To cite this article: Yükcü B, Albayrak M. Association between second trimester maternal hypothyroidism and congenital heart diseases in fetuses: A retrospective study. Turk J Clin Lab 2025; 2: 322-329.

Research Article

Association between second trimester maternal hypothyroidism and congenital heart diseases in fetuses: a retrospective study

Maternal hipotiroidi ile fetal konjenital kalp hastalıkları arasındaki ilişki: retrospektif bir çalışma

Bekir Yükcü*[1], Mehmet Albayrak[2]

[1]Department of Pediatric Cardiology, Giresun Obstetric and Pediatric Disease Education and Research Hospital, Giresun, Türkiye

[2]Department of Perinatology, Giresun Obstetric and Pediatric Disease Education and Research Hospital, Giresun, Türkiye

Abstract

Aim: This study aimed to investigate the association between second-trimester maternal hypothyroidism and congenital heart diseases (CHDs) in fetuses.

Material and Methods: This retrospective study was conducted at Obstetrics and Pediatrics Training and Research Hospital between June 2022 and December 2024. The patient group comprised mothers of children diagnosed with major CHDs, while the control group included mothers of children without CHDs or with minor anomalies not requiring intervention. Maternal thyroid status was determined by second-trimester TSH levels: >4.0 mIU/mL was classified as hypothyroid, while 0.2–4.0 mIU/mL was considered euthyroid. Statistical analyses, including ROC analysis, regression analysis, Chi-square test, Fisher's exact test, and Mann-Whitney U test, were performed using SPSS 25, with $p < 0.05$ considered significant.

Results: The median TSH level was significantly higher in the CHD group compared to controls ($p = 0.002$). Logistic regression analysis revealed that each unit increase in maternal TSH levels increased the risk of fetal CHD by 1.47 times (95% CI: 1.212–1.792, $p < 0.001$). ROC analysis determined an optimal TSH cutoff of 1.795 mIU/mL (AUC = 0.627; sensitivity: 59.6%, specificity: 59.4%). While differences in CHD subgroups were observed, including conotruncal and valvular defects, these did not reach statistical significance ($p > 0.05$).

Conclusion: The study suggests a potential association between maternal hypothyroidism and fetal CHD.

Keywords: maternal hypothyroidism, congenital heart disease, fetal echocardiography, thyroid function

Corresponding Author*: Bekir Yükcü, MD. Giresun Obstetric and Pediatric Disease Education and Research Hospital, Pediatric Cardiology Department.
E-mail: byukcu@gmail.com
Orcid: 0000-0003-1661-7024
Doi: 18663/tjcl.1613893
Recevied: 05.01.2025 accepted: 13.05.2025

TJCL Volume 16 Number 1 p: 39-47

Öz

Amaç: Bu çalışma, ikinci trimesterdeki maternal hipotiroidi ile fetal konjenital kalp hastalıkları (KKH) arasındaki ilişkiyi araştırmayı amaçladı.

Gereç ve Yöntemler: Bu retrospektif çalışma, Haziran 2022 ile Aralık 2024 tarihleri arasında Kadın Doğum ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi'nde gerçekleştirildi. Hasta grubu, majör konjenital kalp hastalığı tanısı alan çocukların annelerinden oluşurken, kontrol grubu KKH olmayan veya müdahale gerektirmeyen minör anomalilere sahip çocukların annelerini içeriyordu. Annelerin tiroid durumu, ikinci trimesterde ölçülen TSH seviyelerine göre belirlendi: >4,0 mIU/mL hipotiroid, 0,2-4,0 mIU/mL ötiroid olarak kabul edildi. İstatistiksel analizler arasında ROC analizi, regresyon analizi, Ki-kare testi, Fisher'ın kesin testi ve Mann-Whitney U testi yer almakta olup, tüm analizler SPSS 25 kullanılarak gerçekleştirildi ve $p < 0,05$ anlamlı kabul edildi.

Bulgular: Medyan TSH seviyesi, KKH grubunda kontrol grubuna göre anlamlı derecede daha yüksek bulundu ($p = 0,002$). Lojistik regresyon analizinde, maternal TSH seviyelerindeki her bir birimlik artışın fetal KKH riskini 1,47 kat artırdığı tespit edildi (95% CI: 1,212–1,792, $p < 0,001$). ROC analizi, TSH için optimal eşik değerini 1,795 mIU/mL olarak belirledi (AUC = 0,627; duyarlılık: %59,6, özgüllük: %59,4). Konotrunkal ve valvüler defektler gibi KKH alt gruplarında farklılıklar gözlenmiş olsa da, bu farklar istatistiksel anlamlılığa ulaşmadı ($p > 0,05$).

Sonuç: Çalışma, maternal hipotiroidizm ile fetal KKH arasında potansiyel bir ilişki olabileceğini göstermektedir.

Anahtar Kelimeler: maternal hipotiroidizm, konjenital kalp hastalığı, fetal ekokardiyografi, tiroid fonksiyonları

Introduction

Congenital heart diseases (CHDs) occur in approximately 1% of live births and account for one-third of all major congenital anomalies [1]. However, this prevalence may vary depending on regional and environmental factors [2,3]. As one of the most common congenital anomalies in newborns, CHDs are responsible for 30-50% of infant mortality associated with congenital anomalies [4-7].

The causes of CHDs have been linked to a combination of genetic predisposition and various environmental risk factors, such as maternal illnesses, teratogen exposure, and maternal phenylketonuria [2,8]. However, the genetic, epigenetic, and environmental foundations of these defects remain incompletely understood [9]. Despite advancements in diagnosis and treatment, CHDs continue to play a significant role in childhood morbidity and mortality, underscoring the critical importance of early detection and identification of risk factors [4].

Thyroid hormones play a critical role in maintaining the health of both the mother and fetus during pregnancy. During this period, the thyroid gland increases its production of thyroxine (T4) and triiodothyronine (T3) by approximately 50%, with a corresponding rise in daily iodine requirements. While these physiological changes occur seamlessly in healthy pregnancies, thyroid dysfunctions can emerge in many women as a result of pathological processes. Common thyroid disorders during pregnancy include hypothyroidism, hyperthyroidism, and nodular thyroid diseases, all of which can lead to significant complications before, during, or after pregnancy [10].

Maternal hypothyroidism can have significant adverse effects on pregnancy outcomes and fetal development [11-15]. Overt hypothyroidism, in particular, has been associated with an increased risk of complications such as preterm birth, low birth weight, pregnancy loss, gestational hypertension, and impaired neurodevelopment in the fetus [13,16,17]. Studies have also shown that maternal hypothyroidism can impact various systems, including the cardiovascular system, and has been linked to CHD [18-20]. Population-based studies in this field have yielded conflicting results regarding the risk posed by thyroid disorders on CHD [18,21].

In this study, we aimed to investigate the relationship between CHDs and second-trimester maternal hypothyroidism, considering the high prevalence of maternal hypothyroidism in our region.

Material and Methods

Study design

This retrospective study was conducted at the Giresun Obstetrics and Pediatrics Training and Research Hospital between June 2022 and December 2024. Initially, pediatric cardiology clinic records were reviewed to identify children diagnosed and followed with major CHDs during this period. The maternal second-trimester thyroid function tests of these children were collected, forming the patient group. For the control group, children without CHD or with minor cardiac anomalies that did not require intervention were identified during the same period, and their mothers' second-trimester thyroid function tests were gathered.

Thyroid function testing

Pregnant women with a TSH level above 4.0 mIU/mL were classified as hypothyroid and referred to an endocrinologist for further evaluation and levothyroxine treatment. Women with TSH levels between 0.2 and 4.0 mIU/mL were considered euthyroid [10].

Exclusion criteria

Participants meeting any of the following criteria were excluded: presence of systemic diseases, pregnancies achieved via in vitro fertilization, smoking, biochemical or hematological abnormalities, congenital fetal anomalies such as liver or neurological defects, gestational diabetes or hypertension, chronic hypertension, acute or chronic infections (e.g., fever, urinary tract infections, hepatitis), renovascular diseases, maternal morbid obesity, pre-pregnancy hypothyroidism or use of thyroid medication due to other endocrine disorders, other endocrine conditions, missing medical records or unavailable data.

Echocardiographic evaluation

Transthoracic echocardiographic assessments were performed using a Philips Affiniti 50 device (Philips Healthcare, Best, Netherlands) by an experienced pediatric cardiologist. Congenital heart diseases identified in the study were categorized into two groups as (1) Major CHDs: Moderate-to-large ventricular septal defects (VSD), moderate-to-severe pulmonary stenosis/atresia, moderate-to-severe aortic stenosis (valvular), arcus hypoplasia/aortic coarctation, situs inversus totalis/dextrocardia, atrioventricular septal defects (AVSD), Tetralogy of Fallot, truncus arteriosus, transposition of the great arteries (TGA), pulmonary artery sling, double outlet right ventricle (DORV), hypoplastic left heart syndrome (HLHS), and Ebstein's anomaly and (2) Minor CHDs: Defects not requiring surgical or transcatheter intervention, such as patent ductus arteriosus (PDA), patent foramen ovale (PFO), atrial septal defects (ASD), and mild valvular regurgitation or stenosis.

Thyroid hormone measurement

Venous blood samples were collected in BD Vacutainer SST II Advance tubes during routine second-level ultrasonography. The samples were centrifuged at 1500×g for 10 minutes to obtain serum. Thyroid-stimulating hormone (TSH) and free T4 levels were measured using a Roche Cobas e601 analyzer (Roche Diagnostics GmbH, Mannheim, Germany).

This study was approved by the Giresun Education and Research Hospital Ethics Committee (approval date: 25.12.2024; approval number: 2024/02). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from the patients prior to inclusion in the study.

Statistical Analysis

All analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro-Wilk test. As a result, numerical variables, including maternal age, maternal weight, TSH levels, and FT4 levels, were found not to follow a normal distribution. Therefore, non-parametric tests were used for these variables. Numerical data were expressed as median (25–75 percentiles), while categorical data were presented as counts and percentages [n (%)]. Differences between categorical variables were evaluated using the Chi-square test. In cases where expected cell counts were insufficient, Fisher's exact test was applied. Comparisons between numerical variables across groups were conducted using the Mann-Whitney U test. For TSH levels, which showed statistical significance, receiver operating characteristic (ROC) analysis was performed to determine diagnostic value and cutoff points. A significance level of $p < 0.05$ was considered statistically significant for all analyses. Confidence intervals were calculated at a 95% confidence level.

Results

A total of 301 pregnancies were included in the study. The median age of the participants was 28 years (25–32), and the median weight was 68 kg (61.5–78). Among the pregnancies, 99.3% were singleton, and 0.7% were twin pregnancies. According to laboratory data, the median TSH level measured during the second trimester was 1.79 mIU/mL (Table 1).

When comparing the control group with the CHD group, TSH levels were found to be significantly higher in the CHD group ($p = 0.002$). However, no significant differences were observed between the groups in terms of maternal age, weight, thyroid status, history of diabetes, smoking, or trisomy ($p > 0.05$) (Table 2).

The area under the curve (AUC) was calculated as 0.627 (95% confidence interval: 0.563–0.690) and found to be statistically significant ($p < 0.001$). According to the Youden index, the optimal cutoff value for TSH was determined to be 1.795 mIU/mL, providing a sensitivity of 59.6% and a specificity of 59.4% (Table 3) (Figure 1).

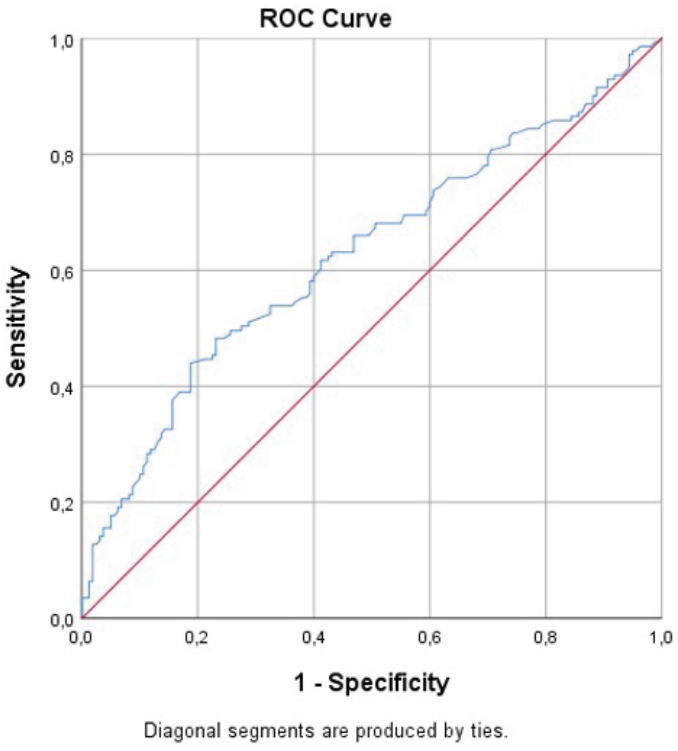

Figure 1. Receiver operating characteristic (ROC) curve for TSH levels in predicting congenital heart disease.

Table 1. Demographic, clinical, and laboratory characteristics of all participants.		
Characteristics		All participants (n=301)
Demographic data		
Maternal age (years)	28 (25–32)	
Maternal weight (kg)	68 (61.5–78)	
Number of fetuses n(%)	1	299 (99.3%)
	2	2 (0.7%)
Gestational weeks		21 (18-24)
Laboratory data		
TSH (mIU/mL)		1.79 (1.28–3.50)
T4 (ng/dl)		1.2 (0.5-3.3)
Clinical findings		
Diagnostic groups n(%)	Normal echocardiographic findings/minor anomalies (PFO, PDA, ASD, small VSD)	160 (53.2)
	VSD (At least moderate VSD)	59 (19.6)
	Pulmonary stenosis	22 (7.3)
	Arcus hypoplasia/aortic coarctation	9 (3.0)
	Tetralogy of Fallot	8 (2.7)
	Situs inversus totalis	13 (4.3)
	TGA	1 (0.3)
	Truncus arteriosus	1 (0.3)
	Pulmonary artery sling	2 (0.7)
	DORV	1 (0.3)
	HLHS	1 (0.3)
	AVSD	7 (2.3)
	Aortic stenosis/Bicuspid aortic valve	16 (5.3)
	Ebstein's anomaly	1 (0.3)
History of diabetes n(%)	No	298 (99.0)
	Yes	3 (1.0)
Smoking status n(%)	No	285 (94.7)
	Yes	16 (5.3)
History of trisomy n(%)	No	296 (98.3)
	Yes	5 (1.7)
Thyroid status n(%)	Euthyroidism	250 (83.1)
	Hypothyroidism	51 (16.9)
Cardiac anomaly classification n(%)	Healthy group and Minor CHD	160 (53.2)
	Major CHD	141 (46.8)

Abbrev.: ASD: Atrial Septal Defect, AVSD: Atrioventricular Septal Defect, CHD: Congenital Heart Disease, DORV: Double Outlet Right Ventricle, HLHS: Hypoplastic Left Heart Syndrome, PDA: Patent Ductus Arteriosus, PFO: Patent Foramen Ovale, TGA: Transposition of the Great Arteries, TSH: Thyroid-Stimulating Hormone, VSD: Ventricular Septal Defect.
Numerical variables are presented as median (25–75 percentiles). Categorical variables are presented as counts and percentages(%)..

Table 2. Comparison of participants with and without congenital heart disease.				
Characteristics		Control group (n=160)	Major CHD group (n=141)	p
Maternal age (years)		28 (25-32.75)	28 (25.5-31)	0.377*
Maternal weight (kg)		67 (62-77)	70 (60.5-78)	0.134*
TSH (mIU/mL)		1.55 (0.5-6.8)	3.05 (0.5-11.58)	0.002*
T4 (ng/dl)		1.2 (0.7-2.2)	1.3 (0.6-2.7)	0.234*
Thyroid Status	Euthyroid	144 (90)	106 (75.2)	0.001***
	Hypothyroidism	16 (10)	35 (24.8)	
History of diabetes n(%)	No	158 (98.8)	140 (99.3)	1.000**
	Yes	2 (1.2)	1 (0.7)	
Number of fetuses n(%)	1	160 (100)	139 (98.6)	0.219**
	2	0 (0)	2 (1,4)	
Smoking status n(%)	No	151 (94.4)	134 (95)	1.000***
	Yes	9 (5.6)	7 (5)	
History of trisomy n(%)	No	158 (98.8)	138 (97.9)	0.668**
	Yes	2 (1.2)	3 (2.1)	

Abbrev.: CHD: Congenital Heart Disease, TSH: Thyroid-Stimulating Hormone
Numerical variables are presented as median (minimum-maximum values). Categorical variables are presented as counts and percentages (%). *Mann-Whitney U test, ** Fisher Exact test, *** Pearson Chi-Square test. Statistical significance was set at p< 0.05. Bold values indicate statistically significant differences.

Table 3. ROC Analysis results of TSH levels for predicting congenital heart disease.

Risk Factor	AUC (95% Confidence Interval)	Cuttoff According to Youden index	p	Sensitivity (%)	Specificity (%)
TSH	0.627 (0.563-0.690)	1.795	<0.001	59.6%	59.4%

Abbrev.: AUC: Area Under the Curve, CI: Confidence Interval, TSH: Thyroid-Stimula ing Hormone.

Table 4. Logistic regression results for TSH and CHD risk.

Variable	B	S.E.	Wald	df	Sig. (p-value)	Exp(B) (Odds ratio)	95% CI for Exp(B) (Lower - upper)
TSH	0.388	0.100	15.089	1	0.000	1.474	1.212 - 1.792

Abbrev.: B: Coefficient, CHD: Congenital Heart Disease, CI: Confidence Interval, df: Degrees of Freedom, Exp(B): Exponentiated Coefficient (Odds Ratio), S.E.: Standard Error, Sig.: Significance, TSH: Thyroid-Stimulating Hormone, Wald: Wald Test Statistic.

It was found that each unit increase in maternal TSH levels increased the risk of fetal CHD by 1.47 times, and this relationship was statistically significant ($p < 0.001$) (Table 4).

In this table evaluating the impact of maternal hypothyroidism on subgroups of major CHD, differences were observed in certain subgroups such as conotruncal defects, septal defects, and valvular anomalies in the hypothyroid group; however, these differences did not reach statistical significance ($p > 0.05$) (Table 5).

Table 5. Distribution of embryologic and clinical cardiac classifications and TSH levels among participants with and without hypothyroidism.

Characteristics	Euthyroid (n=106)	Hypothyroidism (n=35)	p
TSH Levels (mIU/mL) median (min-max)	1.55 (0.5-2.96)	4.26 (3.03-11.58)	<0.001*
Embryologic heart classification			
Conotruncal (Fallot, TGA, DORV, Truncus, pulmonary artery sling)	8 (7.5%)	5 (14.3%)	0.157**
Left ventricular outflow obstruction (Aortic coarctation, arcus hypoplasia, HLHS, aortic stenosis)	6 (5.7%)	6 (17.1%)	
Valvular defects (pulmonary stenosis, bicuspid aorta, AVSD, Ebstein's anomaly)	34 (32.1%)	10 (28.6%)	
Septal defects (VSD)	48 (45.3%)	11 (31.4%)	
Situs anomalies (Situs inversus)	10 (9.4%)	3 (8.6%)	
Detailed cardiac classification			
VSD	48 (45.3%)	11 (31.4%)	0.291**
Pulmonary stenosis	17 (16.0%)	5 (14.3%)	
Aortic coarctation/arcus hypoplasia	5 (4.7%)	4 (11.4%)	
Fallot tetralogy	4 (3.8%)	4 (11.4%)	
Situs inversus totalis-dextrocardia	10 (9.4%)	3 (8.6%)	
TGA	0 (0.0%)	1 (2.9%)	
Truncus arteriosus	1 (0.9%)	0 (0.0%)	
Pulmonary artery sling	2 (1.9%)	0 (0.0%)	
DORV	1 (0.9%)	0 (0.0%)	
HLHS	0 (0.0%)	1 (2.9%)	
AVSD	6 (5.7%)	1 (2.9%)	
Aortic stenosis/bicuspid aorta valve	11 (10.4%)	5 (14.3%)	
Ebstein's anomaly	1 (0.9%)	0	

Abbrev.: ASD: Atrial Septal Defect, AVSD: Atrioventricular Septal Defect, CHD: Congenital Heart Disease, DORV: Double Outlet Right Ventricle, HLHS: Hypoplastic Left Heart Syndrome, PDA: Patent Ductus Arteriosus, PFO: Patent Foramen Ovale, TGA: Transposition of the Great Arteries, TSH: Thyroid-Stimulating Hormone, VSD: Ventricular Septal Defect.
*Mann Whitney U test, **Fisher Exact test. Statistical significance was set at $p< 0.05$. Bold values indicate statistically significant differences. Categorical variables are presented as counts and percentages (%).

Discussion

Our study results, consistent with the literature, indicate an association between maternal hypothyroidism and fetal CHD. Through regression analysis, we determined that each one-unit increase in TSH levels raises the risk of fetal CHD by 1.47 times.

Maternal hypothyroidism is a frequently encountered clinical condition, with its prevalence ranging from 2% to 17%, influenced by factors such as diagnostic criteria, the stage of pregnancy, and regional differences [22-24]. Numerous studies have indicated an association between maternal hypothyroidism and a heightened risk of congenital heart defects in the fetus, as well as cardiovascular conditions later in life during long-term follow-up [20, 25, 26]. The

precise pathways through which maternal hypothyroidism may lead to fetal heart disease remain unclear. However, it is thought to disrupt the normal developmental processes of the fetal heart in various ways. Research has also demonstrated that cardiac remodeling is influenced by the reactivation of embryonic genes, a process that may be influenced by thyroxine [20]. Hypothyroid mothers have been found to experience placental dysfunction, suggesting that thyroid hormones may have both direct and indirect roles in the maturation of the cardiovascular system. Additionally, thyroid hormones play a critical role in the formation of cardiac septa and the development of outflow tracts [27,28].

Ahad et al. [28] investigated the impact of maternal hypothyroidism on both the structural and functional aspects of the fetal heart. This study holds particular significance as it was conducted in Pakistan, where the prevalence of hypothyroidism is notably high. Unlike our study, they did not find a significant difference between the groups in terms of CHDs. However, in their evaluation of functional parameters, a significant difference was observed only in isovolumetric relaxation time. Additionally, while no significant differences in CHDs were found, the study identified significant differences in tricuspid, mitral, and aortic annulus measurements between the groups, with lower measurements reported in the hypothyroid group [28]. This reduction was particularly emphasized in the fetal left heart structures of the hypothyroid group. However, it is believed that this reduction does not lead to structural stenosis or hypoplasia. In our study, when groups were formed based on thyroid status, no significant impact of maternal hypothyroidism was observed in the analysis comparing subgroups of CHDs, particularly those related to left heart structures.

In a cross-sectional case-control study conducted by Grattan and colleagues over a 17-month period, a significantly higher prevalence of CHD was observed in infants born to mothers with maternal hypothyroidism [29]. Regression analysis revealed that maternal hypothyroidism was associated with a 1.68-fold increased risk of CHD [29]. In our study, we found that each one-unit increase in maternal TSH levels increased the risk of fetal CHD by 1.47 times. Furthermore, in the same study by Grattan et al. [29], heterotaxy, a subgroup of CHDs, was reported to occur significantly more frequently in the maternal hypothyroidism group. However, in our study, no significant differences were found among the subgroups of CHDs.

In the studies conducted by Liu et al. [18] and Browne et al. [21], it was similarly observed that maternal thyroid disorders, without detailed categorization, significantly increased the risk of fetal CHDs. Liu et al. [18] reported the most significant associations between maternal thyroid disorders and conotruncal defects, while Browne et al. [21] highlighted a notable relationship with left ventricular outflow tract obstruction heart defects. However, since these studies did not differentiate between hypothyroidism and hyperthyroidism, it is unclear which specific thyroid dysfunction contributed to these outcomes. As a result, a direct comparison with our study cannot be made.

In a nationwide population-based cohort study using Danish national registry data, Miao et al.[30] observed a significant increase in the incidence of cardiovascular diseases, such as hypertension, arrhythmias, and acute myocardial infarction, in children born to mothers with hypothyroidism. However, since infants with congenital anomalies were excluded from the study design, the relationship between maternal hypothyroidism and CHDs could not be assessed [30].

In their study, Dong et al. identified an association between elevated maternal FT4 levels and an increased risk of fetal CHDs. Additionally, they demonstrated that the free-to-total thyroxine proportion serves as a better indicator for this relationship. This association was found to be stronger when these markers were assessed between the 12th and 18th weeks of pregnancy, while measurements taken after the 18th week showed no significant changes [19]. In our study, while we found a significant relationship between elevated TSH levels and CHDs, FT4 levels did not exhibit any significant effect. Based on the findings of Dong et al.[19], evaluating thyroid function tests between the 12th and 18th weeks of gestation might have influenced the FT4 results in our patient population.

Limitations of the study

This study primarily focused on evaluating maternal hypothyroidism based on TSH and FT4 parameters, without accounting for potential risk factors such as diet, genetic predisposition, and environmental influences. Additionally, the small sample size, reliance on data from a single center, and the relatively short study period are significant limitations that should be acknowledged. Additionally, we did not gather information on the duration of maternal hypothyroidism before achieving a state of euthyroidism, nor did we evaluate the extent of fetal exposure to maternal hypothyroidism during this time. Furthermore, our study does not provide information on whether patients received medication or were monitored clinically without treatment. These factors are significant limitations, as they may impact fetal outcomes and should be taken into account in future research. We believe that to better understand the relationship between maternal hypothyroidism and fetal cardiac health, larger-scale,

multicenter, and prospective studies are needed. Such studies should also investigate the effects of maternal hypothyroidism on fetal cardiac rhythm and functional heart disorders.

In conclusion, This study suggests a potential association between maternal hypothyroidism and fetal structural heart diseases, emphasizing the importance of routine thyroid function screening during the second trimester of pregnancy. Future large-scale studies are needed to further elucidate this relationship and to better understand how optimizing maternal thyroid function may positively impact fetal cardiac health.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

Ethics approval

The study was approved by the Institutional Ethics Review Board for Clinical Research of Giresun Education and Research Hospital Ethics Committee (approval date: 25.12.2024; approval number: 2024/02). Written informed consent was obtained from the patients prior to inclusion in the study.

Author contributions

Conceptualization, visualization, investigation, formal analysis, data curation writing – original draft: BY, methodology, resources, supervision writing – review & editing: MA,BY, Each author reviewed and approved the published version of the study.

References

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002; 39: 1890-900.
2. Kula S, Cevik A, Olguntürk FR, Tunaoğlu FS, Oğuz AD, Ilhan MN. Distribution of congenital heart disease in Turkey. Turk J Med Sci 2011; 41: 889-893.
3. Botto LD. Epidemiology and prevention of congenital heart defects. Cong Heart Dis Karger Publishers; 2015:28-45.
4. Gilboa SM, Salemi JL, Nembhard WN, Fixler DE, Correa A. Mortality resulting from congenital heart disease among children and adults in the United States, 1999 to 2006. Circulation 2010; 122: 2254-63.
5. Petrini J, Damus K, Johnston RB. An overview of infant mortality and birth defects in the United States. Teratology 1997; 56: 8-10.
6. Petrini J, Damus K, Russell R, Poschman K, Davidoff MJ, Mattison D. Contribution of birth defects to infant mortality in the United States. Teratology 2002; 66: S3-S6.
7. Yang Q, Khoury MJ, Mannino D. Trends and patterns of mortality associated with birth defects and genetic diseases in the United States, 1979–1992: An analysis of multiple-cause mortality data. Gen Epidemiol 1997; 14: 493-505.
8. Atiq M. Early Diagnosis of Congenital Heart Disease Improves Outcome. LNJPC 2020; 2 : 39-42.
9. Sun R, Liu M, Lu L, Zheng Y, Zhang P. Congenital heart disease: causes, diagnosis, symptoms, and treatments. Cell Biochem Biophys 2015;72:857-60.
10. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C 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: 315-89.
11. van den Boogaard E, Vissenberg R, Land JA, van Wely M, van der Post JA, Goddijn M et al. Significance of (sub) clinical thyroid dysfunction and thyroid autoimmunity before conception and in early pregnancy: a systematic review. Hum Reprod Update 2011; 17: 605-19.
12. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999; 341: 549-55.
13. Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle O. Overt and subclinical hypothyroidism complicating pregnancy. Thyroid 2002; 12: 63-8.
14. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. Arch Gynecol Obstet 2010; 281: 215-20.
15. León G, Murcia M, Rebagliato M, Álvarez-Pedrerol M, Castilla AM, Basterrechea M et al. Maternal thyroid dysfunction during gestation, preterm delivery, and birthweight. The Infancia y Medio Ambiente Cohort, Spain. Paediatr Perinat Epidemiolr 2015; 29: 113-22.
16. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011; 21: 1081-125.
17. Leung AS, Millar LK, Koonings PP, Montoro M, Mestman JH. Perinatal outcome in hypothyroid pregnancies. Obstet Gynecol 1993; 81: 349-53.
18. Liu S, Joseph KS, Lisonkova S, Rouleau J, Van den Hof M, Sauve R et al. Association between maternal chronic conditions and congenital heart defects: a population-based cohort study. Circulation 2013; 128: 583-9.

19. Dong J, Peng T, Li M-Q, Xie F, Wu J-N. Association between Maternal Thyroxine and Risk of Fetal Congenital Heart Defects: A Hospital-Based Cohort Study. Int J Endocrinol 2022; 2022(1): 3859388.
20. Zhang Y, Zhang L, Zhao W, Li N, Chen G, Ge J et al. Cardiac structural and functional remodeling in the fetuses associated with maternal hypothyroidism during pregnancy. Matern Fetal Neonatal Med 2023; 36: 2203796.
21. Browne ML, Rasmussen SA, Hoyt AT, Waller DK, Druschel CM, Caton AR et al. Maternal thyroid disease, thyroid medication use, and selected birth defects in the National Birth Defects Prevention Study. Birth Defects Res A Clin Mol Teratol 2009; 85: 621-8.
22. Ghanbari M, Ghasemi A. Maternal hypothyroidism: An overview of current experimental models. Life sciences. 2017;187:1-8.
23. Gupta P, Jain M, Verma V, Gupta NK. The study of prevalence and pattern of thyroid disorder in pregnant women: a prospective study. Cureus. 2021;13(7)
24. Ezzeddine D, Ezzeddine D, Hamadi C, et al. Prevalence and correlation of hypothyroidism with pregnancy outcomes among lebanese women. Journal of the Endocrine society. 2017; 1: 415-22.
25. Sohail R, Yasmin H, Tasneem N, Khanum Z, Sachdeve PS, Pal SA et al. The Prevalence of Subclinical Hypothyroidism During Early Pregnancy in Pakistan: A Cross-Sectional Study. Cureus 2021; 13: e20316.
26. Turunen S, Vääräsmäki M, Männistö T, Hartikainen AL, Lahesmaa-Korpinen AM, Gissler M et al. Pregnancy and Perinatal Outcome Among Hypothyroid Mothers: A Population-Based Cohort Study. Thyroid 2019; 29: 135-41.
27. Mittag J, Lyons DJ, Sällström J, Vujovic M, Dudazy-Gralla S, Warner A et al. Thyroid hormone is required for hypothalamic neurons regulating cardiovascular functions. J Clin Invest 2013; 123: 509-16.
28. Abdul Ahad FA, Maria Murtaza, Midhat E Zahra Naqvi, Mehnaz Atiq. Cardıac ınvolvement ın fetuses of mothers wıth hypothyroıdısm. Res Medical Sci Rev 2024; 2: 1929-35.
29. Grattan MJ, Thomas DS, Hornberger LK, Hamilton RM, Midodzi WK, Vohra S. Maternal hypothyroidism may be associated with CHD in offspring. Cardiol Young 2015; 25: 1247-53.
30. Miao M, Liu H, Yuan W, Madsen N, Yu Y, László KD et al. Association of Maternal Hypothyroidism With Cardiovascular Diseases in the Offspring. Front Endocrinol (Lausanne) 2021; 12: 739629.