# No association found between decreased ovarian reserve and low thyroid function

## J.H. Check, J. Stegonshek, C. Wilson

The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden, Cooper Hospital/University Medical Center, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ (USA)

#### Summary

*Purpose:* To determine if women with diminished egg reserve are more likely to have in addition diminished thyroid reserve compared to women with normal egg reserve. *Methods:* Serum thyroid stimulation hormone levels and history of thyroid hormone replacement therapy was determined according to three ranges of elevated serum follicle stimulating hormone (FSH) in donor egg recipients with diminished egg reserve, and comparisons were made to women having embryo transfers on the same day. *Results:* No difference or trends were found of diminished thyroid function in egg recipients vs controls in women aged 39 or under. *Conclusions:* Since autoimmune damage to an endocrine gland is more commonly associated with damage to other endocrine glands because of sharing of common proteins, autoantibody damage to the ovaries does not seem to be a common cause of diminished ovarian egg reserve.

Key words: Ovarian failure; Hypothyroidism; Autoimmunity.

#### Introduction

One theoretical cause of premature diminished egg reserve is autoimmune destruction of the ovaries, similar to the common cause of hypothyroidism as seen in Hashimoto's disease. Due to the existence of common proteins among various endocrine glands, autoimmune damage to the ovaries could theoretically be part of a generalized autoimmune endocrine destruction process involving multiple endocrine glands.

One study found ten cases of hypothyroidism in 119 women with normal karyotypes with premature ovarian failure [1]. The same group found a 3.2% incidence of adrenal insufficiency detected by using the commercially available assay for measuring adrenal antibodies to the 21-hydroxylase enzyme, the primary adrenal autoantigen [2].

Hypothyroidism is a common problem. Thus the question arises as to whether the aforementioned 8.4% incidence of hypothyroidism in a population of women with idiopathic diminished egg reserve is greater than what would be expected in women with normal egg reserve or not [1].

#### **Materials and Methods**

A retrospective cohort analysis was performed on donor oocyte recipients aged  $\leq 40$  years of age. Participants were divided into three groups based upon serum FSH (mIU/ml) levels: FSH 11-15, FSH 16-30, and FSH > 30. Serum thyroid stimulating hormone (TSH) levels were recorded at the time of initial visit and it was determined if they were taking any thyroid replacement therapy. Controls included all women having embryo transfers on the same day as the recipients, who were using their own eggs, and had a serum  $FSH \le 5$  mIU/ml.

A TSH level > 5 uIU/ml was considered elevated, and if a woman was currently taking thyroid hormone replacement, her TSH level was excluded in the determination of mean TSH levels.

#### Results

TSH levels according to recipient groups are given in Table 1. The ranges of day 3 serum FSH (mIU/mL) in the three groups were 6.9-15 (median 11.2), 17-28 (median 20.6), and 36.7-90 (median 50.3). The average age in the three groups were  $36.3 \pm 2.7$ ,  $32.7 \pm 2.7$ , and  $35.1 \pm 4.4$ .

No association was seen between elevated FSH and elevated TSH (Table 1). None of the recipients were receiving thyroid hormone replacement. Only two of 30 (66%) had a TSH > 5 uIU/ml.

For the controls, the average age was  $36 \pm 5$ , with 11 controls (24%) aged  $\geq 40$ . Six of the 46 controls (13%) were taking L-thyroxin, with three of the six in the age  $\geq$  40 group (thus they had a history of elevated serum TSH levels). There were three additional women with TSH > 5 uIU/ml, yielding a percentage of 19.5% (9/46) with elevated TSH levels. If one eliminates the six control women  $\geq$  age 40 there were three of 40 or 7.5% with diminished thyroid reserve.

### Discussion

These data do not support a correlation between high day 3 serum FSH levels and a high TSH level. Though the 6.6% frequency of diminished thyroid reserve is consistent with the findings of 8.4% by Kim *et al.* [1], control women with normal ovarian reserve less than age

Revised manuscript accepted for publication August 22, 2008

Table 1. — Comparison of TSH levels by FSH levels in oocyte recipients < 40 years of age.

TSH levels (uIU/ml)	Group 1 FSH $\ge 15$ (n = 11)	Group 2 FSH 16-30 (n = 8)	Group 3 FSH > 30 (n = 11)
Minimum	.77	.6	.65
Maximum	8.10	4.3	7.9
Median	1.3	1.4	2.1
Mean + SD	2.1 + 2.1	1.7 + 1.2	2.6 + 2.0
95% confidence interval for mean	(.7 - 3.5)	(.7 - 2.7)	(1.2 - 3.9)
% with elevated	9.1%	0.0%	9.1%
TSH (> 5)	(1/11)	(0/8)	(1/11)
p = NS.			

40 also had a similar frequency of 7.5%. Thus the trend for a higher incidence of diminished thyroid reserve in women with normal egg reserve seems to have been agerelated.

Specific anti-ovarian antibodies may exist, but the lack of an association with damaged thyroid glands makes autoimmune damage to the ovaries a less likely etiology for premature ovarian failure.

#### References

- Kim T.J., Anesti J.N., Flack M.R., Kimzey L.M., Defensor R.A., Nelson L.M: "Routine endocrine screening for patients with karyotypically normal premature ovarian failure". *Obstet. Gynecol.*, 1997, 89, 777.
- [2] Bakalov U.K., Vanderboof U.H., Bondy C.A., Nelson L.M.: "Adrenal antibodies detect asymptomatic auto-immune adrenal insufficiency in young women with spontaneous premature ovarian failure". *Hum. Reprod.*, 2002, *17*, 2096.

Address reprint requests to: J.H. CHECK, M.D., Ph.D. 7447 Old York Road Melrose Park, PA 19027 (USA) e-mail: laurie@ccivf.com