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## Subclinical Hypothyroidism And Conception In A Woman With Primary Infertility.

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### ABSTRACT

Hypothyroidism is the most common endocrinological problem affecting women who present with ovulatory dysfunction resulting in infertility. Its milder form, subclinical hypothyroidism (SH) characterized by mildly elevated thyroid stimulating hormone levels and normal free thyroxine levels, may also contribute to disturbed reproductive function. We report a case highlighting the beneficial effects of levothyroxine replacement therapy in women with subclinical hypothyroidism presenting with infertility.

**Keywords:** Hypothyroidism, Conception, Infertility, Nulliparous

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## INTRODUCTION

Hypothyroidism is the most common endocrinological problem affecting women who present with ovulatory dysfunction resulting in infertility. Its milder form, subclinical hypothyroidism (SH) characterized by mildly elevated thyroid stimulating hormone (TSH) levels and normal free thyroxine (fT4) levels, may also contribute to disturbed reproductive function.[1] We report a case highlighting the beneficial effects of levothyroxine (LT4) replacement therapy in women with SH presenting with infertility.

### Case Report

A 27-year-old nulliparous woman, married for three years, was referred to our endocrinology clinic with primary infertility and regular cycles. Laboratory evaluation revealed an altered thyroid profile with an elevated Thyroid Stimulating Hormone [8.24 mIU/L (normal values in 1st trimester pregnancy = 0.2-2.5 mIU/mL)]. Work-up for male infertility was noncontributory. Other investigations were as follows: haemoglobin of 14 g/dL, fasting plasma glucose 82 mg/dL. Urine examination was normal. Ultrasonography of the pelvis showed normal uterus, ovaries and adnexa. She had no symptoms suggestive of hypothyroidism and no family history of thyroid disease. On clinical examination, she had a diffuse and firm grade II goitre. Rest of the clinical examination was normal [1,2].

Thyroid hormone profile [hypersensitive (hTSH), anti-thyroid peroxidase (Anti-TPO) and fT4] were performed using Access Immunoassay analyzer from Beckman Coulter Inc., Brea, CA. Quality control serum (Lyphocheck - Immunoassay Plus from Bio-Rad, Hercules, CA) was used to assess performance quality.

The fT4 was 1.0 ng/dL (normal 0.61-1.12 ng/dL) and anti-TPO antibody levels were greater than 500 U/ $\mu$ L. She was started on a small dose of oral LT4 (50  $\mu$ g, once daily) and monitoring of TSH with titration of LT4 dosage was carried out [3]. After two months, the TSH level was 0.81 mIU/L. She was able to conceive following 5 months of LT4 replacement therapy. A first trimester ultrasonography at 9 weeks of gestation, revealed a viable foetus of 9 weeks and 4 days. She was monitored every four weeks during the initial three months and once every two months thereafter. Throughout her pregnancy the TSH levels were maintained between 0.4 to 2.5 mIU/L. There was no change in her LT4 requirement throughout the pregnancy. She gave birth to a healthy male baby weighing 3.1 kg. She continued to receive LT4 replacement therapy in the postpartum period [4,5]

## DISCUSSION

Hypothyroidism is being increasingly recognized as a known cause of infertility. Infertility is defined by the failure to achieve a successful pregnancy after 12 months or more of regular unprotected intercourse or after 6 months for women over the age of 35 years.<sup>2</sup> Severe hypothyroidism is commonly associated with ovulatory dysfunction and, thus, with infertility. In mild hypothyroidism, ovulation and conception can occur, but the resulting pregnancies are often associated with abortions, stillbirth or prematurity.

Thyroid hormones have direct effects on granulosa cells, luteal cells and oocytes, indicating a direct interference with normal ovarian function. They play a role in the modulation of the luteinizing hormone (LH) and follicle stimulating hormone (FSH) mediated control of granulosa cell function.[6] They act as amplifiers of differentiated trophoblast function and therefore contribute to the stability of the foeto-placental unit, protecting from early loss of the conceptus.

Also, elevated thyrotropin releasing hormone (TRH) levels due to hypothyroidism are often associated with increased prolactin levels, and a delayed LH response to LH-releasing hormone (LHRH). Previous data have demonstrated that thyroid hormone replacement therapy increased the success rate of ovulation induction by clomiphene citrate in women with subclinical hypothyroidism.<sup>3</sup> Taken together, hypothyroidism may, even at an early stage, have an important impact on conception.[7]

Hypothyroidism has been suggested to jeopardize the fetoplacental unit of early pregnancy. A positive linear relationship between pregnancy loss and increased TSH values has been observed, with the incidence of child loss augmented by 60% for every doubling in TSH concentration.<sup>4</sup>

Thyroid autoimmunity (TAI) represents the most common autoimmune disorder, affecting 5%-10% of the female population of reproductive age. It is the most common aetiological factor leading to or associated with hypothyroidism (subclinical or overt).<sup>5</sup> Results from historical studies have concurred that TAI, without overt thyroid dysfunction, is associated with a three- to fivefold increase in the rate of miscarriages.<sup>6-8</sup>. Further TAI could act by delaying the occurrence of pregnancy, because of its frequent association with subfertility [6,9].

### CONCLUSION

Infertile women should be screened for hypothyroidism, as it often remains undiagnosed despite its high frequency in them.<sup>[9]</sup> As illustrated by our patient, appropriate treatment of subclinical hypothyroidism<sup>4</sup> by achieving TSH levels below the trimester specific upper limits (2.5 mIU/L in the first-trimester and 3 mIU/L thereafter) may result in conception and a normal outcome of pregnancy [9,10].

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