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Original article

Thyroid-stimulating hormone (TSH) and pregnancy outcome in patients undergoing in vitro fertilization (IVF)

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Abstract

Bacjground: Subclinical hypothyroidism is related to poor outcome of pregnancy, which is reported in more recent researches. The aim of this study was to determine the correlation between pre-conception of thyroid-stimulating hormone (TSH) level and pregnancy outcomes in patients undergoing in vitro fertilization (IVF).

Method: This retrospective cohort study was done on 115 IVF candidate patients undergoing long protocol of ovulation induction that became pregnant from 2007 to 2012. Pregnancy outcomes, including abortion rate, termination age of pregnancy and birth weight in women with low pre-conception TSH (≤2.5 mIU/L) and high pre-conception TSH (>2.5 mIU/L) were compared with each other.

Results: Among 115 pregnancies, 30.2% of the women had pre-conception TSH >2.5 mIU/L. Preterm delivery (<32 weeks) was higher in patients with a pre-conception TSH >2.5 than them with a pre-conception TSH ≤2.5 (P= 0.044). There was no statistically significant difference in abortion, pregnancy termination, and birth weight between two groups.

A pre-conception thyroid-stimulating hormone level >2.5 mIU/L is associated with a lower gestational age at delivery and low birth weight in women undergoing in vitro fertilization.

Conclusion: The results of this research indicated that a pre-conception thyroid-stimulating hormone level >2.5 associated with preterm labor in women undergoing IVF therefore it is Suggested that screening for hypothyroidism before IVF could be have significant public health implications.

Key words: TSH, IVF, subclinical hypothyroidism, pregnancy

Introduction

Subclinical hypothyroidism is defined as normal levels of serum free thyroxin (T4) and a brief enhancement in serum thyroid-stimulating hormone (TSH) (1). Patients with subclinical hypothyroidism may have ambiguous and nonspecific symptoms of hypothyroidism, however, efforts to diagnose the disease based on specific symptoms associated with thyroid has not been successful (2). This disorder is

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detectable only by laboratory (3).

In a study, subclinical hypothyroidism was documented in 2.2% of pregnant women (4). Since the prevalence of subclinical hypothyroidism in infertile due to an ovulation was higher than fertile women (5), the recent researches have been shown subclinical hypothyroidism during pregnancy linked with preterm labor (< 32 weeks) (6), placenta abruption (7), and fetal death (8). Some routine therapeutic recommendations have been presented that the treatment according to levels of TSH was formerly attributed normal (9). TSH levels <5.5 mIU/L is known as normal, but the American Thyroid Association has suggested in pregnant women with TSH levels > 2.5 mIU/L, the treatment should begin with levothyroxine (9). Moreover, the prevalence of subclinical hypothyroidism has been reported high in infertile women with ovulation disorders and the women who have failed to become pregnant after IVF (5, 10). Accordingly, this study was designed to investigate pregnancy outcome in patients undergoing IVF with a TSH > 2.5 mIU/L compared with cycles with TSH ≤ 2.5 mIU/L.

Materials and Methods

In this study, 115 patients underwent ovulation induction (long protocol) of IVF with a preconception TSH ≤ 5.5 mIU/L that became pregnant at Fatemehzahra Infertility and Reproductive Health Research Center in Babol, Iran, (from December 2007 to January 2012) were participated. The subjects had a normal uterus cavity (confirmed with hysterosalpangiography) and normal prolactin levels before beginning IVF. The patients with high risk of miscarriage, age over 35 years, history of recurrent abortion, systemic diseases (diabetes, chronic hypertension, and hypothyroidism), endometriosis, and smokers were excluded. All women had an assessment of TSH serum 15 days after egg retrieval.

Controlled Ovarian Hyper stimulation (COH) which was used for all patients as follows:

Oral Contraceptive Pills (made in Iran-Hormone, Tehran) administered the cycle before treatment, and then patients received a GnRH analogue (Suprefact, 50 IU, subcutaneously, Aventis Pharma Deutschland GMBH, and Germany) from the 20th days of the previous cycle. At the 2-3th day of menstruation, Human Menopausal Gonadotropin (Merional 75 IU, intramuscularly, IBSA, Institute Biochimique, Switzerland) were started up to 3 follicles 17 mm in size which were seen in a transvaginal ultrasound. Mylab 40, Esaote, Italy Human Chorionic Gonadotropin (HCG 10000 IU, intramuscularly, Pregnyl; Darou Pakhsh, Iran) was injected 36-38 hours after HCG injection, oocytes were removed and embryos were cultured in a special environment in the lab. After 48 hours the egg retrieval, when the zygotes have divided to form 4-8cell masses, several of the embryos were transferred to the uterus. All patients used progesterone (Cyclogest suppositories 400 mg daily, inserted vaginally or rectally) until 12 weeks of gestation for luteal support. Preparations of the recipients' uterus were performed oral estrogen and progesterone. Serum ßhCG was determined 2 weeks after egg retrieval. Vaginal ultrasound was performed in our clinic at 6 weeks gestation (4 weeks after egg retrieval) and was repeated 2 weeks later. Delivery outcome was determined for each cycle by contacting the patient after the expected date of delivery.

Table1. Pregnancy outcome according to TSH level

Variables	TSH >2.5 mIU/L N=35 N(%)	TSH ≤2.5 mIU/L N=80 N(%)	P-value
Ectopic pregnancy	0 (0.0%)	3(3.8%)	0.552
Abortion	5(14.3%)	8(10%)	0.531
pregnancy termination	34. 8 ± 4.7	35.3 ± 4.1	0.584
Preterm delivery (<32 weeks)	9(30%)	9(13%)	0.044
pregnancy termination (weeks) (mean±SD)	34. 8 ± 4.7	35.3 ± 4.1	0.584

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TSH was measured before IVF treatment using the gamma method. The normal range of TSH in the method was 0.2-5.5 mIU/L. Inter-assay and intra-assay coefficients of variation were 4.1% and 2.5% for TSH, respectively. The women were classified with optimal preconception TSH (≤2.5 mIU/L) and near optimal preconception TSH (>2.5 mIU/L) (9). Then, abortion rate, premature delivery ≤32 weeks and low birth weight were compared in women with TSH ≤2.5 mIU/L vs. TSH > 2.5 mIU/L.

All analyses were performed with SPSS (version 18.0). Chi-square Test and T-Test were used. In all tests; P-value <0.05 was statistically considered significant.

Results

A total of 115 women were selected with mean age of 27.1 ± 4.9 years (range 18 to 35 years). Thirty five women (30.2%) had pre-conception TSH > 2.5 mIU/L. Preterm delivery (<32 weeks) was higher in patients with a pre-conception TSH > 2.5 than the patients with a pre-conception TSH ≤2.5 (P=0.044). The comparison between TSH > 2.5 (n=35) and TSH ≤ 2.5 (n=80) revealed no significant differences between TSH and abortion, pregnancy termination, and birth weight (Table 1).

Discussion

The main finding of this study was that in women underwent IVF, rate of preterm labor (<32 weeks) was higher in cycles with a preconception TSH >2.5 mIU/L compared with cycles with preconception TSH ≤2.5 mIU/L.

Our data was consistent with a study which found preterm labor (before 34 weeks gestation) is high in women with subclinical hypothyroidism (11). While in Stagnaro-Green research no significant associations between TSH level and preterm labor was shown; however the cutoff of TSH was selected 3 mIU/L and it was a little higher than our selected cut off (6). A possible explanation for higher preterm labor is that hypothyroidism during pregnancy could progress to more serious degree of dysfunction during pregnancy (12). Since we were not measured TSH level during pregnancy, therefore our study cannot be compared with other studies in which TSH was evaluated during pregnancy. There is also a possibility that in women with subclinical hypothyroidism, who are undergoing ovarian stimulation experience, a drop in thyroxin and a rise in TSH during ovulation induction were observed (13). Caliskan et al. reported that in women with subclinical hypothyroidism fertility rate was lower than the women without hypothyroidism disease. While, several studies revealed hypothyroidism was no associated with pregnancy rate and IVF outcome (14, 15). Baker showed that gestational age and birth weight in the women with subclinical TSH was higher than our study (10).

Conclusion

since hypothyroidism is a common problem (3), applying these simple screening programs like measurement of TSH would be useful in order to develop public health strategies for prevention of preterm labor in women undergoing IVF. Since maternal thyroid function may be important, our study was not repeated measurement of TSH level during pregnancy. Therefore, the role of TSH level is unclear and our results did not consistently agree with the hypothesis that a higher TSH is closely related with both abortion and ectopic pregnancy. A large prospective study is proposed to elucidate association between pregnancy outcome in patients undergoing IVF with a TSH >2.5 mIU/L compared with cycles with TSH ≤2.5 mIU/L.

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Conflict of interest

None declared.

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