



Journal of Acute Disease

Original Article



jadweb.org

doi: 10.4103/jad.jad_89_24

Impact Factor® 0.5

Thyroid dysfunction prevalence in high-risk pregnant women and maternal and neonatal consequences after delivery: A retrospective cohort study

Roghaye Ahangari¹, Abolfazl Mohammadbeigi², Sepideh Miraj^{1✉}, Keivan Ghassami³, Azadeh Asgarian⁴

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Qom University of Medical Sciences, Qom, Iran

²Department of Epidemiology and Biostatistics, Faculty of Health, Qom University of Medical Sciences, Qom, Iran

³Department of Neurology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran

⁴Clinical Research Development Center, Forghani Hospital Qom University of Medical Sciences, Qom, Iran

ABSTRACT

Objective: To evaluate thyroid dysfunction prevalence and its consequences in high-risk pregnant women and their children.

Methods: In this retrospective cohort study, data from high-risk pregnant women who were referred to a governmental referral hospital in Qom, Iran from March to August 2022 were collected. The thyroid disorders were determined according to the 2017 American Thyroid Association guidelines. The predictors of a mother's hypothyroidism and its fetal and maternal consequences were assessed. Independent *t*-test, *Chi*-square test, and logistic regression were used for bivariate and multivariate analysis.

Results: 293 women were included. The prevalence of hypothyroidism and hyperthyroidism based on the thyroid stimulating hormone classification was 32.5% and 2.0%. The prevalence of subclinical and overt hypothyroidism was 6.1% and 4.1%, and the prevalence of subclinical and overt hyperthyroidism was 2.4% and 1.4%, respectively. Family history of thyroid disorders was the most important predictor of hypothyroidism during pregnancy ($OR=2.6$, 95% $CI=1.0-6.6$, $P=0.002$), while preterm delivery ($OR=2.2$, 95% $CI=1.3-6.8$, $P=0.220$) and elevated neonate thyroid stimulating hormone ($OR=1.2$, 95% $CI=1.1-1.3$, $P=0.041$) were the most important consequence of hypothyroidism.

Conclusions: Hypothyroidism is a highly prevalent thyroid disorder in high-risk pregnant women. Thyroid function screening should be performed in all pregnant women to increase the detection of subclinical and overt hypothyroidism during pregnancy.

KEYWORDS: Hypothyroidism; Thyroid disorder; Thyroid dysfunction; Thyroid stimulating hormone; Pregnancy

1. Introduction

Thyroid dysfunction in pregnancy is one of the main clinical problems and is associated with negative outcomes for the

Significance

Thyroid dysfunction in pregnancy is one of the main clinical problems and is associated with different consequences for mothers and their children. Hypothyroidism prevalence is very high in pregnant women with suspected endocrine disorders. Thyroid function screening should be performed in all pregnant women to increase the detection of subclinical and overt hypothyroidism during pregnancy.

✉ To whom correspondence may be addressed. E-mail: miraj.sepideh@gmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

©2024 Journal of Acute Disease Produced by Wolters Kluwer-Medknow.

How to cite this article: Ahangari R, Mohammadbeigi A, Miraj S, Ghassami K, Asgarian A. Thyroid dysfunction prevalence in high-risk pregnant women and maternal and neonatal consequences after delivery: A retrospective cohort study. J Acute Dis 2024; 13(5): 185-192.

Article history: Received 13 August 2024; Revision 15 August 2024; Accepted 25 November 2024; Available online 29 November 2024

mother and her baby[1,2]. Thyroid disorders including a variety of thyroid dysfunction from subclinical hypothyroidism and isolated maternal hypothyroxinemia to hyperthyroidism are responsible for possible adverse effects on the health of the mother and her child[3,4]. Hypothyroidism in pregnancy is related to a higher risk of maternal-fetal complications and lower cognitive outcomes in offspring such as a higher risk of intrauterine growth restriction, reduced Apgar score at birth, and reduction of future intellectual development[4,5].

According to reports, the prevalence of thyroid dysfunction such as iodine deficiency, hypothyroidism, and hyperthyroidism varied from 1% to more than 20% in different studies[1,3,4,6]. It is reported that 2% to 10.5% of women in pregnancy were affected by thyroid disorders and the incidence of hypothyroidism in pregnancy varied from 0.5%-3.5%[6-9]. Studies in Iran by Borzouei *et al.* showed that the hypothyroidism prevalence in pregnant women is high. A large study in Hamadan showed that the prevalence of hypothyroidism was 28.2% and 0.2% were affected by subclinical hyperthyroidism[10].

Hyperthyroidism and hypothyroidism during pregnancy have adverse effects on the mother and her neonate. As thyroid hormone is important for normal fetal growth, hypothyroidism can cause adverse obstetric and child neurodevelopmental outcomes[11,12]. Hypothyroidism is the most common thyroid dysfunction in pregnancy and occurs in 0.2%-0.4% of pregnant women[9].

Hypothyroidism incidence in pregnant women is between 0.2%-0.4% and Grave's disease is the most common cause of this type of thyroid disorder[9,10]. However, the prevalence of thyroid dysfunction and its consequences on the mother and her neonate are understudied or controversial in pregnant women[13]. Moreover, the prevalence of thyroid disorders in pregnancy has not yet been fully demonstrated in Qom, Iran as a multicultural region with different migrate ethnicities such as Afghan and Arab people. Therefore, this study was designed and conducted to evaluate the thyroid dysfunction prevalence and its consequences on high-risk pregnant women and their babies in Qom, Iran.

2. Patients and methods

2.1. Study setting

A retrospective cohort study was conducted on high-risk pregnant women who referred to the governmental referral hospital in Qom, Iran from March to August 2022. This center delivers prenatal and postnatal care for all pregnant women and all of the target population can receive this care, but only high-risk pregnant women fulfill the complete thyroid function test during pregnancy. High-risk pregnant women in this study were defined as women with a positive history of thyroid dysfunction in first-degree relatives,

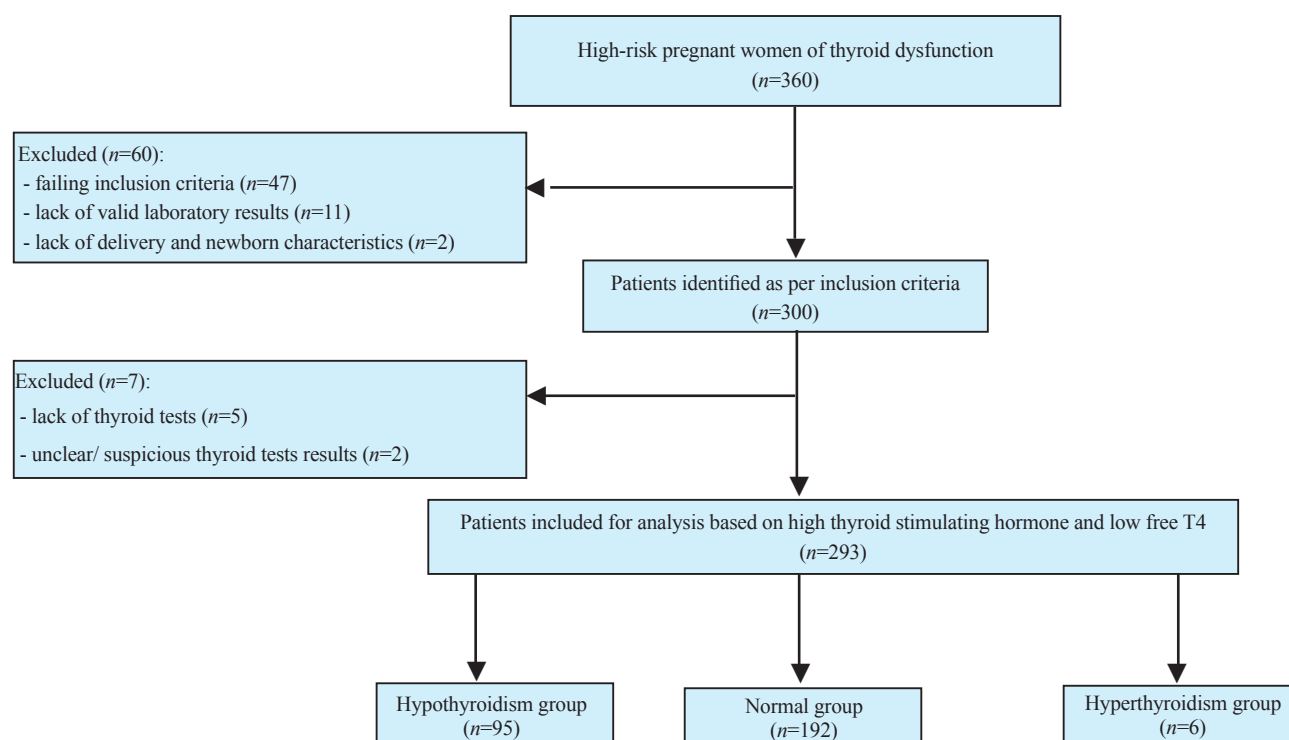


Figure 1. The study flowchart.

Table 1. Prevalence of hypothyroidism and hyperthyroidism according to TSH, T4, subclinical and overt definitions (n, %).

Groups	High TSH and low free T4	T4	Subclinical	Overt
Hypothyroidism	95 (32.5)	130 (44.4)	18 (6.1)	12 (4.1)
Normal	192 (65.5)	159 (54.3)	-	-
Hyperthyroidism	6 (2.0)	4 (1.4)	7 (2.4)	4 (1.4)

TSH: thyroid stimulating hormone.

Table 2. Demographic, reproductive, and neonate quantitative variables between normal and hypothyroidism mothers.

Variables	Normal group (n=192)	Hypothyroidism group (n=95)	t/U	P
Mother age (years, mean±SD)	29.1±6.1	30.7±5.6	-2.21	0.028
Pregnancy age (years, mean±SD)	37.8±6.6	36.4±4.3	2.16	0.032
Gravidity (median, Q1, Q3)	2 (1-2)	2 (1-3)	-3.26	0.001
Abortion numbers (median, Q1, Q3)	0 (0-1)	0 (0-1)	-1.53	0.121
Mother height (cm, mean±SD)	160.0±14.3	161.7±6.6	-0.89	0.374
Mother weight (kg, mean±SD)	76.3±15.3	79.4±19.3	-1.27	0.206
Mother BMI (mean±SD)	30.1±6.4	26.6±5.0	-0.63	0.531

BMI: body mass index, which is calculated as weight in kilograms divided by height in meters squared.

prior thyroid disorder, having thyroid nodules, and mothers who did thyroid tests based on the physician's suggestion. A sample of eligible subjects based on eligible criteria of high-risk women was selected and demographic and clinical data were extracted from her medical records. The subjects entered to study and the information of their delivery and required data were extracted. First, the thyroid disorder occurrence was evaluated according to the laboratory tests in recruited women in their medical records. Second, related factors of thyroid disorders were assessed. Finally, the complications of hypothyroidism for the mother and her newborn during pregnancy after delivery were listed for the mother and her baby. Preeclampsia, gestational diabetes, and anemia in mothers were extracted from medical records, and neonatal consequences including premature birth, low birth weight, hospitalization in neonatal intensive care unit, hyperbilirubinemia, and hypothyroidism were checked and these data were collected.

We include 300 eligible subjects to study, and finally, data from 293 subjects were analyzed. Inclusion criteria included pregnant women with active medical records in referral hospitals, having medical records during the pregnancy and having delivery at the same hospital, and having full clinical and laboratory examination during the pregnancy period, especially thyroid test results. However, pregnant women who were affected to secondary hypothyroidism due to other diseases or causes, subjects with incomplete thyroid

function tests, or outlier thyroid test results were excluded. Therefore, the medical records of 300 high-risk pregnant women were extracted and recorded in our checklist. The study flowchart shown in Figure 1.

2.2. Ethical consideration

The study was approved by ethical committee of Qom University of Medical Sciences (Approval No. IR.MUQ.REC.1400.049) on 14 March 2021. Written informed consent was obtained for participation in the study and use of the patient data for research and educational purposes. The procedures in the study follow the guidelines laid down in the Declaration of Helsinki (2000).

2.3. Data collection

Data collection conducted by a demographic questionnaire and a clinical checklist. Mother age, pregnancy age, gravidity, abortion numbers, mother height, weight and body mass index (BMI), and neonate sex were gathered by demographic questionnaire. Moreover, the medical history of subjects including used salt, thyroid function, drug medication, hypothyroidism history, family history of thyroid disorders, diabetes history, uterine cyst history, blood pressure, gestational diabetes and anemia extracted from medical records. The consequences data of hypothyroidism in mother and fetal including abortion, breach delivery, preterm delivery, abnormal bleeding, uterine rupture, prenatal death, in mother and neonate weight, neonate height, Apgar 0 and 5 minutes, neonate thyroid stimulating hormone (TSH), NICU hospitalization and respiratory distress were recorded in the checklist.

The hypothyroidism or hyperthyroidism were diagnosed based on TSH and T4 classifications by ELISA method and according to the diagnostic kit of disease and the pregnancy age of the patients. The normal range for TSH in the first trimester is 3.9 mIU/L and 4.1 mIU/L in the second and third trimesters in pregnant women according to the 2017 guidelines of the American thyroid association for the diagnosis and management of thyroid disease during pregnancy and the postpartum[2]. The same determined reference intervals by an Iranian national study were also used for different pregnancy trimesters[14, 15]. The normal range of thyroid function tests in the first, second, and third trimesters of pregnancy were including for TSH (0.2-3.9, 0.5-4.1, and 0.6-4.1 mIU/L), TT4 (8.2-18.5, 10.1-

Table 3. The relationship between hypothyroidism and medical history of studied* pregnant women (n, %).

Variables	Normal group <i>n</i> (%)	Hypothyroidism group <i>n</i> (%)	χ^2	<i>OR</i> (95% <i>CI</i>)	<i>P</i>
Idolized salt consumption					
Refined salt	59 (100)	31 (93.9)	1.36	0.3 (0.26-0.46)	0.243
Sea salt	0 (0)	2 (6.1)			
Thyroid function					
Normal	50 (100)	26 (96.3)	0.10	0.3 (0.25-0.47)	0.753
Abnormal viscos	0 (0)	1 (3.7)			
Drug medication					
Levothyroxine	158 (96.3)	82 (98.8)	0.63	1.1 (0.69-1.71)	0.425
Other drugs	6 (3.7)	1 (1.2)			
Hypothyroidism history					
Yes	180 (93.8)	76 (81.7)	9.33	3.4 (1.54-7.40)	0.002
No	12 (6.2)	17 (18.3)			
Family history of thyroid disorder					
Yes	60 (32.4)	51 (54.8)	12.84	1.8 (1.31-2.54)	<0.001
No	125 (67.6)	42 (45.2)			
Diabetes history					
Yes	36 (18.9)	14 (14.9)	0.71	0.8 (0.51-1.32)	0.399
No	154 (81.1)	80 (85.1)			
Uterine cyst history					
Yes	1 (0.5)	7 (7.5)	10.48	2.7 (2.01-3.77)	0.002
No	185 (99.5)	86 (92.5)			
Blood pressure					
Yes	32 (16.7)	17 (17.9)	0.04	1.0 (0.68-1.60)	0.837
No	160 (83.3)	78 (82.1)			
Gestational diabetes mellitus					
Yes	46 (23.9)	31 (32.6)	2.51	1.3 (0.94-1.86)	0.113
No	146 (76.1)	64 (67.4)			
Anemia					
Yes	14 (7.3)	12 (12.6)	2.49	1.4 (0.89-2.23)	0.117
No	178 (92.7)	83 (87.4)			

OR is calculated by Haldane-Anscombe correction method; DM: diabetes mellitus.

20.6, and 9-19.4 $\mu\text{g/dL}$), and TT3 (137.8-278.3, 154.8-327.6, and 137.0-323.6 ng/dL), respectively. Anti-TPO lower than 40 IU/mL was considered normal[1,15]. If the TSH is higher than 4 mU/L and free T4 is lower than the normal range, the patient is considered as hypothyroidism[15].

2.4. Statistical analysis

Descriptive statistics including mean and standard deviation (SD), median and IQR as well as frequency and percent used to describe the quantitative and qualitative variables, respectively. Comparison between pregnant women with and without hypothyroidism was conducted by independent *t*-test or *U* test for continuous data and by *Chi*-square for categorical data in bivariate analysis using SPSS version 20 (SPSS Inc., Chicago, IL, USA) and Stata 17 StataCorp, 2017. A multivariate logistic regression model with stepwise forward Wald method was used to assess the most important predictors of hypothyroidism in pregnant women as well as the most

consequences of it in their neonates. Hosmer-Lemeshow statistic checked the goodness of fit of the model and *P* value lower than 5% was considered a significant level.

3. Results

Sample size calculation was conducted based on the hypothyroidism prevalence ($P=18.1\%$) in pregnancy based on a recent review study in Iran[4] and type one error equal $\alpha=0.05$ and precision $d=0.1$. Therefore, the minimum required sample size was estimated as 232 subjects. The mean age of patients was (29.6 ± 6.0) years varied from 14 to 47 years old and the mean gestational age was (37.1 ± 2.8) weeks. From all 293 required high-risk pregnant women, 192 subjects (65.5%) were normal, and the prevalence of hypothyroidism and hyperthyroidism based on the TSH and free T4 classification was 95 subjects (32.5%) and 6 subjects (2.0%), respectively. The classification of T4 showed that 130 subjects

Table 4. Relationship between hypothyroidism and its consequences in under study pregnant women.

Variables	Normal group (n=192)	Hypothyroidism group (n=95)	χ^2/t	OR (95% CI)	P
Neonate sex (n, %)					
Female	97 (50.5)	44 (47.8)	0.2	0.9 (0.66-1.30)	0.671
Male	95 (49.5)	45 (52.2)			
Abortion history (n, %)					
Yes	22 (11.45)	22 (23.2)	6.3	1.6 (1.15-2.34)	0.012
No	170 (88.5)	73 (76.8)			
Breach presentation (n, %)					
Yes	23 (12)	13 (13.7)	0.1	1.1 (0.68-1.7)	0.742
No	169 (88)	82 (86.3)			
Preterm delivery (n, %)					
Yes	29 (15.1)	252 (26.7)	5.3	1.5 (1.09-2.19)	0.021
No	163 (84.9)	70 (73.7)			
Abnormal bleeding (n, %)					
Yes	33 (17.2)	20 (21.1)	0.7	1.2 (0.80-1.75)	0.416
No	159 (82.8)	75 (78.9)			
Uterine rupture (n, %)					
Yes	32 (16.7)	19 (20)	0.3	1.1 (0.75-1.68)	0.582
No	160 (83.3)	76 (80)			
Prenatal death (n, %)					
Yes	4 (2.1)	1 (1.1)	0.4	0.7 (0.14-3.52)	0.540
No	188 (97.9)	94 (98.9)			
NICU hospitalization (n, %)					
Yes	10 (5.2)	2 (2.1)	1.5	0.5 (0.14-1.78)	0.225
No	182 (94.8)	93 (97.9)			
Respiratory distress (n, %)					
Yes	16 (8.6)	9 (10.1)	0.2	1.1 (0.65-1.96)	0.684
No	170 (91.4)	80 (89.9)			
Neonate weight (g, mean±SD)	3 258.4±2039.6	3 204.6±693.9	0.2	-	0.826
Neonate height (cm, mean±SD)	49.1±2.6	49.3±2.2	0.8	-	0.434
Apgar 0 (mean±SD)	8.7±0.9	8.9±0.7	-1.5	-	0.133
Apgar 5 (mean±SD)	9.7±1.0	9.9±0.6	-1.3	-	0.197
Neonate TSH (mU/L, mean±SD)	3.6±2.6	6.3±4.3	2.2	-	0.032

NICU: neonatal intensive care unit; TSH: thyroid stimulating hormone.

(44.4%) were affected by hypothyroidism and 4 cases (1.4%) were hyperthyroidism. Based on the definition (Table 1), the prevalence of subclinical and overt hyperthyroidism was 2.4% and 1.4%, while the prevalence of subclinical and overt hypothyroidism was 6.1% and 4.1%, respectively.

Hypothyroidism subjects were compared with normal women regarding thyroid disorders based on risk factors and maternal and neonatal consequences due to the high prevalence of this disorder. Comparison of the mean of demographic and reproductive variables between normal and hypothyroidism mothers (Table 2) showed that there was a significant difference between the two groups based on mother age ($P=0.028$), pregnancy age ($P=0.032$), and gravidity ($P=0.003$). Whereas, no significant difference was observed in abortion, mother height, weight, or BMI ($P>0.05$).

According to results in Table 3, there was no significant relationship between hypothyroidism in pregnant women with type consuming salt, thyroid function, Levothyroxine consumption,

history of diabetes and gestational diabetes, high blood pressure, and anemia ($P>0.05$). But hypothyroidism history in patient ($OR=3.4$, 95% $CI=1.5-7.4$, $P=0.002$), having family history of hypothyroidism ($OR=1.8$, 95% $CI=1.3-2.5$, $P<0.001$), and history of uterine cyst ($OR=2.7$; 95% $CI=2.0-3.8$, $P=0.002$) were significant factors of hypothyroidism in pregnancy. The history of neck surgery, goiter disease, preeclampsia, and eclampsia did not show a significant relationship with hypothyroidism ($P>0.05$). Smoking and alcohol consumption were not reported in study subjects and only one patient with hypothyroidism has reported neck radiotherapy.

The effect of hypothyroidism during pregnancy on neonatal outcomes is presented in Table 4. Based on bivariate analysis, there was no significant relationship between mother hypothyroidism with neonate sex, breach presentation, abnormal bleeding, rupture, prenatal death, neonatal intensive care unit hospitalization, and respiratory distress after delivery ($P>0.05$).

Nevertheless, mother hypothyroidism was related to abortion

history ($OR=1.6$, 95% $CI=1.1-2.3$, $P=0.012$), and preterm delivery ($OR=1.5$, 95% $CI=1.1-2.2$, $P=0.021$). Moreover, tachypnea, meconium excretion and congenital abnormalities did not show a significant relationship with hypothyroidism during pregnancy ($P>0.05$). Moreover, hypothyroidism did not show a significant effect on neonate variables such as neonate weight, Height, and Apgar score ($P>0.05$), but the neonate TSH after delivery was significantly higher in children of the hypothyroidism group ($P=0.032$). The results of multivariate logistic regression showed that a family history of thyroid disorders is the most important predictor of hypothyroidism during pregnancy ($OR=2.6$, 95% $CI=1.0-6.6$, $P=0.002$). While other variables including used salt, BMI, age, pregnancy age, and other chronic diseases during pregnancy (blood pressure, anemia, diabetes mellitus, and uterine cyst history) were excluded from the regression model. In addition, the most important consequence of hypothyroidism during pregnancy was the increase in neonate TSH ($OR=1.2$, 95% $CI=1.1-1.3$, $P=0.041$) and preterm delivery ($OR=2.2$, 95% $CI=1.3-6.8$, $P=0.220$).

4. Discussion

The current study showed that the prevalence of hypothyroidism and hyperthyroidism in high-risk pregnant women was estimated as 32.5% and 2.0%, and the prevalence of subclinical and overt hypothyroidism was 6.1% and 4.1%, respectively. It seems that the hypothyroidism prevalence in our study was very high and it could be due to higher thyroid function screening and more completed tests in high-risk pregnant women with suspected endocrine disorders. The results of a meta-analysis study on 17 670 Iranian women showed thyroid dysfunction prevalence in pregnant women was 18.1% and the prevalence of hypothyroidism, and hyperthyroidism were 13.01% and 3.31%, respectively[4]. Another study in Istanbul, Turkey showed the prevalence of hypothyroidism, subclinical hypothyroidism and hyperthyroidism was 0.5%, 8.9%, and 2.8%, respectively[9]. Moreover, a national population-based cross-sectional study on 1080 pregnant women from 12 provinces of Iran[3], showed that Isolated hypothyroxinemia and subclinical hypothyroidism were the most prevalent thyroid disorders by 9.9% and 8%, respectively and were lower than our results. Mother age, pregnancy age, and gravidity were the significant risk factors of hypothyroidism in our study. Another large study in Iran showed that isolated maternal hypothyroxinemia is the most common thyroid disorder in Iranian pregnant women[3].

Pregnancy causes some changes in the thyroid gland and increases the production of thyroid hormone in pregnant women to 50%. Therefore, daily iodine needs increase and cause insufficient iodine

and consequently, some maternal and fetal complications may occur due to pathologic or immunologic changes during pregnancy such as hypothyroidism[16,17]. The isolated maternal hypothyroxinemia is defined as a decrease in maternal T4 during the pregnancy in the absence of TSH increase[18] and is related to some feto-maternal outcomes including gestational hypertension, preterm delivery, fetal distress, spontaneous abortion, and placental abruption, especially in the second trimester[13,18-20]. In addition, Hernández *et al.* study showed that an increase in maternal TSH in the first trimester is correlated with a higher incidence of perinatal loss, miscarriage and hypothyroidism[6,21]. Our results based on multivariate logistic regression showed that family history of thyroid disorders is the most important predictor of hypothyroidism during pregnancy. The results of a review study showed that post-partum thyroiditis prevalence is about 5%-10% and many of these women affected ultimately develop permanent hypothyroidism[22]. Moreover, based on the results of the current study, the most important consequence of hypothyroidism during pregnancy was an increase in neonate TSH and preterm delivery. Similar results showed in another study that showed that maternal hypothyroidism can increase the chance of post-partum hyperthyroidism[16,21-23]. In another study TSH>4 mIU/L increased the premature delivery and respiratory distress more than twofold in compare to mother who have TSH<4 mIU/L[11].

According to the results of a national study in Iran, the iodine deficiency in pregnant women in Iran is moderate in spite the adequate intake of iodine by the general population after the iodine replete since 2000[7]. Nevertheless, the long-term trend of thyroid disorders in Iranian pregnant women is increasing and health policymakers should make necessary interventions and policies regarding this problem[1,3]. Although the results of a national interventional study showed that the coverage of iodized salt coverage is more than 95% in Iranian households[7]. Based on the results of current study, there was no significant relationship between iodized salt consumption and hypothyroidism, but the effect of iodine deficiency to thyroid disorders is more evident and more considerable in pregnant women than other non-pregnant women in other studies[7,24]. Based on Etemadi *et al.* study, isolated hypothyroxinemia in pregnant women was associated with age higher 30 years, being in the second and the third trimesters, history of multiparity and residing in rural areas[3]. However, the results of Delshad *et al.* study showed that iodine supplementation with at least 150 µg of iodine per day is necessary in pregnancy and can improve the iodine intake of pregnant women and decrease the prevalence of clinical hypothyroidism, clinical/subclinical thyrotoxicosis, TPO-Ab positivity, and isolated hypothyroxinemia significantly[7]. Also, similar results were shown in a Sweden study[24].

In this study, pregnant women in different trimesters were

evaluated based on the medical records. However, interpretation of thyroid function tests in pregnancy should be considered based on trimester-related reference intervals due to changes in thyroid function tests and different physiological changes during pregnancy[1,15,25]. Applying trimester-specific reference ranges of thyroid hormones is warranted to avoid misclassification of thyroid dysfunction during pregnancy[15]. The TSH value decreases during pregnancy in both the lower and the upper limit of maternal TSH about 0.5-0.2 mU/L with the highest descending in TSH at the first trimester due to increased levels of serum human chorionic gonadotropin[2], but the serum TSH and its reference range slowly increase in the second and third trimesters[26]. Therefore, the classification of pregnant women for thyroid dysfunctions needs to understand the reference range of thyroid function tests and we used a valid interval range for the classification of hypothyroidism according to Iranian studies[1,10,14,15].

Overall, our results showed a high prevalence of hypothyroidism as shown in another meta-analysis study in Iran[4]. Therefore, mass screening of all pregnant women during pregnancy should be recommended by health policymakers to prevent of missing subclinical hypothyroidism. Based on our study, 32% of thyroid disorders were not detected if only high-risk women were screened. With all of these, there was no evidence for the recommendation of thyroid screening in pregnant women and its effect on pregnancy outcomes, although, it is performed by a large percentage of obstetricians and gynecologists in Iran[4].

Our study has some limitations. First, the medical records were used for data gathering and some of the information was missed. In contrast, the high prevalence of thyroid disorder in our study is probably due to evaluating the higher-risk patients who were referred in the referral centers and it can cause an overestimation due to higher thyroid function screening and more completed tests in suspected endocrine patients. Second, we assessed subjects in different trimesters of pregnancy because the thyroid function tests were done at different times during pregnancy among selected women. Moreover, the effect of physiological changes during pregnancy was not assessed in our study. Finally, we did not have data on TPO-Ab and urine iodine to assess the prevalence of TPO-Ab positive. However, the authors suggest more strong studies to cover these limitations and assess the role of iodine deficiency in developing such disorders in future studies.

In conclusion, hypothyroidism is a prevalent thyroid disorder in Iranian pregnant women probably due to higher thyroid function screening and more completed tests in suspected endocrine patients. Therefore, screening of thyroid dysfunctions should be performed in all pregnant women instead of high-risk groups to increase the detection of subclinical and overt hypothyroidism during pregnancy. Moreover, it seems that for a more exact evaluation of

thyroid dysfunction prevalence, more specific values for defined people should be determined and the reference intervals need to be calculated for each community. Therefore, mass screening for thyroid dysfunction is suggested for all pregnant women especially in the second trimester of pregnancy to prevent preterm delivery and fetal thyroid disorder.

Conflict of interest statement

The authors report no conflict of interest.

Funding

This study is funded financially by the Vice Chancellor for Research and Technology Development at Qom University of Medical Sciences.

Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

All authors worked on manuscript drafting and final approval. AA, AM and K GH: data collection and data analysis. RA, AM, SM: study concept and design, management, data collection. AM, SM, RA; analysis and interpretation of data, critical revision of the manuscript for important intellectual content. AM, AA and K GH: statistical analysis and interpretation of data.

References

- [1] Gholami S, Namiranian N, Shukohifar M, Kalantari F, Azizi R. Maternal thyroid function test level during the first trimester of pregnancy at a center Yazd, Iran: A cross-sectional study. *Int J Reprod Biomed* 2021; **19**(3): 255-260.
- [2] Erik KA, Elizabeth NP, Gregory AB, Rosalind SB, Herbert C, Chrysoula D, et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* 2017; **27**(3): 315-389.
- [3] Etemadi A, Amouzegar A, Mehran L, Tohidi M, Azizi F, Moradi K, et al. Isolated hypothyroxinemia in Iranian pregnant women, the role of iodine

- deficiency: A population-based cross-sectional study. *Thyroid* 2020; **30**(2): 262-269.
- [4] Sepasi F, Rashidian T, Shokri M, Badfar G, Kazemi F, Azami M. Thyroid dysfunction in Iranian pregnant women: A systematic review and meta-analysis. *BMC Pregnancy Childb* 2020; **20**(1): 405.
- [5] Menotti S, Mura C, Raia S, Bergianti L, De Carolis S, Romeo DM, et al. Overt hypothyroidism in pregnancy and language development in offspring: is there an association? *J Endocrinol Invest* 2024. doi: 10.1007/s40618-024-02317-2.
- [6] Dhanwal DK, Bajaj S, Rajput R, Subramaniam KA, Chowdhury S, Bhandari R, et al. Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India. *Indian J Endocrinol Metab* 2016; **20**(3): 387-390.
- [7] Delshad H, Raeisi A, Abdollahi Z, Tohidi M, Hedayati M, Mirmiran P, et al. Iodine supplementation for pregnant women: A cross-sectional national interventional study. *J Endocrinol Invest* 2021; **44**(10): 2307-2314.
- [8] Askari S, Abdi H, Ahmadi S, Bahadoran Z, Amouzegar A. Knowledge of thyroid disorders during pregnancy among general practitioners in Iran. *Int J Endocrinol Metab* 2017; **15**(3): e55450.
- [9] Dulek H, Vural F, Aka N, Zengin S. The prevalence of thyroid dysfunction and its relationship with perinatal outcomes in pregnant women in the third trimester. *North Clin Istanb* 2019; **6**(3): 267-272.
- [10] Borzouei S, Goodarzi MT, Biglari M, Nazari F, Shivapour Z. The prevalence of thyroid disorders in pregnant women of Hamadan. *Avicenna J Nurs Midwifery Care* 2019; **27**(1): 11-17.
- [11] Lee SY, Cabral HJ, Aschengrau A, Pearce EN. Associations between maternal thyroid function in pregnancy and obstetric and perinatal outcomes. *J Clin Endocrinol Metab* 2020; **105**(5): e2015-23.
- [12] Pande A, Anjankar A. A narrative review on the effect of maternal hypothyroidism on fetal development. *Cureus* 2023; **15**(2): e34824.
- [13] Li P, Cui J, Li L, Chen X, Ouyang L, Fan J, et al. Association between isolated maternal hypothyroxinemia during the first trimester and adverse pregnancy outcomes in southern Chinese women: A retrospective study of 7 051 cases. *BMC Pregnancy Childb* 2022; **22**(1): 866-872.
- [14] Mir F, Chiti H, Mazloomzadeh S. Short-term adverse pregnancy outcomes in women with subclinical hypothyroidism: A comparative approach of Iranian and American guidelines. *J Thyroid Res* 2022; **2022**: 9315250.
- [15] Mehran L, Amouzegar A, Delshad H, Askari S, Hedayati M, Amirshakeri G, et al. Trimester-specific reference ranges for thyroid hormones in Iranian pregnant women. *J Thyroid Res* 2013; **2013**: 651517.
- [16] Lee SY, Pearce EN. Assessment and treatment of thyroid disorders in pregnancy and the postpartum period. *Nat Rev Endocrinol* 2022; **18**(3): 158-171.
- [17] Croce L, Chiovato L, Tonacchera M, Petrosino E, Tanda ML, Moleti M, et al. Iodine status and supplementation in pregnancy: an overview of the evidence provided by meta-analyses. *Rev Endocr Metab Disord* 2023; **24**(2): 241-250.
- [18] Ramezani TF, Nazarpour S, Behboudi-Gandevani S. Isolated maternal hypothyroxinemia and adverse pregnancy outcomes: A systematic review. *J Gynecol Obstet Hum Reprod* 2021; **50**(7): 102057.
- [19] Gong X, Liu A, Li Y, Sun H, Li Y, Li C, et al. The impact of isolated maternal hypothyroxinemia during the first and second trimester of gestation on pregnancy outcomes: An intervention and prospective cohort study in China. *J Endocrinol Invest* 2019; **42**(5): 599-607.
- [20] Avramovska M, Karanfilski B, Dimitrov G, Dzikova E, Daneva Markova A, Hadzi Lega M, et al. Isolated maternal hypothyroxinemia and its perinatal outcome in north Macedonia. *Acta Clin Croat* 2021; **60**(2): 246-253.
- [21] Hernández M, López C, Soldevila B, Cecenarro L, Martínez-Barahona M, Palomera E, et al. Impact of TSH during the first trimester of pregnancy on obstetric and foetal complications: Usefulness of 2.5 mIU/L cut-off value. *Clin Endocr* 2018; **88**(5): 728-734.
- [22] Cooper DS, Laurberg P. Hyperthyroidism in pregnancy. *Lancet Diabetes Endo* 2013; **1**(3): 238-249.
- [23] Campos-Martorell A, Ramon AM, Barros KN, Soria JLM, Galera RML, Fernández DY, et al. Thyroid function in 509 premature newborns below 31 weeks of gestational age: Evaluation and follow-up. *J Clin Res Pediatr Endocrinol* 2022; **14**(4): 453-462.
- [24] Manousou S, Andersson M, Eggertsen R, Hunziker S, Hulthén L, Nyström HF. Iodine deficiency in pregnant women in Sweden: A national cross-sectional study. *Eur J Nutr* 2020; **59**(6): 2535-2545.
- [25] Marwaha RK, Chopra S, Gopalakrishnan S, Sharma B, Kanwar RS, Sastry A, et al. Establishment of reference range for thyroid hormones in normal pregnant Indian women. *BJOG* 2008; **115**(5): 602-606.
- [26] Haddow JE, Knight GJ, Palomaki GE, McClain MR, Pulkkinen AJ. The reference range and within-person variability of thyroid stimulating hormone during the first and second trimesters of pregnancy. *J Med Screen* 2004; **11**(4): 170-174.

Publisher's note

The Publisher of the Journal remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.