SCREENING AND MANAGEMENT OF HYPOTHYROIDISM IN PREGNANCY: A CROSS-SECTIONAL SURVEY

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ABSTRACT

Background: To study prevalent current practice of our clinicians related to the treatment of both overt and subclinical hypothyroidism during pregnancy in Kurdistan region, Iraq.

Materials and methods: In June 2020, we sent an electronic questionnaire on current practice relating to management of hypothyroidism in pregnancy to 213 clinicians of the three governorates of Kurdistan region, Iraq including Duhok, Sulmani, and Erbil who are managing pregnant patients with thyroid disease. Subsequently, we have analyzed responses from physician members.

Results: 194 of responders represent clinicians from three governorates of Kurdistan region, Iraq were involved in this survey. With regard to screening , 76 (39%) of all the responders screened all pregnant females for the presence of thyroid gland dysfunction, and the remaining 119 (61%), consisting majority of responders, did not carry out any systemic screening for the thyroid dysfunction in pregnant females. For women with known hypothyroidism, 36.9% of responders only would recommend TSH level less than 2.5mIU/L as a best target for diagnosing hypothyroidism in first trimester of pregnancy. Regarding monitoring of the treatment of hypothyroidism in pregnancy, a minority of responders 27.2% suggested doing TSH as monitoring tool.

Conclusion: Deficiencies in diagnosis and management of hypothyroidism during pregnancy were observed in our survey, highlighting the need for improvement of specialist education and quality of care offered to patients with thyroid disease during pregnancy in Kurdistan region, Iraq.

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Keywords: hypothyroidism, pregnancy, clinical practice.

Thyroid dysfunction is the second most common endocrine disease affecting female of reproductive age with the prevalence rate of overt hypothyroidism was (0.3% to 0.5%) and subclinical hypothyroidism was (2% to 3%)[1,2,3,4]. However, other study showed a higher prevalence rate of hypothyroidism up to 12.3% as it affected by many factors[5]. Overt hypothyroidism and, to some extent, subclinical hypothyroidism are associated with multiple adverse outcomes for the mother and fetus, including preterm delivery, gestational diabetes, gestational hypertension, spontaneous abortion, fetal growth

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retardation, impaired neuropsychological development with decrease IQ in the offspring[8,9]. In 2011 and 2012; two guidelines including Endocrine Society Guideline and American Thyroid Association guideline for treatment of thyroid diseases in pregnancy including overt and subclinical hypothyroidism were published[10,11]. However, in our locality, it remains uncertain to what extend our clinicians follow these guidelines in their clinical practice. Therefore, this study was carried out to study the prevalent current practice of our clinicians related to the treatment of both overt and subclinical hypothyroidism during pregnancy in Kurdistan region, Iraq.

SUBJECTS AND METHODS

In 2020 and with a continuation of two months (1st June to 30th July), an electronic questionnaire survey on current practice concerning the management of hypothyroidism in pregnancy was sent through e-mail to 213 clinicians. Thirteen of them were apologized to complete the survey. The remaining clinicians 200 have completed the survey and were of different specialty (endocrinologist, general internist, obstetricians, Family medicine, general practitioners), from different cities (Duhok, Sulmani, Erbil) and they worked in different hospitals in Kurdistan region, Iraq. The survey was based on 4 questions concerning the screening and management of hypothyroidism in pregnancy and these were based on the Endocrine Society Guideline and American Thyroid Association Guideline. Table 1.

Table 1: Shwoing the clinical questions which were asked.

Q1	Do you screen routinely all pregnant ladies for hypothyroidism?
Q2	For a known case of hypothyroidism, who she is recently pregnant and taking levothyroxine, what is your first action?
Q3	For a known case of hypothyroidism, who she is recently pregnant and taking levothyroxine, what is your TSH target in the first trimester?
Q4	For a known case of hypothyroidism, who she is recently pregnant and taking levothyroxine, how do you monitor treatment?

Then answers of the physicians were matched with the guidelines of both the Endocrine Society and American Thyroid Association concerning the management of hypothyroidism during pregnancy. Table 2.

Table 2: Showing the ideal answers according to the guidelines of the Endocrine Society Guideline and American Thyroid Association.

A1	Yes, Routine screening is indicated.
A2	Increase dose of levothyroxine.
A3	Keep the TSH less than 2.5.
A4	TSH.

Statistical analyses: The descriptive data are shown in frequencies and percentages for categorical data and mean and standard deviation for continuous data. Correlations between the variables are done using the linear regression test, P-values of less than 0.05 is considered significant. Data are analyzed using the Statistical Package for Social Sciences (SPSS 25 IBM: USA).

RESULTS:

Characteristics of responders

Two hundred and two submissions have been received from clinicians and 194 of them agreed to participate in this survey. Responses were received from clinicians of three governorates of Kurdistan region, Iraq including Duhok 64 (32%), Sulmani 53 (26.5%) and Erbil 83 (41.5%), with their mean age (40.4 ± 9.5years), females were 119 (59.5%) and males 81 (40.5%). The responders were of different specialty: endocrinologist 10 (5%), general internist 75 (37.5%), obstetricians 86 (43.0%), Family medicine 24 (12%), and general practitioners 5 (2.5 %). Table 3.

Table 3: Showing the general characteristics of the involved physicians.

Main category	Subcategories	Frequency	Percentage
Agreement for participation in the study	No	8	4.0
	Yes	194	96.0
Specialty	Endocrinologist	9	4.6
	Family medicine	26	13.3
	General Practitioner	8	4.1
	Internist	73	37.4
	Obstetrician	79	40.5
Gender	Female	111	56.9
	Male	84	43.1
Age	25-35	38	19.5
	36-45	106	54.4
	46-55	37	19.0
	56-65	13	6.7
	> 65	1	.5
City of practice	Duhok	68	34.9
	Halbja	2	1.0
	Erbil	95	48.7
	Sulaymania	30	15.4

The below is the result of questions which they were asked during our survey:

1. Do you screen routinely all pregnant ladies for hypothyroidism?

Whilst 76 (39%) of all the responders screened all pregnant females for the presence of thyroid gland dysfunction, and the remaining 119 (61%), consisting majority of responders, did not carry out any systemic screening for the thyroid dysfunction in pregnant females. Table 4.

2. For a known case of hypothyroidism, who recently become pregnant and taking levothyroxine, what is your next action?

It has been appropriately answered by 79 (40.5%) of responders, that is to increase dose of levothyroxine. While 116 (59.5%) of the responders were answered the question inappropriately.

3. The TSH target in the first trimester for a hypothyroid pregnant lady

It has been appropriately answered by 72 (36.9%) of responders which is to keep TSH recommended TSH level less than 2.5 mIU/L while the question has been answered inappropriately by 123 (63.1%) of responders. Table 4.

4. Monitoring treatment of a hypothyroid pregnant lady:

It has been appropriately answered by 53 (27.2%) of responders which is TSH. While the question has been answered inappropriately by 142 (72.8%) of responders. Table 4.

Table 4: showing the response of the physicians to the questions.

Question	Response	Frequency	Percent
Do you screen routinely all pregnant ladies for hypothyroidism?	Appropriately answered	76	39.0
	Inappropriately answered	119	61.0
For a known case of hypothyroidism, who recently become pregnant and taking levothyroxine, what is your next action?	Appropriately answered	79	40.5
	Inappropriately answered	116	59.5
The TSH target in the first trimester for a hypothyroid pregnant lady	Appropriately answered	72	36.9
	Inappropriately answered	123	63.1
Monitoring treatment of a hypothyroid pregnant lady	Appropriately answered	53	27.2
	Inappropriately answered	142	72.8

All in all, one step of management was inappropriate in 9.74% of responders, while two steps of management were inappropriate in 32.82%, the three steps of management were inappropriate in 41.03% and all steps of management were

inappropriate in 14.36% of reponders. Figure 1.

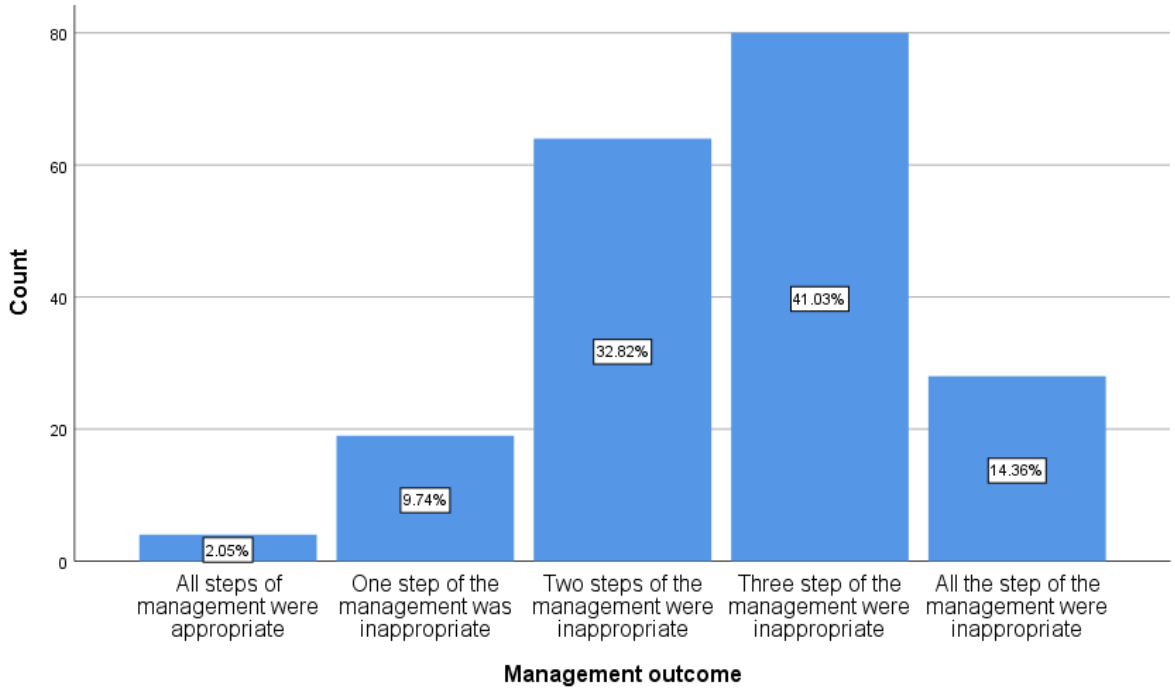

Figure 1: A simle bar chart showing the outcome of the clinicians management based on the questions asked.

Also our results show no impact of clinician's characteristics like gender, age, specialty and their cities on the management outcome Table 5. However the P value was very significant regarding our four questions which they have been asked during the survey, the routine screening of hypothyroidisim during pregnancy, the first action to do for a pregnant lady on thyroxine, the TSH target in the first trimester of pregnancy, and for monitoring of treatment during pregnancy (P value of 0.001 for the first two questions and 0.000 for the last two questions). Table 5.

Table 5: Showing the correlation between the management outcome and different clinician's charecteristics and management steps.

Category	Subcategories	Outcome of management *		Sig. (2-sided)
		Appropriate 24(12.3%)	Inappropriate 171(87.7%)	
Gender	Male	13(54.2%)	71(41.5%)	0.241**
	Female	11(45.8%)	100(58.5%)	
Age groups	25-35	3(12.5%)	35(20.5%)	0.830***
	36-45	15(62.5%)	91(53.2%)	
	46-55	5(20.8%)	32(18.7%)	
	56-65	1(4.2%)	12(7.0%)	
	> 65	0(0.0%)	1(0.6%)	
Specialty	Obstetrician	8(33.3%)	71(41.5%)	0.307***
	Internist	10(41.7%)	63(36.8%)	
	Family doctor	3(12.5%)	23(13.5%)	
	Endocrinologist	3(12.5%)	6(3.5%)	
	General practitioner	0(0.0%)	8(4.7%)	
City of practice	Duhok	14(58.3%)	54(31.6%)	0.085***
	Erbil	7(29.2%)	88(51.5%)	

Category	Subcategories	Outcome of management *		Sig. (2-sided)
		Appropriate 24(12.3%)	Inappropriate 171(87.7%)	
	Sulaymania	3(12.5%)	27(15.8%)	
	Halabja	0(0.0%)	2(1.2%)	
Q1- Routine screening of hypothyroidisim for pregnant ladies	Appropriately answered	17(70.8%)	59(34.5%)	0.001**
	Inappropriately answered	7(29.2%)	112(65.5%)	
Q2- The first action for a pregnant lady and taking thyroxine	Appropriately answered	17(70.8%)	62(36.3%)	0.001**
	Inappropriately answered	7(29.2%)	109(63.7%)	
Q3- The TSH target in the first trimester for a hypothyroid pregnant lady	Appropriately answered	19(79.2%)	53(31.0%)	0.000**
	Inappropriately answered	5(20.8%)	118(69.0%)	
Q4- For a known case of hypothyroidism, who she is recently pregnant and taking levothyroxine, how do you monitor treatment?	Appropriately answered	20(83.3%)	33(19.3%)	0.000**
	Inappropriately answered	4(16.7%)	138(80.7%)	

* Appropriate management: when all steps were correct or at least one not appropriate, Inappropriate management: when 2 or more steps were incorrect.
** Pearson Chi-Square test, *** Fisher's Exact test.

DISCUSSION:

With respect to maternal hypothyroidism diagnosed during pregnancy, the current survey provide recommendations to start treatment and normalize thyroid function of clinical practice relating to the screening and treatment of maternal overt hypothyroidism and subclinical hypothyroidism in pregnant females in Kurdistan region, Iraq, demonstrating a wide variation in its results. There was some degree of consistency between Endocrine Society and American Thyroid Association guidelines and some aspects of the responders clinical practice such as targeting TSH level in first trimester for pregnant females with hypothyroidism on L-T4 treatment, however; at the same time, there was some contradictory between guidelines and other aspects of responders clinical practice such as screening program of pregnant females.

Universal screening for thyroid gland dysfunction in pregnant females has been widely debated in recent years[12,13]. The American Thyroid Association and Endocrine Society Guidelines have two types of recommendations, some recommended universal screening for hypothyroidism in pregnancy and another group recommended targeted case finding; however, several studies have shown that the targeted case finding misses a significant number of pregnant females with thyroid gland dysfunction[14]. There are several uncertainties about screening thyroid function in pregnant females in the current study including time of testing and type of tests used in screening. Identification and treatment of hypothyroid dysfunction in the first antenatal visit may be so late to prevent complications associated with pregnancy; however, implementation of systemic screening for the presence of hypothyroidism in pregnancy would be an enormous challenge, particularly in developing countries[15]. A study done by Moleti M et al reported that, if the screening only limited to first trimester, near half of pregnant female with overt and subclinical hypothyroidism could be missed. In current survey, therefore; it is remarkable that, contrary to the recommendations of guidelines, two third of our clinicians did not do any screening program for thyroid

gland dysfunction in pregnancy, whereas, almost one third of the responders did a screening program for all pregnant females with hypothyroidism despite uncertainties in choosing the type of thyroid function tests.

Thyroid hormones in pregnant females play a critical role in the early fetal neurological development; therefore, diagnosed maternal hypothyroidism in pregnancy should be corrected as early as possible[16,17]. It is well known that most pregnant females with hypothyroidism need an increased dose of L-T4 from early stage of pregnancy[18,19]. Indeed, some study reported that one quarter of females on L-T4 treatment have biochemical evidence of under replacement at their first antenatal visit[20,21]. In this survey and it is unfortunate that 40% of the responders initiated an increased dose of the L-T4 for pregnant females with hypothyroidism as soon as the pregnancy is confirmed according to previous recommendations.

There was general consensus on the targeting the level of TSH in the first trimester of pregnant females with hypothyroidism on L-T4 treatment, with most responders aiming to achieve TSH less than 2.5mIU/L[16,17]. However; in this study, only one third of the responders aimed to achieve the maternal level of TSH less than 2.5mIU/L in the first trimester of pregnancy, and this consistent with that recommended by the guidelines.

In this study, majority of the responders in Kurdistan region choose an inappropriate tool for monitoring the treatment of pregnant females. It is remarkable that only less than one third of the responders reported that they used TSH alone for this purpose. This is in contrast to the American Thyroid Association guidelines and Endocrine Society Guidelines, both of them recommend TSH only.

Compared to the survey reported screening and treatment of maternal thyroid dysfunction in pregnancy in Europe and united states, the results of this study in much different in multiple aspects of management of hypothyroidism in pregnancy. Clinicians of Kurdistan often do not adhere to the clinical practice guidelines.

This survey has several limitations: first, the responders may not represent all clinicians in all governorates in Kurdistan region, Iraq. Second, variation in the clinical practices in different governorates could have influences the overall results of the survey. Near half of the responders of the survey are gynecologist, and their approach to screening and treatment of hypothyroidism in pregnancy may be different from that of endocrinologist, internist and general practitioners.

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