

## Case Report:

# Subclinical hypothyroidism and conception in a woman with primary infertility

J.V. Mascarenhas, S. Vageesh Ayyar, G. Bantwal

Department of Endocrinology, St.John's Medical College and Hospital, Bengaluru

## 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.

**Key Words:** *Subclinical hypothyroidism, Infertility, Levothyroxine therapy, Pregnancy*

Mascarenhas JV, Vageesh Ayyar S, Bantwal G. Subclinical hypothyroidism and conception in a woman with primary infertility. *J Clin Sci Res* 2012;1:94-6.

## 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. The prevalence of SH has been reported to be 0.7%-2.3% in large series of unselected infertile women.<sup>1</sup> In addition, the role of thyroid autoimmunity (with or without thyroid dysfunction) as a contributor to increased foetal wastage has been investigated earlier. Several studies have demonstrated beneficial effects of thyroxine replacement therapy in improving fertility and pregnancy outcomes in women with overt and subclinical hypothyroidism.<sup>1</sup> 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 TSH [8.24 mIU/L (normal values in 1<sup>st</sup> 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.

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. Basing on these results she was detected to have SH associated with autoimmunity. 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. 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

Received: 31 December 2011.

**Corresponding Author:** Dr S. Vageesh Ayyar, Department of Endocrinology, St.John's Medical college and Hospital, Bengaluru 560034, India. **e-mail:** vagayyar@yahoo.com

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.

### 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. 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.

Hypothyroidism has indirect effects, for instance by altering the pituitary-ovarian axis, by decreasing the binding activity of sex hormone-binding globulin (SHBG) resulting in increased serum free testosterone and oestradiol and by decreasing the metabolic clearance of androstenedione and estrone. 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.

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 five-fold increase in the rate of miscarriages.<sup>6-8</sup> Two explanations may be advocated for these associations: reduced functional reserve or an unfavorable autoimmune environment. When systematically screened in the early stages of pregnancy, 5% to 10% of women have thyroid autoantibodies with normal thyroid function. However, the parameters of thyroid function show a gradual deterioration towards subclinical hypothyroidism in a significant fraction of women with TAI.

The precise aetiology of pregnancy loss in women with TAI remains largely unknown. However, three hypotheses have been proposed, none of which are mutually exclusive.<sup>9</sup> It may be that pregnancy loss is not directly related to the presence of circulating thyroid antibodies. In this view, TAI would only represent a marker of an underlying (yet to be defined) more generalized immune imbalance that, in turn, would explain a greater rejection rate of the foetal graft. Alternatively despite apparent euthyroidism, the presence of TAI could be associated with a subtle deficiency in thyroid hormone concentrations or with a lesser ability of the thyroid economy to adapt to the necessary changes associated with the pregnant state, because of the reduced functional reserve characteristic of chronic thyroiditis. Further TAI could act by delaying the occurrence of pregnancy, because of its frequent association with subfertility. Women with thyroid antibodies tend to become

pregnant at an older age (average of 3 to 4 years later) and are therefore more prone to pregnancy loss.

Infertile women should be screened for hypothyroidism, as it often remains undiagnosed despite its high frequency in them. 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.

---

### REFERENCES

---

1. Mascarenhas JV, Anoop HS, Patil M, Kulkarni S, George B, Ananthraman et al. Improvement in fertility outcome follows initiation of thyroxine for women with subclinical hypothyroidism. *Thyroid Res Pract* 2011;8:3-6.
2. The American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss. *Fertil Steril* 2008;90:S60.
3. Maruo T, Katayama K, Barnea ER, Mochizuki M. A role for thyroid hormone in the induction of ovulation and corpus luteum function. *Horm Res* 1993;37 (Suppl 1):12-8.
4. Negro R, Mestman JH. Thyroid disease in pregnancy. *Best Pract Res Clin Endocrinol Metab* 2011;25:927-43.
5. Poppe K, Glinoe D. Thyroid autoimmunity & hypothyroidism before & during pregnancy. *Hum Reprod Update* 2003;9:149-61.
6. Vaquero E, Lazzarin CD, Valensise H, Moretti C, Ramanini C. Mild thyroid abnormalities and recurrent spontaneous abortion: diagnostic and therapeutic approach. *Am J Reprod Immunol* 2000;43:204-8.
7. Abramson J, Stagnaro-Green A. Thyroid antibodies and fetal loss: an evolving story. *Thyroid* 2001;11:57-63.
8. Glinoe D, Soto MF, Bourdoux P, Lejeune B, Delange F, Lemone M, et al. Pregnancy in patients with mild thyroid abnormalities: maternal and neonatal repercussions. *J Clin Endocrinol Metab* 1991;73:421-7.
9. Glinoe D. Thyroid disease during pregnancy. In: Baverman LE, Utiger RG, editors. *Werner & Ingbar's the thyroid: a fundamental & clinical text*. 9th edition. Philadelphia: Lippincott Williams & Wilkins; 2005.p.1087-108.