Thyroid and its indispensability in fertility

Sir,

Thyroid hormones are instrumental in reproductive physiology. In hypothyroidism, there is decreased synthesis of factors VII, VIII, IX, and XI[1] and estrogen break through bleeding secondary to anovulation, which may explain the frequent, prolonged, and heavy menstruation. Hyperthyroidism may be characterized by infrequent scanty menstruation or amenorrhea. Thyrotoxicosis (usually from Graves' disease/gestational transient thyrotoxicosis) increases the risk of spontaneous abortions and especially if on methimazole, there is an amplified risk of congenital anamolies and aplasia cutis.

In males, thyrotoxicosis causes abnormal sperm motility, while hypothyroidism may result in abnormal sperm morphology and both may cause erectile abnormalities.

Ovarian surface epithelium and oocytes of primordial, primary, and secondary follicles, endometrial stromal and Ishikawa cells feature strong immunostaining of thyroid-stimulating hormone (TSH)-Receptor, thyroid hormone receptor TRα1 and TRβ1. TSH stimulated granulosa cells show a significant increase in cAMP concentrations via

activation through TSH-receptor.[2] Thyroid dysfunction may cause short luteal phase, failure to sustain a fertilized egg, and loss of early pregnancy. More than half of hypothyroid patients have menstrual irregularities and one third of subfertile patients have thyroid disease. Pituitary hormones such as TSH, prolactin, or growth hormone act synergistically with follicle-stimulating horomone (FSH) and luteinizing hormone (LH) to usher the follicles into the growth phase. About 46.1% of infertile patients with hypothyroidism exhibit hyperprolactinemia.[3] Hyperprolactinemia from longstanding primary hypothyroidism impairs pulsatile secretion of gonadotrophin-releasing hormone (GnRH) and causes ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated to oligomenorrhea or amenorrhea and polycystic ovaries when levels are high. Thyroid supplementation restores prolactin levels and normalizes ovulatory function. Thyroid hormones are vital for the production of both estradiol and progesterone lack of which may cause infertility independent of hyperprolactinemia.

Maternal thyroid dysfunction marrs fetal neuropsychological development and increases risk of preterm delivery, small for date offspring, fetal distress in labor, and probably gestation-induced hypertension and placental abruption. The recommended dose for iodine intake during pregnancy is increased from 200 to 250 μg/day.

A study showed that women who never achieved basal TSH <2.5 mIU/l or Thyrotropin releasing hormone-stimulated TSH <20 mIU/l had lower conception rates.[4] Women with TSH ≥2.5 mIU/l have significantly higher BMI, fasting insulin concentrations, total testosterone and free androgen indices and decreased sex hormone–binding globulin concentrations.

During super-ovulation for *in vitro* fertilization high estradiol enhances Thyroid Binding Globulin-TBG binding of thyroxine and may have effects on ovum quality, fertilization, conception, or ongoing pregnancy. Pregnancy rate and delivery rate are significantly higher in those treated with levothyroxine than placebo (35% and 10% vs 26% and 3%, respectively) and miscarriage rate is considerably lower (9% vs 13%).[5] Anti-thyroid peroxidase-TPO levels (>121 IU/mL) significantly correlate with early miscarriage (may affect post-implantation embryo development). In threatened abortions lower HCG, free T3 and free T4, but higher TSH serum concentrations are observed. In infertile women suffering from PCOS, clomiphene-resistant patients tend to have significantly more anti-TPO values compared to clomiphene and metformin responders

Thyroid function is of paramount importance in fertility and adequate screening and treatment accordingly can improve conception and delivery rates apart from overall health.

Dilip Gude
Department of Internal Medicine, AMC,
Medwin Hospital, Nampally, Hyderabad,
Andhra Pradesh, India

Address for correspondence:
Dr. Dilip Gude,
Registrar,Internal Medicine, AMC, 3rd Floor, Medwin Hospital,
Chirag Ali lane, Nampally, Hyderabad - 500 001,
Andhra Pradhesh, India.
E-mail: letsgo.dilip@gmail.com

REFERENCES

1. Poppe K, Velkeniers B, Glinoer D. The role of thyroid autoimmunity in fertility and pregnancy. Nat Clin Pract Endocrinol Metab 2008;4: 394-405.
2. Aghajanova L, Lindeberg M, Carlsson IB, Stavreus-Evers A, Zhang P, Scott JE, *et al*. Receptors for thyroid-stimulating hormone and thyroid hormones in human ovarian tissue. Reprod Biomed Online 2009;18:337-47.
3. Goswami B, Patel S, Chatterjee M, Koner BC, Saxena A. Correlation of prolactin and thyroid hormone concentration with menstrual patterns in infertile women. J Reprod Infertil 2009;10:207-13.
4. Raber W, Nowotny P, Vytiska-Binstorfer E, Vierhapper H. Thyroxine treatment modified in infertile women according to thyroxine-releasing hormone testing: 5 year follow-up of 283 women referred after exclusion of absolute causes of infertility. Hum Reprod 2003;18:707-14.
5. Rahman AH, Abbassy HA, Abbassy AA. Improved *in vitro* fertilization outcomes after treatment of subclinical hypothyroidism in infertile women. Endocr Pract 2010;16:792-7.

Access this article online	
Quick Response Code:	Website: www.jhrsonline.org
	DOI: 10.4103/0974-1208.82368