positive group. In both negative group, there were 10 fetal

malformation (4 congenital heart malformations, 2 hexadactyly, 1 thoracic deformity, 1 agenesis of kidney, 1 anal atresia, 1 cervical hygroma) and 4 chromosomal abnormalities (2 trisomy 21 syndrome and 2 ambiguous chromosomal abnormalities).

There was no difference in birthweight (P = 0.096), this efficacy was evaluated via analysis of covariance (ANCOVA) for eliminating gestational week disturbance. All complications during pregnancy were observed in the third trimester. The most common complication during pregnancy was gestational diabetes mellitus (GDM) (43/214, 23/87, 32/159 and 291/1580, P = 0.289). No postpartum thyroiditis was reported in our study.

We performed ROC analysis to identify TPOAb and/or TgAb concentration cutoff predicting the complications during pregnancy. There were no best TPOAb or TgAb concentration cutoff as the upper limit to elevate complications during pregnancy (Fig. 2, supplement Fig. 1, supplement Fig. 2).

Pregnancy outcomes in women with TSH reduction and elevation

To assess the effect of L-T4 treatment on pregnancy outcomes, we performed subgroup analyses of intervention according to both TSH level and TPOAb status only for pregnant women with TSH 2.5 to 4.94mIU/L. The pregnancy outcomes of the intervention subgroup analysis were shown in Table 5. There were no differences between the treated and untreated groups. In both negative group, LT4 intervention may reduce the risk of premature rupture of membranes (P = 0.033).

Table 5
Pregnancy Outcomes in the Intervention Subgroups and Control Group

	TPOAb + TgAb+			TPOAb + TgAb-			TPOAb-TgAb+			TPOAb-TgAb-		
	LT4-treated	Untreated	P	LT4-treated	Untreated	P	LT4-treated	Untreated	P	LT4-treated	Untreated	P
Number of events	34	25		6	11		8	16		79	143	
Timing of vaginal delivery (week)	39.46 ± 0.87	39.38 ± 0.79	0.805	39.29 ± 1.03	39.35 ± 1.23	0.938	39.86 ± 0.47	39.17 ± 1.20	0.219	39.22 ± 1.03	39.31 ± 1.16	0.667
Timing of cesarean section (week)	38.29 ± 1.22	39.10 ± 1.45	0.191	38.95 ± 1.64	39.93 ± 0.91	0.130	39.57 ± 0.81	39.00 ± 1.08	0.502	39.08 ± 1.19	38.80 ± 1.33	0.292
Birthweight†	3236.71 ± 383.11	3173.20 ± 360.91	0.281	3240.00 ± 332.44	3465.45 ± 393.99	0.260	3437.50 ± 480.53	3182.50 ± 91.62	0.433	3359.81 ± 409.89	3359.97 ± 445.44	0.870
Number of neonatal asphyxia	0	1	0.424	0	0	1.000	0	0	1.000	0	2	0.538
Number of neonatal malformations	0	0	1.000	0	0	1.000	0	0	1.000	0	0	1.000
Number of neonatal chromosomal abnormalities	0	0	1.000	0	0	1.000	0	0	1.000	0	1	1.000
Complications during pregnancy												
Preterm labor	1	1	1.000	0	1	1.000	0	0	1.000	2	7	0.605
Gestational diabetes mellitus	10	4	0.231	1	1	1.000	1	3	1.000	22	35	0.581
Hypertension in pregnancy	0	0	1.000	0	0	1.000	0	0	1.000	2	4	1.000
Postpartum hemorrhage	0	1	0.417	0	0	1.000	0	0	1.000	1	1	1.000
ICP	1	0	1.000	0	0	1.000	1	2	1.000	3	1	0.257
Oligohydramnios	2	1	1.000	0	0	1.000	0	0	1.000	2	5	1.000
Premature rupture of membranes	7	3	0.605	1	3	1.000	1	0	0.333	9	33	0.033*
Placental abruption	0	0	1.000	0	0	1.000	0	0	1.000	0	2	0.539
Placenta previa	0	1	0.424	0	0	1.000	0	1	1.000	1	4	0.792
Abnormal morphology of placenta previa	0	0	1.000	0	0	1.000	0	0	1.000	0	7	0.110

* means statistically significant differences between the two groups.

† Birthweight was adjusted via analysis of covariance excluding the confounder mentioned (gestational week).

The continuous variables that were nonnormally distributed were compared using the Kruskal-Wallis test. The $\chi 2$ test or Fisher exact test was used to compare categorical variables among the LT4-treated and untreated groups.

Discussion

In our study, 328 (9.94%), 124 (3.76%), 228 (6.91%) and 2620 (79.39%) women are both positive, only TPOAb positive, only TgAb positive and both negative, respectively. All test results came after pregnancy. During the follow-up, we detected that part of women had regular physical examinations of thyroid gland at employment examinations, but they didn't know the specific laboratory items and the significance of them. Thus, we cannot evaluate the affluence of pregnancy on thyroid gland on normal women who receive pregnant spontaneously.

At early pregnancy, TPOAb and/or TgAb are positive in pregnant women with the highest titer, then decreased during pregnancy[5]. In Chen's study[6], whose subject population is similar to ours, the prevalence of ATAs was lower than our study. Both studies are conducted in neighboring iodine-sufficient areas of

China. This controversial result may be due to the fact that Chen collect blood samples from each participant in the delivery day.

Much of the literature on rats demonstrated that hyperthyroidism and hypothyroidism may delay or throw off estrus cycles[7, 8]. From our data, age of menarche similar in all groups. 9.15% women with TPOAb and TgAb had irregular menstruation. This result may be explained by the fact that a variety of factors affect menstruation, such as nutrition and mood. Furthermore, women with ATAs may accompany other autoimmune syndromes[9–11]. We excluded the confounding factor in the experimental design phase.

In our study, 15 women with both positive-TPOAb and TgAb had higher titer of TSH (> 4.94 IU/ml). In four groups, 61, 18, 25 and 236 women had a borderline TSH level (2.5 IU/ml < TSH ≤ 4.94 IU/ml). We demonstrated that women who had positive antithyroid antibodies had a higher risk of abnormal thyroid function (F = 70.711, P = 0.000).

The academic literature on human has revealed that embryo quality was significantly impaired in women with at least one ATA[12]. HT mice with normal thyroid function were liable to suffer from a series of complications, containing implantation failure, fewer pinopodes and retarded pinopode maturation[13]. Multiple studies have shown that TPOAb may have impact on miscarriage, preterm delivery, and low birth weight17-19, however, Yan et al.20 demonstrated that TPOAb did not increase the incidence of unexplained recurrent miscarriage. From our results, fewer women (6/221, 4/92, 4/163, 68/1656) have miscarriages in this pregnancy. And there are no significant differences in timing of delivery, mode of delivery and birthweight. The malformation of progeny in this study may be an individual case. A relationship exists between ATAs and cognitive ability of offspring[14–16], thus, further studies and follow-up are required to evaluate the impact of ATAs.

There are many complications during pregnancy. The incidence of GDM is higher than other diseases. In another study, positive TPOAb in early pregnancy was able to increase the risk of GDM[17]. It has the disadvantage that the family history is not taken into account. According to Montaner[18], maternal age, prior GDM, and diabetes mellitus in first-degree relatives may have a greater impact on the onset of GDM.

Han 2018[19] reports that women with positive-TPOAb and positive-TgAb in the first trimester had a higher risk of hypertensive disorders of pregnancy, even they were euthyroid. However, Medici 2014[20] found little evidence that TPOAb status had relationship with hypertensive disorders. It's a pity that we do not have enough cases to verify it. For further researches, a wide range of confounding factors should be taken into account, such as individual history of thyroid diseases and thyroid medication usage.

Abbassi-Ghanavati found that subjects with TPOAb suffered a threefold risk of the onset of placental abruption, and the blood samples screened in the first 20 weeks of gestation[21]. In our study, there were 13 cases of placental abruption, and the result showed no significance between TPOAb and/or TgAb positive group and both positive group. But whether this relationship of ATAs and the morphology and location of placenta exists is worthy of further research.

We performed ROC analysis to verify the value of TPOAb or TgAb or TSH as an independent risk factor predicting complications during pregnancy. From our data, any combination of TPOAb, TgAb and TSH were far from perfect in terms of positively or negatively predicting pregnancy related diseases.

A special focus is that weather Women with a borderline TSH level (2.5 IU/ml < TSH ≤ 4.94 IU/ml) need to treat. In our study, of the women with one or two ATAs, there were no significant differences between LT4 therapy group and untreated group in pregnancy outcomes. The limitation is that the events of ATAs-positive women treated with LT4 were insufficient. In both negative group, LT4 therapy may reduce the risk of premature rupture of membranes (PROM) (P = 0.033). And a previous study showed that pregnant women with subclinical hypothyroidism (SCH) were at higher risk for PROM(RR = 1.43, 95% CI 1.04–1.95) [22]. The causes of PROM are complex, and SCH may be one of them. Therefore, further research is necessary to determine whether L-T4 treatment outweighs the disadvantages for PROM.

In conclusion, in this study the presence of TPOAb and TgAb were 13.77% and 16.85%, respectively. The probability of TgAb-positivity was higher in women who had positive TPOAb. ATAs had no effect on age of menarche and menstrual cycle. Even if women were ATA positive, their pregnancy outcomes showed no significant differences compared to negative ones. And any combination of TPOAb, TgAb and TSH showed no positive predictive values. Administration of L-T4 to pregnant women with TSH 2.5-4.94mIU/ml may reduce the risk of PROM in ATA- women. Although our data are flawed, this study still provides indirect evidence that TPOAb or TgAb is probably not the main reason for poor pregnancy outcomes. However, conclusively determining whether L-T4 treatment outweighs the disadvantages requires further research in the setting of randomized controlled clinical trials.

Declarations

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Authors' contributions

All authors were involved in the clinical work. Jilai Xie, Changchang Huang, Qiaohang Zhao, Ping Zhou and Lihong Jiang worked in the extraction of data from the data base. Jilai Xie, Danqing Yu, Yayu Shen and Chun Feng performed the analysis of data and statistics. Jilai Xie and Min Jin was involved in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

The study was reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine, First People's Hospital of Yuhang, Taizhou Women and Children's Hospital and Changxing People's Hospital. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication

"Not applicable".

Competing interests

The authors declare that they have no competing interests.

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Figures

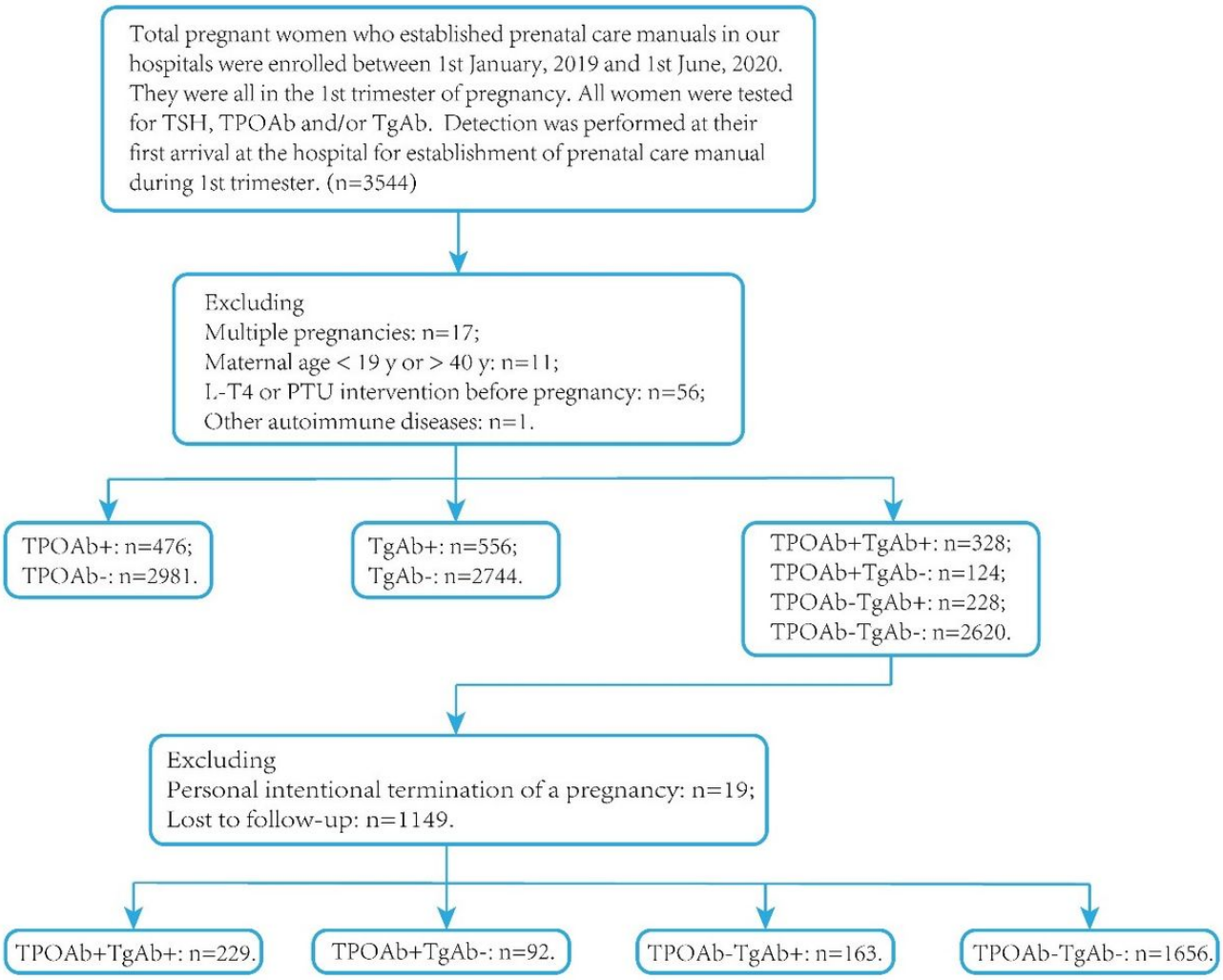

Figure 1

Flowchart illustrating the selection of the pregnant women included in the current study.

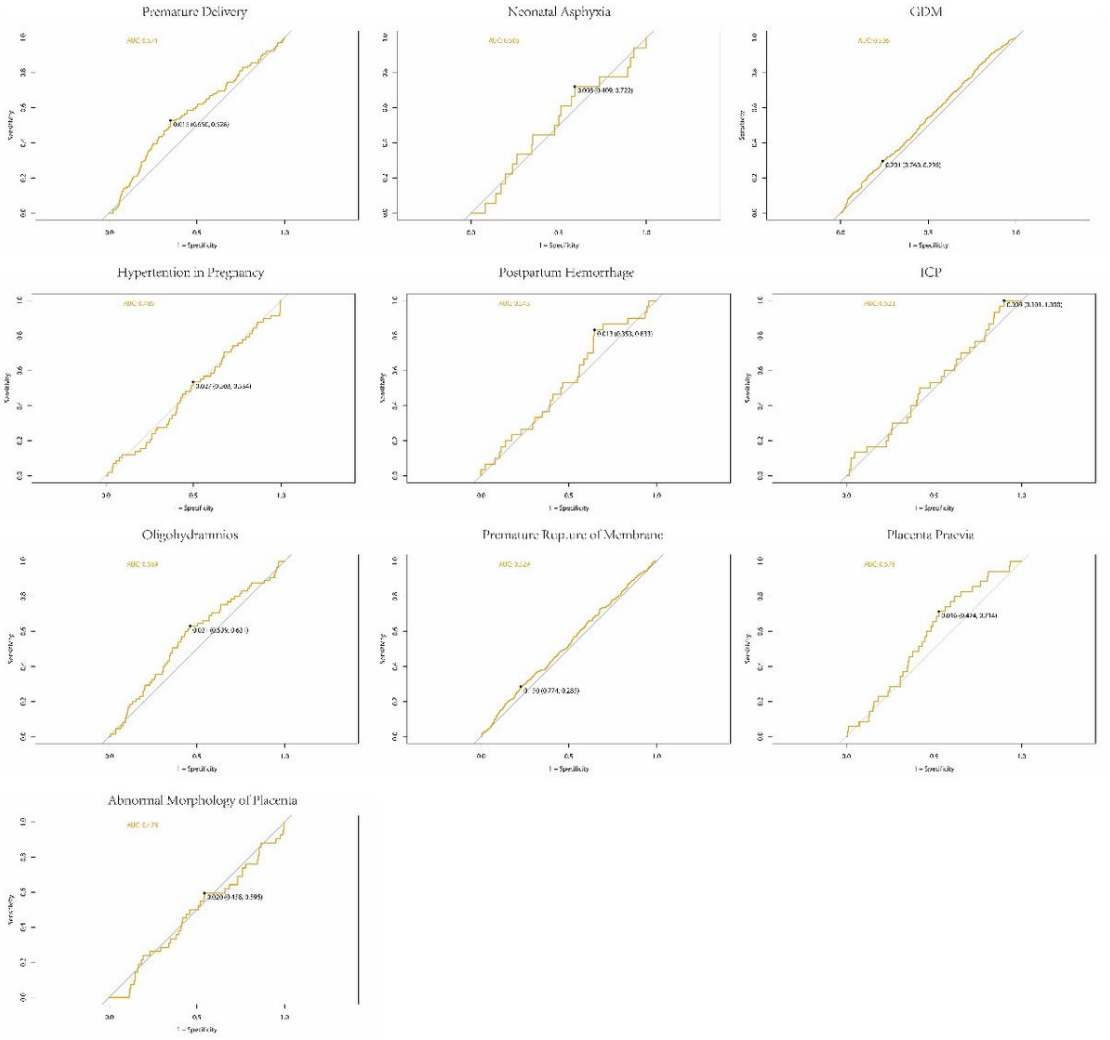

Figure 2

ROC curve analysis depicting the predictive value of TPOAb, TgAb and TSH in combination for predicting the presence of complications during pregnancy.

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