

# EFFECT OF CONTROLLED OVARIAN STIMULATION ON THYROID FUNCTION IN WOMEN WITH AND WITHOUT THYROID AUTOIMMUNITY

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## Introduction

Thyroid hormone plays a crucial role in the proper functioning of the reproductive system. Alterations in thyroid physiology has been linked to reproductive dysfunctions in women including infertility. Assisted reproduction technology (ART) is widely used as the ultimate approach to treat certain causes of infertility.

The preparation for ART is the called controlled ovarian stimulation, necessary to obtain multiple cumulus oocyte complexes. Some evidence suggests that the strain on the hypothalamic-pituitary-thyroid axis put by ovarian stimulation protocols used in ART may have an impact on thyroid function and can induce changes in TSH levels due to marked changes in estradiol levels, high E2 levels stimulate TBG levels that leads to a decrease in free thyroid hormone whereas HCG stimulates the gland. It has been suggested that thyroid dysfunction as well as thyroid autoimmunity have an impact on reproductive outcome of ART.

## Aim of the Work

The aim of this study was to evaluate the effect of controlled ovarian stimulation on thyroid function in euthyroid women with and without thyroid autoimmunity.

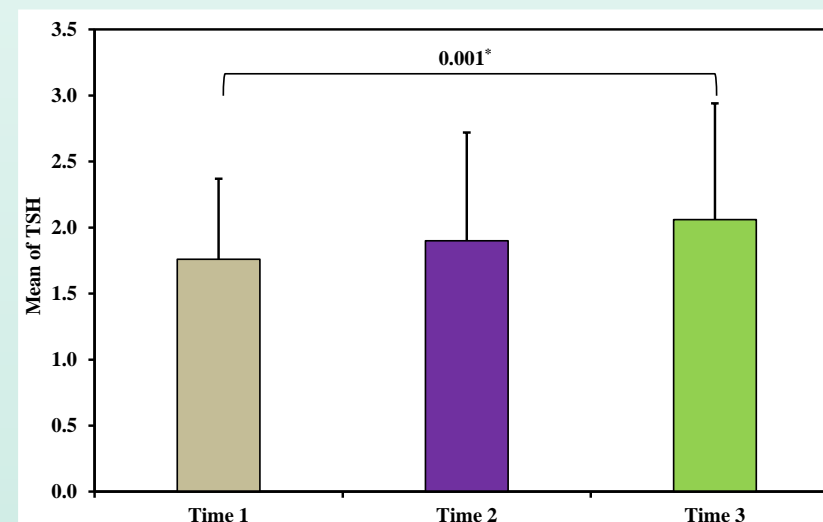
## Subjects and Methods

Eighty euthyroid infertile females scheduled for IVF/ICSI were enrolled. Thyroid profile (TSH, free T<sub>4</sub>) was tested in three different time points during OS (baseline before OS, at time of trigger with hCG and 16 days after trigger). Similar analysis was performed comparing thyroid hormone levels in women with and without thyroid autoimmunity. Thyroid autoimmunity cases were defined by having positive anti-TPO antibodies (>34IU/mL).

## Results

Mean serum levels of TSH at basal assessment (time 1), at the time of hCG administration (time 2) and at 16 days after hCG administration (time 3; time of pregnancy test) were  $1.76 \pm 0.61$ ,  $1.9 \pm 0.82$  and  $2.06 \pm 0.88$ , respectively.

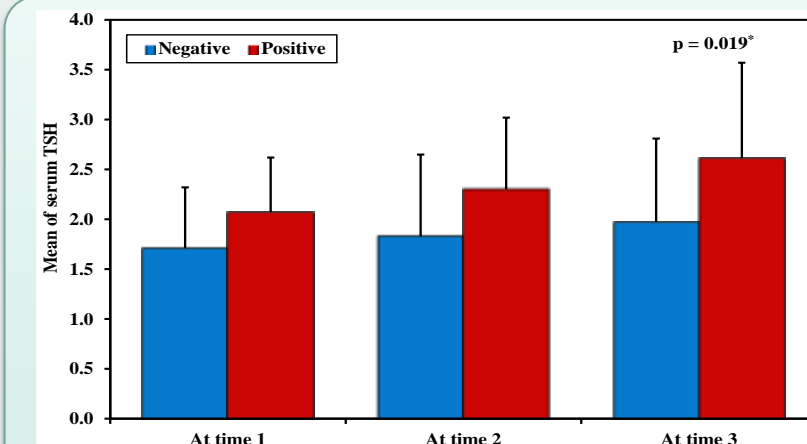
A statistically significant increase occurred between basal levels and 16 days after hCG administration (between time 1 and time 3) ( $p=0.001$ ). There was no statistically significant difference between mean TSH levels at basal assessment and time of hCG administration neither between the latter time point and 16 days after hCG administration ( $p=0.396$ ,  $0.293$  respectively).



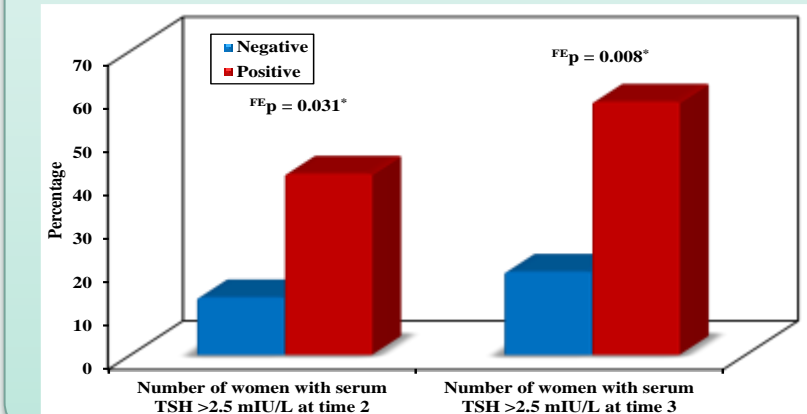
**Figure 1:** Descriptive analysis of the studied cases in all sample according to TSH in different time points during ovarian stimulation. (n = 80)

Mean TSH increased significantly at time 3 in the TAI positive group ( $P=0.019$ ).

Regarding the rate of women whose serum TSH exceeded the recommended threshold 2.5  $\mu$ IU/ml during controlled ovarian stimulation, 9 (13.2%) women of the anti-TPO negative exceeded the threshold at the time of hCG administration while there was 5 (41.7%) women of the anti-TPO positive group ( $FEp=0.031$ ). Similarly, 13 (19.1%) women of the anti-TPO negative exceeded the threshold at the time of pregnancy test while there was 7 (58.3%) women of the anti-TPO positive group ( $FEp=0.008$ ).



**Figure 2:** Comparison between Anti-TPO negative and Anti-TPO positive subgroups according to serum TSH in different time points during ovarian stimulation.



**Figure 3:** Number of women with serum TSH >2.5 mIU/L at time 2 and Number of women with serum TSH >2.5 mIU/L at time 3 and IVF outcomes in Anti-TPO positive and negative women.

## Conclusion

1. Controlled ovarian stimulation protocols used in IVF significantly impact thyroid function in euthyroid infertile females.
2. There is a trend towards a rise in TSH levels in the studied sample at different time points during OS reaching its peak value at time of pregnancy test.
3. Euthyroid patients with thyroid autoimmunity having positive anti-TPO showed higher TSH levels than anti-TPO negative group at the same time points during OS.
4. The rise in TSH levels from baseline to time of pregnancy test in TAI positive group exceeded the recommended threshold of TSH of 2.5 mIU/L before pregnancy.