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Prevalence of Hypothyroidism and Pregnancy Outcomes in Women Referred to Ayatollah Mousavi Hospital in Zanjan in 2018-2019

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Abstract

Background: Hypothyroidism is common during pregnancy. This disorder is associated with adverse maternal and neonatal outcomes.

Objectives: The study of the prevalence and different consequences of hypothyroidism in pregnancy in each region is the special importance in determining prevention and management strategies. Therefore, the aim of this study was to determine the prevalence of hypothyroidism and pregnancy outcomes in women referred to Ayatollah Mousavi Hospital in Zanjan.

Methods: This cross-sectional-analytical study was performed on all pregnant women who gave birth in Ayatollah Mousavi Hospital in Zanjan in 2018-2019. Data were collected through census and using Chi-square, Fisher's exact and independent t-tests and with SPSS software version 22, pregnancy outcomes between the two groups were calculated.

***Results*:** The prevalence of hypothyroidism in pregnant women in the present study was estimated at 8.59%. Hypothyroidism was found to double the chance of gestational diabetes ($p<0.02$) (CI=1.1-3.8). The rate of cesarean delivery was significantly higher in patients ($p<0.001$). The rate of fetal heart rate drop, placental abruption, and placental adhesion was higher in the affected group, but this difference was not significant ($p>0.05$). There was no significant difference between the two groups in terms of preeclampsia, preterm delivery, first minute Apgar score, height, weight and head circumference of the newborn ($p>0.05$).

Conclusion: Considering the adverse maternal and neonatal outcomes of hypothyroidism, it seems that more clinical studies in this field are needed to manage and evaluate the outcomes in pregnant women with hypothyroidism.

Keywords: prevalence, hypothyroidism, pregnancy outcomes, neonatal outcomes

Introduction

During the pregnancy the thyroid undergoes physiology and structure changes, and the fetus is reliant on maternal thyroxine, so the mother's thyroid gland is more prone to hypothyroidism during pregnancy [1].

Various factors influence the function of the thyroid during pregnancy such as adequate iodine intake, habits and diet, environmental factors, and genetic predisposition [2]. Maternal age, number of pregnancies, living area, history of infertility, history of abortion, using birth control pills, presence of ovarian cysts, smoking, high body mass index, thyroid autoimmune diseases, thyroid gland destruction with radioactive iodine for the treatment of hyperthyroidism and a history of thyroid disorders [2-4].

Several studies have mentioned the association between iodine and hypothyroidism, so that in areas of iodine deficiency, the size of the thyroid

increases by 20-40% and the prevalence of hypothyroidism is higher. More than one third of the world's population suffer from iodine deficiency. It's believed that the prevalence of goiter is higher in mountainous areas due to iodine deficiency, and since Zanjan province is also geographically located in a mountainous region, the prevalence of hypothyroidism is on the rise. On the other hand, pregnancy is associated with an increased need for daily iodine intake by 50%, mainly due to increased iodine excretion through the kidneys [1,5,6].

The most common thyroid dysfunction in pregnancy is hypothyroidism [7], nearly 2 to 12 in 1000 pregnancies [1]. According to the literature, the prevalence of this disorder based on the criteria of the American Thyroid Association (ATA), in western countries ranges from 0.5 to 12.3% [8,9]. Meanwhile, its prevalence is higher in Asian countries (13.13-14%) [10,11]. In Iran, the prevalence of hypothyroidism varies according to geography and the amount of iodine intake [6]. Nazarpour et al. have reported a prevalence of 18.9 and 50% for subclinical and overt hypothyroidism in pregnancy in the city of Tehran, respectively [3]. Also, its prevalence is estimated to be 21% and 10.15% in Mashhad (northeast of Iran) and Kerman (east of Iran), respectively [12]. In Hamedan, which is one of the neighboring provinces of Zanjan, the prevalence of hypothyroidism during pregnancy in 2016-2017 was estimated to be 27.7% [13].

Hypothyroidism during pregnancy causes negative consequences for both mother and fetus. Hypothyroidism has two main types of overt and subclinical. Severe hypothyroidism is uncommon during pregnancy; mainly because severe hypothyroidism is less common during pregnancy due to infertility and recurrent miscarriage [1,7].

Ajmani et al. reported that those who suffer from hypothyroidism experience increased incidence of preeclampsia and placental abruption, but Mannisto studies repoeted no association between hypothyroidism and preeclampsia and preterm delivery [14-16]. Turunen et al. reported that maternal hypothyroidism was associated with gestational diabetes, hypertension in pregnancy and severe preeclampsia, cesarean section (C-section), preterm delivery, large infant relative to gestational age, major congenital anomalies, and neonatal hospitalization in the intensive care unit (NICU). While Ezzeddine et al. did not find any association between maternal hypothyroidism and neonatal complications such as low Apgar score, low birth weight, and intrauterine death [2,17].

Based on what was mentioned before, there is a discrepancy in the findings and more studies are needed to evaluate the consequences of pregnancy in people with hypothyroidism. Also, according to the available knowledge, no studies investigated the prevalence of hypothyroidism in Zanjan. Therefore, this study was performed to estimate the prevalence of hypothyroidism in women referred to Ayatollah Mousavi Hospital in Zanjan. Besides pregnancy and neonatal related outcomes are also investigated.

Methods

This cross-sectional analytical study was performed on all pregnant women who had given birth in Ayatollah Mousavi Hospital of Zanjan from September 2018 to March 2019. The study was approved by the ethics committee of Zanjan University of Medical Sciences (code: A-12-1203-1) and ethical code (IR.ZUMS.REC.1397.166). The inclusion criteria were as fallows gestation age of 22 weeks or higher, Iranian nationality, and singleton pregnancy. Exclusion criteria were having an underlying disease.

In the first phase of the study, a census was performed to identify all women who gave birth in the Hospital to determine the prevalence of hypothyroidism. Then, those with hypothyroidism were compared with others gestational diabetes and gestational disorders (Table 2). In the second phase, to compare the pregnancy outcomes in subjects with and without hypothyroidism, 115 mothers without hypothyroidism were selected by systematic random sampling. Therefore, 115 mothers with hypothyroidism and 115 mothers without hypothyroidism were studied, with a total sample size of 230.

Data were collected with a research checklist (maternal age, gestational age, neonatal sex, neonatal resuscitation need, all fetal heart rate deceleration, type of delivery, and neonatal outcome). Diagnosis of hypothyroidism was confirmed based on the medical history of patients, who was taken by a resident of obstetrics and gynecology; and evidence of hypothyroidism were according to the Ministry of Health, TSH

above 3.9 in the first trimester or TSH above 4.1 in the second and third trimesters. Data were analyzed using Chi-square, Fisher's exact test, and independent t-test by SPSS version 22. Statistical significance was considered when p-value<0.05.

Results

Of 1338 deliveries in the hospital, 115 mothers with hypothyroidism were identified, an estimated prevalence of 8.59%.

According to the Chi-square and Fisher's exact test, there was no statistically significant difference between the two groups concerning maternal age, place of residence, level of education, and history of abortion (Table 1). The number of primiparous women with hypothyroidism was higher than primiparous women in the control group, but this difference was not statistically significant (p>0.05).

Table 1: Demographic and midwifery characteristics of participants

variables		hypothyroidism Group Number (percent)	Control Group Number (percent)	P value
Age of Mother (Year)		30±2.6	8.29±6.6	0.822 [a]
Area of Residence	City	71 (7.61)	61 (53)	0.182 [b]
	Village	44 (3.38)	54 (47)	
Educational Status	illiterate	2 (7.1)	6 (2.5)	0.387 [b]
	Secondary	95 (6.82)	93 (9.80)	
	University	18 (7.15)	16 (9.13)	
Parity	Nulliparous	40 (8.34)	27 (5.23)	0.059 [b]
	Multiparous	75 (2.65)	88 (5.76)	
Abortion Record	Yes	30 (26.1)	19 (5.16)	0.076 [b]
	No	85 (9.73)	96 (5.83)	

Independent t-test [a]
Chi-square or Fisher exact test [b]

In this study, hypothyroidism was significantly associated with gestational diabetes (P<0.02), so that those with hypothyroidism were at increased risk of developing gestational diabetes by two times (CI=1.1-3.8). But no significant association was found between hypothyroidism and hypertension disorders (P>0.05) (Table 2).

Table 2: Comparison of gestational diabetes and hypertensive disorders in study participants

variables		Hypothyroidism Yes (115 mothers)	Hypothyroidism No (1223 mothers)	P value[a]	OR (CI)
Disease	hypertensive disorders	8 (0.7)	75 (6.1)	0.720	(0.53-2.43) 1.14
	gestational diabetes	13 (11.3)	71 (5.8)	0.020*	(1.3-1.8) 2.06

Chi-square [a]

In this study, the rate of C-section in the affected group was significantly higher (P<0.001) so that hypothyroidism was associated risk of C-section by 2.5 times. Fetal meconium excretion was more common among those with normal pregnancy (P<0.03). Fetal heart rate deceleration, placental abruption, and placental adhesion were higher in mothers with hypothyroidism, but this difference was not statistically significant (P>0.05) (Table 3).

Table 3: Comparison of pregnancy outcome between two group

variables		Hypothyroidism Group Number (percent)	Control Group Number (percent)	P Value	OR (CI)
Mode of Delivery	Natural	39 (33.9)	65 (56.5)	0.001*a	(1.4-4.3) 2.5
	Cesarean	76 (66.1)	50 (43.5)		
Meconium	Yes	1 (0.9)	7 (6.1)	0.033 b*	(0.1-1.1) 0.13
	No	114 (99.1)	108 (93.9)		
Fetal heart rate deceleration	Yes	19 (16.5)	10 (8.7)	0.076 a	(0.4-92.69) 2.07
	No	96 (83.5)	105 (91.3)		
Placental abruption	Yes	5 (4.3)	1 (0.9)	0.106 b	-
	No	110 (95.7)	114 (99.1)		
Placental adhesion	Yes	4 (3.5)	0 (0)	0.061b	-
	No	111 (96.5)	115 (100)		

a: chi-square
b: Fisher's exact test
*** significant**

According to the independent t-test, neonatal outcomes were not significantly different between the two groups (Table 4).

Table 4: Comparison of neonatal outcomes between two groups

variables	Hypothyroidism Group	Control Group	P-Value a
Age of pregnancy	37.2±5.7	37.2±2.9	0.465
Birth weight	3079.698±39.552	2987.681±72.09	0.313
Height	50.4±2.3	49.3±8.79	0.562
Head circumference	34.2±6	34.2±5.9	0.201
Apgar first minute	8.1±2.8	8.1±2.2	0.762

Independent-Sample T test a

Discussion

In the present study, the prevalence of hypothyroidism in pregnant women referred to Ayatollah Mousavi Hospital in Zanjan was 8.59%, which is consistent with some of the previously conducted studies. For example, the prevalence of this disorder in the cities of Hamadan, Kerman, and Mashhad has been estimated at 1.2%, 10.15%, and 21%, respectively [12,13,18]. A recently conducted study in the city of Tehran reported a prevalence of 9.9% for hypothyroidism during pregnancy [5]. The prevalence of this disorder according to the criteria of the American Thyroid Association in Western countries is estimated at 0.3-2.79% [8,9,19]. In contrast, based on recent studies conducted in Asian countries, the prevalence of hypothyroidism is higher in these countries, ranging from 13.13 to 14% [10,11]. It seems that geography also contributes to the prevalence of hypothyroidism. Besides, sample size and study protocol are also important factors in estimating the prevalence of hypothyroidism.

Based on the findings, the prevalence of hypothyroidism was higher in nulliparous women than their multiparous counterparts but this difference was not significant (p>0.05). Cleary-Goldman et al. also, reported that the prevalence of hypothyroidism was higher in nulliparous women than multiparous women [20]. Consistent with the present study, Nazarpour et al. [3] and Dulek et al. [9] also reported no association between parity and hypothyroidism. It seems that their sample size has influenced the results.

Similar to Kiran et al., this study demonstrated that hypothyroidism was not associated with a history of abortion (p=0.07) [11] which is in contrast to the study by Ajmani et al., Shinohara

et al., and Cakmak et al., who reported that hypothyroidism was associated with abortion and that the prevalence of abortion was higher in people with hypothyroidism [15,21,22]. This difference can be attributed to the fact that whether patients were receiving treatment or not.

Ajmani et al. reported a higher prevalence of preeclampsia among women with hypothyroidism so that these women were twice as likely as there healthy counterparts at risk of developing preeclampsia [15]. Kiran et al. also reported that the incidence of preeclampsia increases following hypothyroidism [11]. These findings are in contrast to the results of the present study, which showed no significant association between hypothyroidism and hypertensive disorders. As in our study, Ezzeddine et al. also found no significant association between hypothyroidism and hypertension during pregnancy [2]. This discrepancy can be attributed to the fact that in the present study, women's hypothyroidism was under control and treatment.

Chen et al. reported no significant association between hypothyroidism and gestational diabetes [23]. But the results of our study showed that people with hypothyroidism are at increased risk of developing gestational diabetes (about two times). Stohl et al. also emphasized that hypothyroidism is strongly associated with gestational diabetes and recommended that screening for diabetes should begin earlier in women with thyroid dysfunction [24]. The observed difference can be attributed to factors such as the methodology of the study and criteria used for diagnosing hypothyroidism.

Based on the findings, the rate of C-section in women with hypothyroidism was 2.5 times higher than in healthy women. This increase may be secondary to an increase in gestational diabetes in women with hypothyroidism. Stohl et al. showed that the prevalence of gestational diabetes is higher in women with hypothyroidism than those with hyperthyroidism [24]. Cakmak et al. also reported similar results. According to their study, the risk of C-section was 1.2 times higher in women with hypothyroidism. They argued that the observed increase in the rate of C-section can be attributed to the enhanced rate of pregnancy related outcomes such as high blood pressure, diabetes, and low birth weight [21]. The findings of the present study are consistent with the results of Kiran et al. who reported that TSH levels> 2.5 were associated with an increased rate of C-section [11]. Ajmani et al. argued that the cause of increased cesarean section was increased fetal distress [15]. In our study, the rate of heart rate drop was higher in the hypothyroidism group. But this difference was not statistically significant and could be related to the small sample size of the present study. In contrast, Dulek et el. reported in their study that there was no association between C-section and thyroid disorders during pregnancy [9]. Lee et al. found no association between high levels of TSH (TSH>4) and C-section [25]. These differences may be related to the study method, sample size, and the occurrence of other consequences.

No significant difference was found between the two groups concerning the neonatal outcomes (gestational age at birth, weight, height, head circumference, and first minute Apgar score). Similar to the results of the present study, Ezzeddine et al. reported no association between hypothyroidism and neonatal outcomes such as neonatal weight, 1 and 5 minutes Apgar scores less than 7, and intrauterine death [2]. Also Dulek et al. found no association between hypothyroidism and birth weight and Apgar scores at 1 and 5 minutes [9]. Cakmak et al. did not report any association between hypothyroidism and other neonatal outcomes such as preterm delivery, Apgar scores less than 7, low birth weight, and premature rupture of membranes, except for an increased risk of NICU (Neonatal Intensive Care Unit) admission [21]. Luisi et al. found no association between hypothyroidism and neonatal outcomes (low birth weight, head circumference, and height) [26]. In contrast, Lee et al. reported an increased risk of preterm infancy and respiratory distress syndrome for those with increased levels of TSH. Low birth weight and NICU admission were not associated with hypothyroidism [25]. Because subjects of the present study were receiving treatment their TSH were in the normal range, hence this difference can be justified.

Conclusion

As women with hypothyroidism are at increased risk of hypothyroidism, it seems that more attention should be paid to screening pregnant women. Besides, to prevent the consequences of

hypothyroidism during pregnancy a series of programs should be developed. Further clinical studies are recommended to investigate other consequences of this disorder. The present research was a cross-sectional study and the subjects were treated with levothyroxine but the dose of the drug was not known. Using other study designs (e.g. cohort or RCT) would provide useful information. Moreover, as various studies have reported different rates of prevalence for hypothyroidism, it seems that newer and more effective criteria should be found for screening these people.

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Conflict of interest
The authors declare no conflict of interest.

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