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Prevalence of Thyroid Dysfunction among Saudi Women in Early Pregnancy at King Abdulaziz University Hospital

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ABSTRACT

Introduction: *Thyroid disorders are common in pregnancy and have been linked to adverse maternal and fetal outcomes. Symptoms of thyroid disorders are sometimes mistaken for those of normal pregnancy, and so often go unnoticed. This study investigates the prevalence of thyroid dysfunction in pregnant women in a tertiary care hospital.*
Subjects and Methods: *This was a cross sectional study conducted at the largest tertiary care hospital in Jeddah, Saudi Arabia enrolling 154 first trimester pregnant Saudi women attending the Obstetrics and Gynecology clinic at King Abdulaziz University Hospital, from October to April 2015. Measurements of serum thyroid-stimulating hormone (TSH) were taken as part of the routine antenatal blood tests.*
Results: *The prevalence of hypothyroidism was 40.25% (n=62) and hyperthyroidism 0.6% (n=1) using the cutoff TSH level based on the guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy.*
Conclusion: *Prevalence of hypothyroidism was found to be high in our study and hence, antenatal thyroid screening should be judiciously offered. Routine testing with serum TSH is a sufficient and cost effective screening tool.*

Key words: *Thyroid dysfunction, first trimester, hypothyroidism, pregnancy, Saudi women*

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INTRODUCTION

Maternal thyroid function undergoes physiological changes during pregnancy and some of the most prevalent endocrine disorders seen in pregnancy are those related to thyroid dysfunction (Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, Mandel SJ, Stagnaro-Green A, 2007). Major, yet reversible changes in thyroid physiology are observed in pregnant women (Lazarus JH, 2011) The increased glomerular filtration rate which occurs in pregnancy can lead to increased losses of urinary iodine, resulting in iodine deficiency and eventually maternal goiter (Lazarus JH, 2011; Idris I, Srinivasan R, Simm A, 2005). Thyroxine-binding globulin rises because of higher estrogen levels, and thyroid-stimulating hormone (TSH) levels fall as human chorionic gonadotropin concentration rises (Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, Mandel SJ, Stagnaro-Green A, 2007; Lazarus JH, 2011; Galofre JC, Davies TF, 2009), In sum, pregnancy-induced stress on the thyroid can lead to hypothyroidism in women with inadequate thyroidal iodine reserve or iodine deficiency.

It is not until the end of the first trimester that the developing fetus starts synthesizing thyroid hormones, so it is dependent on the maternal thyroid hormone supply for the development of its organs and the central nervous system as well as general growth (Fitzpatrick DL, Russell MA, 2010; Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al, 2011). Adverse outcomes including attention deficit and hyperactivity disorder have been observed in children born to mothers with hypothyroidism (Ghassabian A, Bongers-Schokking JJ, de Rijke YB, van Mil N, Jaddoe VW, de Muinck Keizer-Schrama SM, et al, 2012; Männistö T, Vääräsmäki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, et al, 2009).

Normal thyroid hormones levels are key to maintaining a normal pregnancy until delivery (Choksi NY, Jahnke GD, St Hilaire C, Shelby M, 2003). Research points to an association between maternal hypothyroidism and higher risks of miscarriages, stillbirths, premature births, and pregnancy-induced hypertension (Montoro MN ,1977; Davis LE, Leveno KJ, Cunningham EG, 1988; Smallridge RC, Ladenson PW,2001; Wasserstrum N, Anania CA, 1995; Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG, 2005). Conversely, researchers have observed improved pregnancy outcomes in women who have been treated for hypothyroidism (Alexander EK, Marqusee E, Lawrence J, Jarolim P, Fischer GA, Larsen P, 2004). Elevated maternal thyroid hormone levels are also associated with adverse effects such as an increased risk of low birth weight, neonatal morbidity and mortality (Medici M, Timmermans S, Visser W, Timmermans H, Bongers-Schokking JJ, et al, 2013).

Diagnosing women with thyroid dysfunction early in pregnancy allows early treatment and thus reduces the risk of adverse maternal and fetal outcomes (Ozdemir H, Akman I,

Coskun S, Demirel U, Turan S, Bereket A, Bilgen H, Ozek E, 2013). While there is still some debate as to the most appropriate screening test for thyroid disorders in early pregnancy, most research suggests using TSH as the preliminary test, because this hormone is a more sensitive indicator of thyroid function than FT4 and takes into consideration the log-linear TSH-FT4 relationship (Ladenson PW, Singer PA, Ain KB, et al, 2000; Dashe JS, Casey BM, Wells CE, McIntire DD, Byrd EW, Leveno KJ, Cunningham FG, 2005; Dashe JS, Casey BM, Wells CE, McIntire DD, Byrd EW, Leveno KJ, Cunningham FG, 2005). According to the Western literature, hypothyroidism in pregnancy is more prevalent than hyperthyroidism (2.5% vs. 0.2%, respectively) (LeBeau SO, Mandel SJ, 2006). There are only a few reports of the prevalence of pregnancy-related hypothyroidism in the Saudi context (Taha I, Alhazmi J, 2011; Refaat B, 2014). To provide more data on pregnancy-related thyroid disorders in Saudi Arabia, the current study aims to find the prevalence of hypothyroidism in Saudi women in their first trimester of pregnancy.

SUBJECTS AND METHODS

This cross-sectional study was carried out at King Abdulaziz University Hospital (KAUH), the largest tertiary care center in Jeddah, Saudi Arabia. It included 154 first-trimester pregnant Saudi women attending the Obstetrics and Gynecology clinic between October and April 2015. Approval for the study was granted by the Biomedical Committee at the Faculty of Medicine, King Abdulaziz University.

The sample size was based on the number of patients who met the inclusion criteria during the study period. Saudi women with singleton pregnancies, in the first trimester (6-13 weeks) and with a viable fetus were selected for inclusion. Women with a history of complicated or multiple pregnancies, thyroid diseases, treatment with anti-thyroid drugs, family history of thyroid disorders, and medical conditions like hypertension, diabetes mellitus, renal and other autoimmune diseases were excluded from the study.

All the women were informed about the nature of the study and anyone who did not agree to participate was excluded. Socio demographic and medical information was obtained from each participant. Additionally, each subject underwent a complete physical examination including abdominal ultrasound to confirm gestational age and normality of pregnancy. At their first antenatal visit as part of routine laboratory workup, all the participants were screened for thyroid function by measuring TSH levels.

In the KAUH laboratory, TSH assay was performed using the electro-chemiluminescence immunoassay (ECLIA) on Cobas e411 (Roche Diagnostics International Ltd, Switzerland) according to the manufacture protocol. The normal range according to the manufacturer for TSH was 0.27-4.20 μIU/mL and the detection sensitivity was 0.005 μIU/mL. The intra and interassay coefficient of variation for TSH was 1.4% and 3.4%, respectively.

Thyroid dysfunction was classified according to the guidelines set out by the American Thyroid Association (ATA) for diagnosing and managing thyroid disease during pregnancy (Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al, 2011).

- Hypothyroidism: TSH <2.5 μIU/mL
- Hyperthyroidism: TSH ≤ 0.03 μIU/mL

All the subjects with abnormal TSH were requested to come for follow-up for further testing at the endocrine clinic at KAUH. A written informed consent was obtained from all the participants who agreed to participate.

Statistical presentation and analysis of the present data was conducted, using SPSS version 20.0 SPSS Inc., Chicago, IL, USA). Continuous variables were analyzed as mean values ± standard deviation (SD). Percentages were calculated for categorical data.

RESULTS

Characteristics of the study population are given in Table 1. The mean maternal age of the study population ranged from 17-39 years with mean ± SD (24.4 ± 3.6). Sixty-three (40.9%) were nulliparous and 91 (59.09) were multiparous. The mean gestational age was 10.9 ± 2.0 weeks.

Variable	Mean±SD
Age (years)	24.4 ± 3.6
BMI (kg/m^2)	25.48 ± 5.36
GA (weeks)	10.92 ± 2.02

BMI: body mass index; GA: gestational age

Following trimester specific cutoffs of <2.5 μIU/mL for the first trimester as suggested by the ATA (Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al, 2011), we found 40.3% (n=62) of pregnant women to have hypothyroidism in the first trimester (Table 2). Hyperthyroidism was detected in one (0.6%) of the participants.

Variable	N (%)
TSH < 2.5 μIU/mL	62 (40.25)
TSH ≤ 0.03 μIU/mL	1 (0.6)

DISCUSSION

Thyroid disorders are common, and their prevalence rises in pregnancy (Karakosta P, Chatzi L, Bagkeris E, Daraki V, Alegakis D, Castanas E et al, 2011; Moleti M, Trimarchi F, Vermiglio F, 2014). According to research by Casey et al., hypothyroidism during early pregnancy affects about 2.5% of pregnant women (Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG, 2005; Casey BM, Dashe JS, Sponge CY, McIntire DD, Leveno KJ, Cunningham GF, 2007). Similar figures were reported several studies (Männistö T, Vääräsmäki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, et al, 2009; Allan WC, Haddow JE, Palomaki GE, Williams JR, Mitchell ML, Hermos RJ, et al, 2000; Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchison S, et al, 2007). These studies suggesting thyroid disorders are a common problem in

pregnancy, in contrast with Gillett's position that routine screening for thyroid function is not necessary in pregnant women, unless they have increased risk factors for thyroid disease (Gillett M, 2004).

This study aimed to evaluate thyroid function during the first trimester of pregnancy in Saudi women living in the Jeddah area. The major finding is that 40.3% of pregnant women attending KAUH have hypothyroidism.

The prevalence of hypothyroidism in various countries has been reported in recent years (Qian W, Zhang L, Han M, Khor S, Tao J, Song M, et al, 2013; Habimana L, Twite KE, Daumerie C, Wallemacq P, Donnen P, Kalenga MK, et al, 2014; Moreno-Reyes R, Glinoer D, Van Oyen H, Vandevijvere S, 2013). Results of the present study are fairly consistent with recently reported figures from Saudi Arabia. In their hospital-based study of 936 pregnant women (12-30 weeks of gestation) in the Madinah region, Taha et al. observed hypothyroidism in 24.2% of the women (Taha I, Alhazmi J, 2011), Refaat (2014) reported hypothyroidism in 32.4% of 162 pregnant women (4-12 weeks of gestation) in Makkah. While somewhat higher, our results are consistent with these Saudi studies, suggesting a high prevalence of hypothyroidism in pregnant Saudi women. A large study carried out in Delhi, India reported a 14.3% prevalence of hypothyroidism in women in their first trimester (Dhanwal DK, Prasad S, Agarwal AK, Dixit V, Banerjee AK, 2013). A smaller scale study conducted in Hyderabad, India on 163 non pregnant women with repeated pregnancy loss occurring up to 12 weeks of gestation found 4.12% prevalence of hypothyroidism in these women (Rao VR, Lakshmi A, Sadhnani MD, 2008). Similarly, a large-scale study in the US found hypothyroidism to be present in 15.5% of the more than 500,000 pregnant women included in the study (Blatt AJ,

Nakamoto JM, Kaufman HW, 2012). The study demonstrates that hypothyroidism has a statistically significant relationship

with recurrent pregnancy loss in the first trimester. However, another US-based study found hypothyroidism in only 2.2% of the pregnant women, in both their first and second trimesters, with no association with adverse outcomes (Cleary-Goldman J, Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, et al, 2008).

Hypothyroidism in early pregnancy has been linked to various outcomes during pregnancy including recurrent pregnancy loss, preeclampsia, premature birth, and increased fetal mortality and has also been associated with later problems in children such as impaired neuropsychological development (Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al, 2011; Männistö T, Vääräsmäki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, et al, 2009; Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchison S, et al, 2007; Rao VR, Lakshmi A, Sadhnani MD, 2008; Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell ML, Hermos RJ, Wasisbern SE, Faix JD, Klein RZ, 1999; Pop VJ, Brouwers EP, Vader HL, Vulsma T, van Baar AL, de Vijlder JJ, 2003).

The thyroid gland and thyroid function come under increased stress during pregnancy, when physiological changes stimulate increased production of thyroid hormones to meet the needs of the mother and fetus. There is still some debate about the most appropriate method of initial screening for thyroid dysfunction in pregnancy. However, the consensus is that TSH is the best marker in initial tests (Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchison S, et al, 2007; Cleary-Goldman J, Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, et al, 2008; Makedou K, Giomisi A, Mouzaki M, Slavakis A, Kalogiannidis L, et al, 2010; Pop VJ, Brouwers EP, Vader HL, Vulsma T, van Baar AL, de Vijlder JJ, 2003).

The adverse outcomes associated with hypothyroidism in pregnancy tend to be seen when using a threshold of TSH levels greater than 2.5 mIU/L in the first trimester instead of a TSH reference range based on cutoff values derived from apparently euthyroid pregnant women. The ATA gives >2.5 μIU/ml as the recommended cutoff point for diagnosis of hypothyroidism during the first trimester. The high prevalence of gestational hypothyroidism in Saudi Arabia could be considered a major public health burden. Debate on the need for universal screening for hypothyroidism in early pregnancy is ongoing. (Vila L, Velasco I, González S, Morales F, Sánchez E, Torrejón S, et al, 2013). In its recent guidelines, the ATA has withheld recommendations for the universal screening of pregnant women for hypothyroidism, citing lack of evidence (Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al, 2011).

Hyperthyroidism has a much lower prevalence than hypothyroidism, occurring in only 0.5-2/1000 pregnancies (Price A, Obel O, Cresswell J, Catch I, Rutter S, Barik S, et al, 2001). If left untreated, pregnant women with hyperthyroidism have a significantly higher risk of obstetric complications including preeclampsia, preterm labor, low birth weight, fetal and perinatal mortality (Price A, Obel O, Cresswell J, Catch I, Rutter S, Barik S, et al, 2001) In the current study, newly diagnosed hyperthyroidism was seen in one participant (0.6%). This high prevalence of hyperthyroidism in our study population could be explained by a possible population-specific elevated sensitivity of the thyroid gland to thyrotrophic molecules like HCG, resulting in gestational toxicosis. Price et al. reported similar differences between Asian and western Caucasian women in their study comparing thyroid function tests in both pregnant and non-pregnant women.

The strong point of this study is that we have included only healthy pregnant women with no past or present history of thyroid diseases in this study and all samples were analyzed in one laboratory. However, there are a few limitations of this study, which are the small sample size and being confined to only one hospital, which underestimate over all prevalence in the Saudi pregnant women population.

This study suggests that hypothyroidism is more common in Saudi pregnant women in the Western Province of Saudi Arabia than it is in other countries. Given the negative maternal and fetal outcomes associated with maternal thyroid dysfunction, it is crucial that abnormal thyroid status be detected early and treatment started promptly. Therefore, screening pregnant women for maternal thyroid dysfunction as early as possible should be considered, particularly in a country like Saudi Arabia, which has a high prevalence of undiagnosed thyroid dysfunction. This study supports the use of TSH as a marker for pregnancy-induced hypothyroidism, but additional research on TSH during pregnancy without evidence of autoimmune thyroid disease is required to develop trimester-specific TSH reference ranges in the Saudi population. Further studies should be conducted to investigate the impact of gestational thyroid disorders in the Saudi population.

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