

Awareness of the Proper Diagnosis and Management of Thyroid Disorders during Pregnancy among Practitioners in the Medina Region of Saudi Arabia

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Abstract;

Background;Thyroid disease is the second most common endocrine disorder affecting women of reproductive age after diabetes , hypothyroidism being the most common thyroid problem that might face physicians caring for pregnant women in Saudi Arabia .

Objective;To determine the knowledge and practices of physicians dealing with pregnant women sufferingthyroid illness in Madina region.

Methods; A crosssectional study that included 60 physicians from different disciplines in medina . General physicians working in primary health care facilities, endocrinologists and obstetricians were invited through a whats-up link to fill an electronic Multiple Choice Questionnaire (MCQ) .It consisted of 25 questions that were based on the latest American Thyroid Association for Clinical Endocrinologists (AACE) guide lines in diagnosis and management of thyroid illnesses during pregnancy . knowledge assessmentwas based on the percentage of the rightly answered questions . Statistical analyses were conducted using SPSS version 16.0 . Participants' characteristics were compared, using independent t test and Chi square test.

Results: 13.3% of the participants hadagood knowledge and practice, while 56.7% hadan average and safe level of knowledge and practice . 30.0% of the included physicians were found to have poor knowledge and need to improve their practice ofmanaging the pregnant women with thyroid illness. The Highest scoreswere related to knowledge about thyroid screening during pregnancy and adjustment of levothyroxine dose once hypothyroid patient gotpregnant. The lowest scores wererelated to knowledge about thyroid hormone physiology during pregnancy ,Target TSH level , Iodine requirement and managing pregnant patient with Graves diseases or thyroid cancer.

Conclusion: A welldesigned comprehensive education program should be delivered to all physicians caring for pregnant women focusing on the target thyroid function test during pregnancy , iodine replacement and timely referral tospecialized endocrinologist .

Key words; Thyroid illness , Pregnancy , Physician awareness , Iodine requirement ¹Department of Medicine, Taibah University / Madinah / Saudi Arabia

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I. Background

Thyroid disease is the secondmost common endocrine disorder affecting women of reproductive age afterdiabetes. (1) Thyroid diseases affect up to 5% of all pregnancies. (2) Thyroidillnesses during in pregnancy results in adverse outcomes for both the mother and the baby, and adequate treatment can reduce these risks; potential problems include pre-eclampsia, prematurity, and congenital abnormality (3) .Pregnancy has a significant effectson thyroidhormones physiology (4) . There is increased synthesis of thyroxinebinding globulin by the liver in response to high levels of estrogen which results in a high serum concentrations of total thyroxine (T4) and triiodothyronine (T3), without affecting free T4 or free T3 concentrations (4) . Placental human chorionic gonadotrophin (hCG) causes reduction in thyroidstimulating hormone (TSH)level because of its stimulatory effect on the thyroid follicular cellsthat in turn increases the secretion of thyroid hormones , and This is the reason that the reference range for TSH in pregnant women is lower than that in the non-pregnant (4). According to recent American Thyroid Association (ATA) guidelines, the recommended reference ranges for TSH are 0.1 to 2.5 mIU/L in the first trimester, 0.2 to 3.0 mIU/L in the second trimester, and 0.3 to 3.0 mIU/L in the third trimester.(4) .There is also an increased urinary clearance of iodine in pregnancy. Pregnant women living in iodinedeficient regions may develop goiter and thyroid hormonal disturbances during pregnancy. (5) . As a result thyroxine requirements are higherduring pregnancy . Overt hypothyroidism (defined as high TSH associated with low free T4) affects 0.3-0.5% of pregnant women (6). Subclinical hypothyroidism (definedas high TSH with normal free T4) affects 2-3% (6) . Chronic autoimmune

thyroiditis is the most common cause of hypothyroidism, followed by history of previous ablative radioactive iodine treatment or thyroidectomy, and drugs (6). All pregnant women with new diagnosis of overt hypothyroidism in pregnancy, full dose of levothyroxine (2µg/kg body weight) should be started immediately (7). A smaller initial dose of levothyroxine (for example, 50-75µg daily) is used for the newly diagnosed subclinical hypothyroidism. Women with pre-existing hypothyroidism need to keep TSH < 2.5 mIU/l, and once pregnancy is confirmed, levothyroxine dose should be increased by 25-30% (7). Thyroid function should be monitored at regular intervals, during pregnancy and the dose of levothyroxine should be adjusted to a serum TSH within the trimester-specific reference range (7). Following delivery, the dose of levothyroxine should be reduced to pre-pregnancy dose (7). About 10% of pregnant women are positive for thyroid peroxidase or thyroglobulin antibodies (6). In addition to an increased risk of hypothyroidism, these women also have a higher incidence of obstetric complications (6). Adequate iodine intake is essential for normal thyroid hormone synthesis and severe iodine deficiency causes endemic goitre, hypothyroidism, miscarriage, fetal mortality and cretinism (6). Recently, it has been shown that there is a risk for reduced IQ in the offspring of even mild-moderate iodine deficiency pregnant mothers (8). The recommended daily iodine intake is 250µg/day during pregnancy and breastfeeding (6). Transient gestational hyperthyroidism affects 1-3% of pregnancies and is limited to the first half of pregnancy (5). Placental hCG, that peaks at 7-11 weeks of gestation, stimulates thyroid follicular cells and is often presents with mild thyrotoxicosis (a raised serum free T4 and suppressed TSH) without evidence for thyroid autoimmunity, such as thyroid eye disease or TSH receptor antibodies (5). Women with hyperemesis gravidarum have high levels of hCG and they are at an increased risk (5). Graves' disease in pregnancy is associated with severe adverse effects for mother and fetus, and proper treatment can prevent these adverse effects (9). The thyrotoxicosis signs and symptoms may exacerbate in the first trimester but generally improves throughout the rest of the pregnancy. Radioiodine is absolutely contra-indicated in pregnancy. Thyroidectomy has a limited use as a treatment option as it is associated with an increased risk of complications in pregnant women. Therefore, anti-thyroid drugs are the mainstay of treatment of Graves' disease in during pregnancy (9). If anti-thyroid drugs are needed in the first trimester, then propylthiouracil should be used (6). If thyroid malignancy is diagnosed during the first or second trimester, thyroidectomy may be performed during the second trimester. Pregnant women without evidence of an aggressive thyroid cancer should be reassured that if surgical treatment is indicated it should be performed soon after delivery as the delay is unlikely to adversely affect their long-term prognosis (10). When thyroid malignancy is diagnosed during the third trimester, surgical treatment can be deferred until the immediate postpartum period (10).

Despite the common knowledge that proper treatment of maternal thyroid disorders is important to improve the outcome of pregnancy, methods of diagnosis and treatment of thyroid disorders in pregnancy remain controversial among physicians (11). In the Medina region healthcare system, general practitioners typically provide first-line antenatal care for women, followed by internists and obstetricians. However, despite the international agreements on benefits and importance of knowledge of evidence-based medicine, the practice of physicians regarding thyroid disorders during pregnancy has not been fully investigated (12, 13). To our knowledge, the present study is the first to address the awareness of internists, obstetricians/gynecologists, and general practitioners regarding the diagnosis and management of thyroid disorders in pregnant women in Saudi Arabia. The aim was to determine the overall level of awareness and areas of knowledge that require improvement in order to design an education program for these physicians focused on their particular areas of deficiency.

II. Subjects and methods

This cross-sectional study included physicians from all disciplines responsible for the care of pregnant women in Medina. General physicians working in primary healthcare facilities, endocrinologists, and obstetricians were all invited through a WhatsApp link to complete an electronic multiple choice questionnaire. The first section of this survey aimed to determine demographic characteristics of participants; the second section was designed to test basic knowledge regarding changes in thyroid hormones during pregnancy, their impact, and iodine requirement; the third section tested the awareness of causes of thyroid dysfunction and complications related to pregnancy; the fourth section tested the physicians' knowledge regarding differences in laboratory reference ranges of thyroid hormones during each trimester and diagnosis of thyroid dysfunction; and the fifth section addressed the management of thyroid disorders during pregnancy (Table 1).

The questionnaire was confirmed by 3 experts in the management of thyroid disorders during pregnancy. Good knowledge was defined as a score of ≥80% (percentage of correctly answered questions in sections 2-5), average knowledge as a score of 50%-79%, and poor knowledge as a score of <50%. The intraclass correlation coefficient was calculated to test the reliability of the questionnaire. Statistical analyses were conducted using SPSS version 16.0 (Chicago, IL, USA), and $P < 0.05$ was considered to represent statistical

significance. The mean (SD) and frequency (%) of characteristics of participants were compared using independent *t*-test and chi-square test.

III. Results

Sixty physicians [10 males (16.7%) and 50 females (83.3%)] completed the survey, of whom 11 were interns, 12 were obstetricians, and 37 were general practitioners. Majority (47; 78.3%) of participants were working in governmental hospitals or primary healthcare centers, and 31 (51.7%) had ≥ 10 years of experience. In general, physicians had sufficient knowledge about thyroid disorders during pregnancy. Eight (13.3%) participants demonstrated good knowledge and practice, 34 (56.7%) demonstrated an average but safe level of knowledge and practice, and 18 (30.0%) demonstrated poor knowledge and, therefore, needed to improve their management of pregnant women with thyroid disorders. Table 2 presents details of the characteristics of participants on the basis of their knowledge of thyroid disorders during pregnancy.

The mean knowledge score for interns was 73.1 ± 21.9 , and 81.9% of them demonstrated sufficient knowledge; that of obstetricians was 64.0 ± 7.6 , and 100% demonstrated sufficient knowledge; whereas that of general practitioners was 54.2 ± 17.6 , and 70% demonstrated a sufficient level of knowledge to permit safe practice, whereas internists had significantly the best knowledge and practice ($P = 0.0002$) over all groups. With regard to clinical rank, there was a significant difference in knowledge and practice between residents, specialists and consultants in the favors of consultants p value 0.001. There was no significant differences in regards to the duration of clinical experience, P value 0.942. The Highest scores were related to question number 9, 10 and 19 which inquired about thyroid screening during pregnancy and adjustment of levothyroxine dose once hypothyroid patient got pregnant. The lowest scores in our study were related to the questions 3, 4, 5, 8, 13, 23 and 25 that were addressing the basic knowledge about thyroid hormone physiology during pregnancy, Target TSH level, daily Iodine requirement and managing pregnant patient with Graves diseases or thyroid cancer (table 1).

IV. Discussion

The present study assessed the knowledge and practice of 3 groups of physicians caring for pregnant women in different aspects of thyroid function and disorders during pregnancy. By using a 25 question survey, we found that 13.3% of the studied physicians had a good knowledge and practice, while 56.7% of them had an average and safe level and 30.0% were found to have poor knowledge and need to improve their practice in managing a pregnant patient with thyroid illness. The observation that the highest scores were related to the knowledge about thyroid screening during pregnancy and adjustment of levothyroxine dose once hypothyroid patient got pregnant might be a reflection of Hypothyroidism being the most common thyroid problem that might face those physicians, as (9.3%) of pregnant Saudi women have overt hypothyroidism, and (14.9%) subclinical hypothyroidism during pregnancy (14). Our results are in agreement with FVaidya *et al* 2012 (15) who found that for a pregnant woman with newly diagnosed overt hypothyroidism, most responders initiated a full dose of l-thyroxine and for a woman with hypothyroidism planning pregnancy, 50% recommended increasing the dose of levothyroxine as soon as pregnancy is confirmed. The lowest scores in our study were related to the basic knowledge about thyroid hormone physiology during pregnancy, daily Iodine requirement and managing pregnant patient with Graves diseases or thyroid cancer. These data are similar to those reported by Sahar Askarie *et al* 2017 (13). Azizi *et al* similarly found great variance among physicians particularly in diagnosing, following up and treating thyrotoxicosis and thyroid nodules during pregnancy and poor compliance with the guidelines (16). Another study in agreement to the poor knowledge and attitude toward managing graves diseases and thyrotoxicosis is the study reported by Poppe K *et al* (17). They found that for a woman with newly diagnosed GD during pregnancy, only 53% of the physicians would treat with propylthiouracil, while 12% with methimazole, and 34% with propylthiouracil initially and switch to methimazole after the first trimester. Responders' opinions about the target of the thyroid test were inconsistent. Regarding Iodine requirement, our study showed poor knowledge and practice about describing iodine replacement for pregnant women, only 36.6% of them believed that Iodine replacement is indicated for pregnant women and they knew the dose. Similar to our finding is the study done by Furthermore, Kut *et al*. 67.1% of the included 322 clinicians believed that iodine supplementation is unnecessary for pregnant women (18). The available data on routine clinical diagnosis and management of thyroid disorders during pregnancy have revealed great variations in daily practice of European physicians mostly among internists and endocrinologists (19, 20). Same variations were also reported among Asian physicians as well (21, 22). Several studies showed no adherence to guide lines published by international associations (23).

Our data revealed better knowledge and practice among internists and obstetricians than general practitioners. Though more pregnant women are usually managed by general practitioners working in primary health care centers. Our observation is consistent with that of Rinaldi *et al* (24) as they found a suboptimal level of knowledge regarding thyroid diseases during pregnancy among family practitioner and they advised to deliver a comprehensive educational program for these physicians.

V. Conclusion & Recommendations

There is a variation of knowledge and management of thyroid illnesses in pregnant women in Madina region . There is a need for A well designed comprehensive education program that should be delivered to all physicians caring for pregnant women focusing on the target Thyroid function Test during pregnancy , iodine replacement and timely referral to specialized internist or endocrinologist.

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Table 1 :information’s revealed through questions ;

The questions headings addressed ;	n and % of The right answers
1) Thyroid gland size in pregnancy	n(38) 63.3%
2) Production of thyroid hormones; T3 and T4 during pregnancy	n(32) 53.3%
3) Placental human chorionic gonadotropin (HCG)	n(16) 26.67%
4) Thyroid peroxidase(TPO) or thyroglobulin (TG) in the first trimester of pregnancy ;	n (22) 36.67%
5) causes of overt hypothyroidism .	n(24) 40%
6) Neonatal complications if uncontrolled maternal hypothyroidism	n(36) 60%
7) Pregnancy complications if untreated hypothyroid mother include	n(42) 70%
8) The recommended daily Iodine requirement	n(22) 36.67%
9) Indications for Thyroid Testing in Pregnancy	n(50) 83.3
10) routine screening of pregnant women for thyroid diseases	n(54) 90%
11) Euthyroid pregnant women with positive thyroid antibodies	n(42) 70%
12) laboratory thyroid hormones referenc ranges	n(36) 60%
13) Pregnant women with aTSH level > 2.5 mmol/dl	n(18) 30%
14) Monitoring of TSH every 4 weeks until the second trimester and at least once around 30 weeks of gestation	42, 70%
15) TSH level (less than pregnancy adjusted laboratory reference range) in the first trimester of pregnancy	44, 73.3%
16) Pregnant woman with thyrotoxicosis on treatment	n(42) 70%
17) thyroid nodules diagnosed during pregnancy	n (38) 63.3%
18) Hyper emesis gravidarum and Post partum depression as an indication to request thyroid function test .	n(46) 76.67%
19) levothyroxine dose adjustment for hypothyroid patient on pre pregnancy levothyroxine treatment	n(50) 83.3%
20) Following the hypothyroid pregnant woman on treatment	n(46) 76.67%
21) levothyroxine dose adjustment Following delivery	n(44) 73.33%
22) Treatment if thyrotoxic woman got pregnant while was on METHYMAZOLE	n(40) 66.67%
23) Pregnant patients with Graves Disease	n(16) 26.67%
24) following up of pregnant thyrotoxic women who are being treated	n(32) 60%
25) Management of women diagnosed with thyroid cancer during pregnancy	n(22,) 36.67%

Table 2.Characteristics of participating clinicians classified on the basis of their knowledge of thyroid disorders during pregnancy

Variables	Good knowledge (>80/100%) (n=8)	Average knowledge <80-50/100% (n=34)	Poor knowledge <50/100% (n=18)	Mean	Std deviation	Median	Minimum	Maximum
Specialty								
Intern (11)	45.5% (5)	36.4% (4)	18.2 % (2)	73.09	21.916	72	36	96
Obstetrician (12)	0% (0)	100% (12)	0% (0)	64.00	7.628	60	56	76
General practitioner (37)	8.1% (3)	48.6% (18)	43.2% (16)	54.16	16.182	56.00	28	88
Total	13.3% (8)	56.7% (34)	30% (18)	59.60	17.563	60.00	28	96
Pvalue	0.0002 significant			0.004 significant	Kruskal–Wallis Test			
Clinical position								
Resident (10)	0.0% (0)	60% (6)	40% (4)	52.8	15.411	56.00	28	72
Specialist (22)	0% (0)	45.5% (10)	54.4% (12)	51.27	15.301	48.00	32	76
Consultant (28)	28.6% (8)	64.3 % (18)	7.1% (2)	68.57	15.989	64.00	40	96
Total	13.3 % (8)	56.7% (18)	30.0 % (18)	59.60	17.563	60.00	28	96

P value	0.001, significant			0.003, significant	Kruskal–Wallis test			
Experience (years)								
≤5 years (12)	16.7% (2)	50% (6)	33.3% (12)	60.7	19.805	64.00	28	88
6–10 years (17)	11.8% (9)	52.9% (9)	35.3% (17)	58.82	17.191	56.00	36	92
>10 years (31)	12.9% (4)	61.3% (19)	25.8% (31)	59.61	17.446	60.00	32	96
Total	13.3% (8)	56.7% (34)	30.0% (18)	59.60	17.563	60.00	28	96
Pvalue	0.942, non-significant			0.860, non-significant	Kruskal–Wallis Test			

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