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**Title:**

Suppressed thyroid stimulating hormone (TSH) levels associate to decreased IVF gonadotropin dose requirements

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**Objective:**

Auto-antibodies, which act on the thyroid stimulation hormone (TSH) receptor, cause hyperthyroidism and have been identified to cross-react and adversely affect follicular stimulation hormone (FSH) receptors. Since most in vitro fertilization (IVF) regimens stimulate follicular development via the FSH receptor, we sought to determine whether hyperthyroidism patients completing cycles required lower total gonadotropin dosage.

**Materials and Methods:**

Patients whose TSH was measured within 2 weeks of the start date of their fresh IVF cycle from 2002-2015 were included. Total gonadotropin dosage (IU) was modeled by oocyte age ( binned as A <35, B [35-38), C [38-41), D [41-43) and E  $\geq$ 43) and TSH levels (binned as (0-0.5], (0.5-1], (1-2.5], (2.5-5], (5-9] and (9-23) mIU/L). Patients with TSH (1-2.5] were selected as the reference "euthyroid" group. Chi-square of ANOVA was performed.

**Results:**

Patients with TSH  $\leq$ 0.5 required lower total gonadotropin dosage on average than their euthyroid counterparts (-248.33  $\pm$ 111.46, p<0.05). Patients with TSH (0.5-1] experienced a trend toward decreased total gonadotropin needs (-126.60  $\pm$ 82.66, p=0.12). Total gonadotropin requirements in patients with TSH levels in higher categories were not significantly different after adjusting for oocyte age.

**Conclusions:**

Patients with suppressed TSH levels appear to require less total gonadotropin dose to complete an IVF cycle. This may be due in part to anti-TSH antibodies that may cross-react with the FSH



receptor. Clinicians proceeding with an IVF cycle in patients with laboratory evidence of hyperthyroidism should be aware of the possibility of decreased stimulation requirements.

| Oocyte Age | TSH (mIU/L) | n   | Total Gonadotropin Dose (IU) |          |
|------------|-------------|-----|------------------------------|----------|
|            |             |     | Mean                         | SD       |
| A          | (0,0.5]     | 30  | 1694.067                     | 919.759  |
| B          | (0,0.5]     | 15  | 2282.133                     | 1115.758 |
| C          | (0,0.5]     | 23  | 2524.522                     | 1284.576 |
| D          | (0,0.5]     | 18  | 2656.25                      | 712.2387 |
| E          | (0,0.5]     | 6   | 2762.5                       | 726.2489 |
| A          | (0.5,1]     | 47  | 1965.628                     | 961.402  |
| B          | (0.5,1]     | 47  | 2222.021                     | 1047.39  |
| C          | (0.5,1]     | 34  | 2478.618                     | 762.0587 |
| D          | (0.5,1]     | 32  | 2850                         | 929.7502 |
| E          | (0.5,1]     | 11  | 2788.636                     | 751.3624 |
| A          | (1,2.5]     | 270 | 2056.12                      | 967.9956 |
| B          | (1,2.5]     | 170 | 2404.806                     | 931.2044 |
| C          | (1,2.5]     | 188 | 2702.707                     | 928.6653 |
| D          | (1,2.5]     | 119 | 2799.634                     | 915.6454 |
| E          | (1,2.5]     | 76  | 2732.842                     | 823.6002 |
| A          | (2.5,5]     | 118 | 2004.085                     | 1033.077 |
| B          | (2.5,5]     | 88  | 2493.364                     | 1021.905 |
| C          | (2.5,5]     | 94  | 2774.41                      | 919.9409 |
| D          | (2.5,5]     | 59  | 2621.025                     | 768.5306 |
| E          | (2.5,5]     | 40  | 3082.463                     | 753.4157 |
| A          | (5,9]       | 19  | 1675.158                     | 1045.973 |
| B          | (5,9]       | 9   | 2366.056                     | 837.7642 |
| C          | (5,9]       | 9   | 3266.667                     | 701.6721 |
| D          | (5,9]       | 7   | 2694.429                     | 967.3894 |
| E          | (5,9]       | 7   | 2753.571                     | 847.1064 |
| A          | (9,Inf]     | 2   | 1434                         | 1047.932 |
| B          | (9,Inf]     | 3   | 2624.333                     | 1014.656 |
| C          | (9,Inf]     | 2   | 1762.5                       | 159.099  |
| D          | (9,Inf]     | 3   | 2675                         | 646.6259 |
| E          | (9,Inf]     | 1   | 3150                         | NA       |