Effect of thyroxine treatment on pregnancy outcomes in infertile Japanese women with TSH levels between 2.5 μ U/mL and the upper reference limit: a retrospective study

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Abstract. Recent randomized controlled studies have revealed that levothyroxine (LT4) treatment improves pregnancy outcomes only in infertile women with subclinical hypothyroidism who have thyroid autoantibodies (TAs), but not for those with high TSH levels within the normal range who have TAs. Here, we retrospectively investigated pregnancy outcomes in infertile Japanese women with $2.5 \mu\text{U/mL} \leq \text{TSH} < \text{upper reference limit (URL)}$. Between 2012 and 2018, 286 patients diagnosed with infertility were followed for more than 1 year at our institution. Among them, we included 106 patients with $2.5 \mu\text{U/mL} \leq \text{TSH} < \text{URL}$. We divided these patients into four groups based on the combination of TA positivity and LT4 treatment status to assess the effects of LT4 treatment considering TA positivity on the incidence of pregnancy or miscarriage. In this study, we did not find any significant differences in the rates of pregnancy or miscarriage among the four groups ($p = 0.81$ and 0.52 , respectively). In addition, logistic regression analysis showed that age and history of miscarriage were associated with the incidence of pregnancy, but presence of TAs and LT4 treatment status were not and that no variables examined were associated with the incidence of miscarriage. In summary, we were not able to demonstrate the benefit of LT4 treatment for pregnancy outcomes in Japanese euthyroid infertile women with $2.5 \mu\text{U/mL} \leq \text{TSH} < \text{URL}$ regardless of TA status in this study.

Key words: Infertility, Euthyroid, Miscarriage, Thyroid autoantibodies, Levothyroxine

PREGNANT WOMEN with subclinical hypothyroidism are at risk for miscarriage and premature birth [1, 2]. The presence of thyroid autoantibodies (TAs) is associated with poor obstetric prognosis [3]. The 2017 American Thyroid Association (ATA) guidelines [4] recommend to consider strict management of thyroid function for pregnant women with TAs and normal thyroid function,

defined as $2.5 \mu\text{U/mL} \leq \text{TSH} < \text{upper reference limit (URL)}$ by levothyroxine (LT4) treatment. However, the recent The Thyroid AntiBodies and LEvoThyroxine (TABLET) trial, a randomized controlled trial (RCT) [5] did not show that LT4 treatment is beneficial for the live birth rate among TA-positive euthyroid pregnant women.

Two RCTs showed that LT4 treatment to maintain $\text{TSH} < 2.5 \mu\text{U/mL}$ known as the TSH upper-reference during the first trimester in pregnant women [6], is beneficial for pregnancy outcomes such as pregnancy rate and miscarriage rate among TA-positive infertile women with subclinical hypothyroidism [7, 8]. However, some observational studies showed that pregnancy and miscarriage rates in infertile women with $2.5 \mu\text{U/mL} \leq \text{TSH} < \text{URL}$ who underwent artificial insemination were similar to those with $\text{TSH} < 2.5 \mu\text{U/mL}$ [9, 10]. Furthermore, RCTs did not find the benefits of LT4 treatment for TA-positive euthyroid infertile women [11, 12]. Thus, LT4 treatment might not be necessary for infertile women

Submitted Jun. 19, 2020; Accepted Aug. 28, 2020 as EJ20-0380
Released online in J-STAGE as advance publication Oct. 1, 2020
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Abbreviations: AMH, anti-Müllerian hormone; ART, artificial reproductive technology; FT3, free triiodothyronine; FT4, free thyroxine; hCG, human chorionic gonadotropin; IVF, *in vitro* fertilization; LT4, levothyroxine; RCT, randomized controlled trial; TA, thyroid autoantibody; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TRAb, thyrotropin receptor antibody; URL, upper reference limit

with normal thyroid function. In this study, we retrospectively investigated the effect of LT4 treatment on pregnancy outcomes among Japanese euthyroid ($2.5 \mu\text{IU/mL} \leq \text{TSH} < \text{URL}$) infertile women divided by TA status.

Subjects and Methods

Patients

In this study, infertility was defined as the failure to achieve clinical pregnancy over 12 months. Between February 1, 2012, and August 31, 2018, there were 345 Japanese infertile women referred by reproductive clinics to the Diabetes and Endocrine Clinics of Juntendo University Hospital because they showed that TSH was higher than $2.5 \mu\text{IU/mL}$ and/or positive TA (thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb)). Among these 345 patients, 59 who were lost to follow-up at 1 year were excluded from the study. Among 286 patients, 106 infertile women with $2.5 \mu\text{IU/mL} \leq \text{TSH} < \text{URL}$ were divided into four groups based on the combination of TA positivity and LT4 treatment status as follows: TA–LT4–, TA–LT4+, TA+LT4–, and TA+LT4+. Initiation of LT4 treatment for each infertile woman was based on the clinical judgment of the treating physician. All infertile women in the LT4+ groups were started on LT4 with the dose titrated to maintain $\text{TSH} < 2.5 \mu\text{IU/mL}$. Mean LT4 dose was calculated as the cumulative LT4 dose divided by the number of days of LT4 treatment. Reproductive specialists classified causes of infertility based on the results of infertility testing, including serum hormonal level testing, semen analysis, and hysterosalpingography. The study protocol was approved by the ethics committee of Juntendo University.

Measurement of serological markers

Blood samples were collected from all patients during clinic visits. Free thyroxine (FT4), free triiodothyronine (FT3), and TSH were measured using commercially available electrochemiluminescence immunoassays (Roche Diagnostics) with the following normal ranges: FT4, $1.00\text{--}1.70 \text{ ng/dL}$; FT3, $2.40\text{--}4.50 \text{ pg/mL}$; and TSH, $0.56\text{--}4.30 \mu\text{IU/mL}$. Serum TPOAb and TgAb values were measured using an enzyme-linked immunosorbent assay (Roche Diagnostics) with a normal range of $<16.0 \text{ IU/mL}$ and $<28.0 \text{ IU/mL}$, respectively. Serum anti-Müllerian hormone (AMH) values were measured using the AMH GenII enzyme-linked immunosorbent assay kit (Medical & Biological Laboratories) with the limit of quantification of 0.16 ng/mL .

Definition of pregnancy outcomes

Pregnancy was defined as the presence of a fetal sac

with an increase in serum human chorionic gonadotropin (hCG) values. Miscarriage was defined as clinical miscarriage occurring after pregnancy as defined above. Chemical pregnancy only with an increase in serum hCG levels was excluded.

Statistical analysis

Results are presented as frequencies (%) or means $\pm$ standard deviation (SD). After verification of the interaction between TA status and LT4 treatment, baseline clinical features and outcomes of patients in the four groups were compared using the χ^2 test for categorical data and two-way analysis of variance for continuous data. To elucidate factors affecting outcomes, independent variables were included in a logistic regression model. The presence of a significant difference was defined as $p < 0.05$. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL).

Results

Table 1 shows characteristics of the study subjects. Mean age was 36.5 ± 4.5 years, mean TSH was $3.33 \pm 0.55 \mu\text{IU/mL}$, and mean FT4 was $1.2 \pm 0.3 \text{ ng/dL}$. TPOAb, TgAb, or both were present in 36 patients (34.0%). Mean TSH values during the observation period in the groups without LT4 (TA–LT4–, TA+LT4–) was $3.19 \pm 0.79 \mu\text{IU/mL}$. On the other hand, that in the LT4 treatment groups (TA–LT4+, TA+LT4+) was $1.70 \pm 0.81 \mu\text{IU/mL}$ and the mean LT4 dose used was $41.5 \pm 19.3 \mu\text{g/day}$. Mean duration of infertility was 2.2 ± 2.4 years. Mean AMH concentration was $3.3 \pm 3.6 \text{ ng/mL}$. There were 56 (52.8%) patients treated with artificial reproductive technology (ART). Except for TA positivity and TA levels, there were no statistically significant differences among the four groups in characteristics including age, basal TSH value, duration of infertility, AMH concentration, and proportion of patients who underwent ART, which is closely related to infertility. Mean LT4 dose and mean TSH value during LT4 treatment were similar between the TA–LT4+ and TA+LT4+ groups.

Table 2 shows pregnancy outcomes among the four groups. First, the interaction between TA positivity and LT4 therapy status did not have a significant effect on pregnancy or miscarriage rates ($p = 0.907$ and 0.484 , respectively). The number of infertile women who became pregnant during observation period in the TA–LT4–, TA–LT4+, TA+LT4–, and TA+LT4+ groups was 15 (42.9%), 15 (42.9%), 6 (54.5%), and 13 (52.0%), respectively ($p = 0.81$). Likewise, the number of pregnant women who experienced miscarriage during observation period in each group was 3 (20.0%), 4 (26.7%), 1

Table 1 Characteristics of 106 infertile patients by presence of thyroid autoantibodies and levothyroxine treatment status

Group	Overall (n = 106)	TA-LT4- (n = 35)	TA-LT4+ (n = 35)	TA+LT4- (n = 11)	TA+LT4+ (n = 25)	<i>p</i>
Age (years)	36.5 ± 4.5	36.1 ± 4.2	37.0 ± 4.1	36.8 ± 5.0	36.1 ± 5.3	0.83
Smoker	7 (6.6%)	2	2	0	3	0.56
BMI (kg/m ²)	21.3 ± 3.5	22.0 ± 4.3	21.0 ± 3.4	21.4 ± 4.1	20.5 ± 2.2	0.43
<i>Thyroid function at first visit</i>						
TSH (μIU/mL)	3.33 ± 0.55	3.34 ± 0.57	3.35 ± 0.50	3.36 ± 0.68	3.37 ± 0.56	0.75
FT3 (pg/mL)	2.8 ± 0.4	2.9 ± 0.4	2.8 ± 0.4	2.8 ± 0.2	2.7 ± 0.4	0.07
FT4 (ng/dL)	1.2 ± 0.3	1.2 ± 0.2	1.3 ± 0.5	1.2 ± 0.1	1.1 ± 0.2	0.20
TPOAb positive	22 (20.8%)	0	0	8	14	<0.01
TPOAb (IU/mL)	27 ± 56	7 ± 2	8 ± 2	53 ± 60	68 ± 95	<0.01
TgAb positive	26 (24.5%)	0	0	5	21	<0.01
TgAb (IU/mL)	68 ± 125	11 ± 3	12 ± 4	120 ± 138	203 ± 176	<0.01
TA positive	36 (34.0%)	0	0	11	25	<0.01
TRAb (IU/L)	0.4 ± 0.2	0.4 ± 0.2	0.4 ± 0.2	0.4 ± 0.1	0.4 ± 0.2	0.66
Mean TSH value during observation (μU/mL)		3.17 ± 0.83	1.65 ± 0.91	3.25 ± 0.70	1.73 ± 0.72	<0.01
Mean LT4 dose (μg/day)	41.5 ± 19.3		40.7 ± 18.5		42.5 ± 20.6	0.93
<i>Infertility</i>						
Duration of infertility (years)	2.2 ± 2.4	2.0 ± 2.0	2.5 ± 3.0	3.2 ± 2.3	1.7 ± 1.9	0.27
Gravida	0.4 ± 0.7	0.3 ± 0.5	0.4 ± 0.7	0.5 ± 0.5	0.7 ± 1.0	0.11
Para	0.1 ± 0.3	0.1 ± 0.3	0.2 ± 0.4	0.1 ± 0.2	0.1 ± 0.3	0.42
Cause of infertility	1.7 ± 0.9	1.7 ± 1.0	1.8 ± 1.0	1.8 ± 0.9	1.4 ± 0.7	0.45
Ovarian factor	37	9	14	4	10	0.57
Uterine factor	38	11	15	5	7	0.54
Tubal factor	15	6	3	4	2	0.09
Endometriosis	23	7	10	3	3	0.45
Unexplained	22	9	6	1	6	0.60
AMH (ng/mL)	3.3 ± 3.6	3.5 ± 3.6	3.1 ± 3.3	3.4 ± 6.1	3.2 ± 2.6	0.96
<i>ART</i>						
ART (-)	50 (47.2%)	16	14	5	15	0.49
ART (+)	56 (52.8%)	19	21	6	10	0.49

Results are presented as frequencies with percentages (%) or means ± SD.

Ovarian factors include ovulation disorder and diminished ovarian reserve.

Gravida, number of past pregnancies; Para, number of past deliveries.

(16.7%), and 3 (21.4%), respectively ($p = 0.52$).

Table 3 shows characteristics among infertile women divided by the incidence of pregnancy or miscarriage. Infertile women who became pregnant were younger ($p = 0.02$), more likely to have prior pregnancies ($p = 0.03$) or a history of miscarriage ($p = 0.02$), and had higher AMH values ($p = 0.04$) than with those who did not become pregnant. Infertile women who had a miscarriage were more likely to have prior pregnancies than those who did not experience a miscarriage ($p = 0.05$).

The proportion of patients treated with LT4, mean dose of LT4, and TSH level during the observation period were similar for each pregnancy outcome.

Next, logistic regression was used to investigate variables related to pregnancy outcomes. First, univariate logistic regression analysis showed that age ($p = 0.021$; odds ratio (OR), 0.90), gravidity ($p = 0.046$; OR, 1.81) and history of miscarriage ($p = 0.030$; OR, 2.16) were associated with pregnancy (Supplemental Table 1). No variables including TSH value during the observation

Table 2 Pregnancy outcomes of 106 infertile patients by presence of thyroid autoantibodies and levothyroxine treatment status

Outcome	TA-LT4- (n = 35)	TA-LT4+ (n = 35)	TA+LT4- (n = 11)	TA+LT4+ (n = 25)	<i>p</i>
Pregnancy	15 (42.9% [†])	15 (42.9%)	6 (54.5%)	13 (52.0%)	0.81
Miscarriage	3 (20.0% ^{††})	4 (26.7%)	1 (16.7%)	3 (23.1%)	0.52

[†] Calculated by dividing the number of women who became pregnant by the total number of infertile women during observational period in each group.

^{††} Calculated by dividing the number of women who experienced a miscarriage by the number of women who became pregnant during observational period in each group.

period were associated with miscarriage. The multivariate logistic regression analysis was performed using significant variables in the univariate logistic regression analysis and presence of TAs, LT4 treatment, and ART, which are reportedly related to pregnancy outcomes. Except age ($p = 0.03$; OR, 0.90 [95% confidence interval (CI), 0.82–0.98]) and history of miscarriage ($p = 0.04$; OR, 2.15 [95% CI, 1.04–4.45]), no other variables were associated with pregnancy and no variables were associated with miscarriage.

Discussion

In this study, we retrospectively investigated pregnancy outcomes among Japanese euthyroid ($2.5 \mu\text{IU/mL} \leq \text{TSH} < \text{URL}$) infertile women categorized by the combination of TA positivity and LT4 treatment status. We found no difference in pregnancy outcomes across groups. Neither the presence of TAs nor LT4 treatment was associated with pregnancy outcomes.

Previous studies have reported the obstetric characteristics and outcomes of infertile women with $2.5 \leq \text{TSH} < 4.5 \mu\text{IU/mL}$ compared with those with $\text{TSH} < 2.5 \mu\text{IU/mL}$ [9, 10, 13–15]. Infertile women with $\text{TSH} \geq 2.5 \mu\text{IU/mL}$ had similar embryo quality as those with $\text{TSH} < 2.5 \mu\text{IU/mL}$ [14]. In addition, the rates of pregnancy, miscarriage, and live births in infertile women with $\text{TSH} \geq 2.5 \mu\text{IU/mL}$ were similar to those with $\text{TSH} < 2.5 \mu\text{IU/mL}$ [9, 10, 13, 15]. Although a few studies have reported that infertile women with $\text{TSH} \geq 2.5 \mu\text{IU/mL}$ have a lower pregnancy rate [16] and lower ovarian reserve [17] than those with $\text{TSH} < 2.5 \mu\text{IU/mL}$, the present study was not able to show the difference mentioned before, similar to most previous studies [9, 10, 13, 15].

Regarding LT4 treatment as an intervention to improve obstetric prognosis in infertile women, previous retrospective studies reported that LT4 treatment in infertile women with $\text{TSH} > 2.5 \mu\text{IU/mL}$ including subclinical hypothyroidism who underwent ART was associated with better obstetric outcomes compared to no interven-

tion [18, 19]. Two RCTs [7, 8] have reported that LT4 treatment in infertile women with subclinical hypothyroidism ($\text{TSH} \geq 4.5 \mu\text{IU/mL}$) and TAs who underwent *in vitro* fertilization (IVF) had better rates of pregnancy, miscarriage, and live birth than those who did not receive LT4 treatment. On the other hand, a RCT in Italy [11] reported that LT4 treatment in infertile women with $\text{TSH} < 2.5 \mu\text{IU/mL}$ and TAs who underwent IVF is not associated with better rates of pregnancy, miscarriage, or live birth when compared with rates in those without LT4 treatment. Another recent RCT [12] reported that LT4 treatment in 567 euthyroid infertile women with TAs who underwent IVF is not associated with better rates of pregnancy, miscarriage, or live birth when compared with those who did not receive LT4 treatment. Based on the results of these RCTs, infertile women with normal thyroid function do not have better obstetric outcomes with LT4 treatment. Our results with Japanese patients are consistent with these previous reports. In addition, our study supports that LT4 treatment is dispensable for euthyroid infertile women without TAs as with those with TAs.

Logistic regression analysis showed that ART is not significantly associated with pregnancy, which indicates that infertile women who underwent ART do not have a better pregnancy rate. These results could be due to the different characteristics between infertile women who underwent ART and those who did not. Indeed, infertile women who underwent ART were older (38.8 vs. 35.0 years; $p < 0.01$) and had lower serum AMH concentrations (1.5 vs. 3.3 ng/mL; $p < 0.01$) than those who did not. As the interactions between ART and age or AMH were not significantly associated with pregnancy rate ($p = 0.486$ and 0.751 , respectively), age was the most influential variable on pregnancy rate in the present study. Therefore, the effects of ART may be statistically underestimated in the present study.

According to the guidelines of the ATA and European Thyroid Association [4, 20], when infertile women with $2.5 \mu\text{IU/mL} \leq \text{TSH} < \text{URL}$ become pregnant, strict management of thyroid function should be considered only in

Table 3 Characteristics of 109 infertile patients by pregnancy outcome

Characteristic	Pregnancy			Miscarriage		
	(+) (<i>n</i> = 49)	(−) (<i>n</i> = 57)	<i>p</i>	(+) (<i>n</i> = 11)	(−) (<i>n</i> = 38)	<i>p</i>
Age (years)	35.4 ± 4.4	37.4 ± 4.3	0.02	36.7 ± 5.2	35.1 ± 4.2	0.31
Smoker	3	4	0.58	2	1	0.08
BMI (kg/m ²)	21.1 ± 3.0	21.4 ± 3.9	0.98	22.1 ± 2.7	20.8 ± 3.1	0.15
<i>Thyroid function at first visit</i>						
TSH (μIU/mL)	3.31 ± 0.60	3.34 ± 0.52	0.79	3.42 ± 0.50	3.29 ± 0.62	0.68
FT3 (pg/mL)	2.8 ± 0.4	2.8 ± 0.4	0.99	2.8 ± 0.4	2.9 ± 0.3	0.85
FT4 (ng/dL)	1.3 ± 0.5	1.2 ± 0.2	0.69	1.6 ± 1.0	1.2 ± 0.2	0.52
TPOAb (IU/mL)	26 ± 56	27 ± 55	0.93	39 ± 52	23 ± 58	0.11
TPOAb positive	10	12	0.56	3	7	0.26
TgAb (IU/mL)	88 ± 150	80 ± 96	0.74	96 ± 133	88 ± 154	0.81
TgAb positive	15	11	0.23	4	11	0.27
TA positive	19	17	0.22	4	15	0.49
TRAb (IU/L)	0.4 ± 0.2	0.4 ± 0.2	0.96	0.5 ± 0.2	0.4 ± 0.2	0.77
Mean TSH value during observation (μU/mL)	1.81 ± 1.02	1.90 ± 0.84	0.33	1.74 ± 0.93	1.84 ± 1.05	0.55
No. of patients treated with LT4	28	32	0.53	7	21	0.44
Mean LT4 dose (μg/day)	42.0 ± 23.8	41.0 ± 14.6	0.61	47.2 ± 18.4	40.2 ± 25.5	0.30
<i>Infertility</i>						
Duration of infertility (years)	1.8 ± 1.7	2.6 ± 2.8	0.18	2.2 ± 1.7	1.7 ± 1.8	0.28
Gravida	0.6 ± 0.8	0.3 ± 0.6	0.03	1.3 ± 0.7	1.7 ± 0.9	0.05
Para	0.1 ± 0.3	0.1 ± 0.3	0.78	1.0 ± 0.7	0.5 ± 0.8	0.58
H/O miscarriages (<i>n</i>)	0.5 ± 0.7	0.2 ± 0.5	0.02	0.2 ± 0.4	0.1 ± 0.3	0.10
Cause of infertility	1.6 ± 0.9	1.8 ± 0.9	0.24	0.7 ± 0.7	0.4 ± 0.7	0.55
Ovarian factor	14	23	0.14	3	11	0.51
Uterine factor	17	21	0.47	4	13	0.23
Tubal factor	9	6	0.49	1	8	0.47
Endometriosis	9	14	0.19	0	9	0.13
Unexplained	10	12	0.56	1	9	0.40
AMH (ng/mL)	3.7 ± 3.5	2.9 ± 3.7	0.04	2.8 ± 1.5	3.9 ± 3.7	0.41
<i>ART</i>						
ART (−)	24	26	0.44	6	18	0.74
LT4 treatment	13	16	0.77	3	10	1.00
ART (+)	25	31	0.6	5	20	0.74
LT4 treatment	15	16	0.79	4	11	0.12

Results are presented as frequencies or means ± SD.

H/O, History of

those with TAs. However, many studies of euthyroid infertile women with $2.5 \mu\text{IU/mL} \leq \text{TSH} < \text{URL}$, including this study, do not support this recommendation. Indeed, another large-scale retrospective study in 2017 that investigated the effects of LT4 treatment in 5,405

infertile women with $2.5 \leq \text{TSH} \leq 10.0 \mu\text{IU/mL}$ until mid-pregnancy on obstetric prognosis found a lower rate of pregnancy loss only in infertile women with $\text{TSH} \geq 4.1 \mu\text{IU/mL}$ [21]. The TABLET study [5] was a recent RCT involving 952 pregnant women with normal TSH

values (0.44–3.63 $\mu\text{IU/mL}$), TPO positivity, and a history of recurrent miscarriages. It investigated the effect of LT4 (50 μg per day) on the live birth rate and found that LT4 treatment does not improve the live birth rate in these patients. These data also support our finding.

The present study has several limitations. First, this was a small, retrospective study. We cannot deny the possibility that a negative finding may be due to inadequate sample size. However, this is the first report involving Japanese subjects; there are no clear guidelines regarding LT4 treatment in Japanese euthyroid infertile women with $2.5 \mu\text{IU/mL} \leq \text{TSH} < \text{URL}$ and obstetric outcomes, thus, this study provide useful information for the treatment of such women. Second, initiation of LT4 treatment was based on the clinical judgment of each treating physician. However, interactions between LT4 therapy status and other clinical variables examined did not have significant effects on pregnancy or miscarriage rates (data not shown). Thus, LT4 treatment initiation might not be biased. Third, we could not confirm serum TSH levels frequently in patients without LT4 treatment in one year. Finally, we only evaluated whether pregnancy occurred after infertility treatment within one-year observation period.

In conclusion, regardless of TA status, we were not able to demonstrate the benefits of LT4 treatment in Japanese euthyroid infertile women with $2.5 \mu\text{IU/mL} \leq \text{TSH} < \text{URL}$. Our data suggest that LT4 treatment may be dispensable for such subjects.

Acknowledgments

The authors thank the following medical institutions for providing follow-up data: Y's Ladies Clinic, Ginza Kounotori Ladies Clinic, Kato Ladies Clinic, Chiba Newtown Ladies Clinic, ART Okamoto Women's Clinic, Aida Kibo Clinic, Shimbashi YUME Clinic, Manaka Clinic, Sannoh Clinic, Motoyawata Ladies Clinic, Usui Clinic, Toyoshima Sanfujinka, Kasumizawa Sanfujinka, Kyono ART Clinic Takanawa, Takasaki ART Clinic, Tatedebari Sato Hospital, Oak Clinic for Ms. Hospital, Aiiku Hospital, Kuma Hospital, Ibaraki Seinan Medical Center Hospital, Sendai City Hospital, Tokyo-Kita Medical Center, Japanese Red Cross Musashino Hospital, Showa University Koto Toyosu Hospital, Toho University Omori Medical Center, University of Yamanashi Hospital, Tokyo Medical and Dental University Hospital.

Disclosure

The authors have no multiplicities of interest to disclose.

Supplemental Table 1 Results of univariate logistic regression analysis for pregnancy outcomes

Characteristic	Pregnancy		Miscarriage	
	<i>p</i>	OR	<i>p</i>	OR
Age	0.021	0.90	0.335	
Smoker	0.853		0.062	
BMI	0.615		0.269	
<i>Thyroid function</i>				
TSH	0.810		0.573	
FT3	0.795		0.693	
FT4	0.279		0.183	
TPOAb value	0.996		0.325	
TPOAb positive	0.935		0.296	
TgAb value	0.113		0.884	
TgAb positive	0.180		0.325	
TA positive	0.333		0.700	
TRAb value	0.177		0.574	
LT4 treatment	0.917		0.181	
TSH during observation	0.328		0.546	
<i>Infertility</i>				
Duration of infertility	0.104		0.413	
Gravida	0.046	1.81	0.130	
Para	0.781		0.325	
H/O miscarriages	0.030	2.16	0.178	
Cause of infertility	0.269		0.335	
Ovarian factor	0.206		0.727	
Uterine factor	0.818		0.499	
Tubal factor	0.253		0.540	
Endometriosis	0.442		0.999	
Unexplained	0.935		0.454	
AMH	0.314		0.372	
<i>ART</i>				
ART (+)	0.729		0.663	

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