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Original Research Article

Relationship between infant hypothyroidism and maternal thyroid disease

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ABSTRACT

Background: Due to the very high complications of neonatal hypothyroidism in the country, neonatal screening program is performed for timely diagnosis and treatment of neonates. The aim of this study to investigate the relationship between infant hypothyroidism and maternal thyroid disease.
Methods: This cross-sectional study was done on 195 neonates with a diagnosis of hypothyroidism. Necessary data were collected by a checklist and then analyzed by statistical methods in statistical package for the social sciences (SPSS) version 21 by statistical methods.
Results: Of all mothers, 21.0% had a history of thyroid disease. There was no statistically significant relationship between maternal age and infant thyroid stimulating hormone (TSH). There was no significant relationship between the history of maternal hypothyroidism and maternal hypothyroidism (during experiments) with the amount of TSH in the newborn. There was a direct and significant relationship between maternal TSH level and maternal free T4. But there was no statistically significant relationship between infant TSH level and maternal TSH level and free T4. There was no significant difference in neonatal TSH levels with maternal anti-TPO status. There was no significant relationship between the history of maternal diabetes and the history of maternal hypertension with neonatal TSH. There was no significant difference in neonatal TSH levels by maternal thyroid status.
Conclusions: In the present study, no significant relationship was found between the incidence of neonatal hypothyroidism and the presence of thyroid disease in mothers. The existence of different genetic and environmental factors and the significant impact of each of these factors can justify this result.

Keywords: TSH, Hypotension, Neonatal hypothyroidism

INTRODUCTION

Hypothyroidism or hypothyroidism is an endocrine disorder in which the thyroid gland does not produce enough thyroid hormone.[1] Neonatal hypothyroidism is a condition in which there is a lack of thyroid hormone from birth, which may initially be asymptomatic or with symptoms such as infant hypotonia, sleepiness, weak or harsh crying, bowel dysfunction, severe jaundice, and body temperature it should be low which, if not diagnosed and treated after a few months, will cause problems such as growth disorder and permanent mental retardation in the baby.[2] In the study conducted by Mirzarahimi and colleagues in Ardabil province on 160 babies, they showed that the prevalence of permanent hypothyroidism in Ardabil province was 1 in 4000.[3] Considering the complications of this disease and the importance of its timely diagnosis and treatment for babies up to 6 weeks old, screening for congenital thyroid disease is done from the heel and suspicious cases are diagnosed and treated. If

the baby's TSH is above 20, hypothyroidism is considered and treated. If it is between 10 and 20 mU/l, serum TSH is requested at the age of 2-3 weeks, if TSH is between 5 and 10 mU/l, repeat the heel sample test, and if it is below 5 mU/l, it is necessary there is no other action, but if it is above 5 mU/l, serum TSH test will be done and if it is disturbed, it will be treated.[4] If treated with levothyroxine in this period, the baby will not have any problems in terms of intelligence and growth, but if it is delayed until 6 months, the patient will develop cretinism.[5]

Several studies have been conducted in relation to hypothyroidism in mother and baby and its effects on the baby as well as on the fetus during pregnancy. In a study conducted by Goldman and his colleagues on the effect of maternal hypothyroidism on the outcome of pregnancy on 10,990 pregnant mothers in the first and second trimesters of pregnancy, they showed that hypothyroidism in the first trimester was associated with premature birth and in the second trimester with gestational diabetes and hypothyroidism in pregnancy causes disorders in the brain development of the fetus.[6] In a study that was conducted on the effect of maternal hypothyroidism on fetal growth and thyroid activity status on 27,386 full-term infants, it was shown that infants with intrauterine growth disorder and serum TSH levels were higher than the control group.[7] Considering the very high complications of neonatal hypothyroidism in the country, for the timely diagnosis and treatment of newborns, a newborn screening plan is carried out. Various studies have shown the impact of maternal hypothyroidism in the form of pregnancy complications and its adverse effects on the health and growth of the fetus, but no study has investigated the relationship between neonatal hypothyroidism and maternal thyroid status. The aim of this study was to investigate the relationship between infant hypothyroidism and maternal thyroid disease.

METHODS

This cross-sectional descriptive study was carried out in the year 2021 in the department of children's diseases of Bo Ali hospital in Ardabil. The statistical population of the present study was infants diagnosed with hypothyroidism. Mothers in the age group 15-49 years and term neonates were entered the study and pre-term neonates and the file of patients with missing paraclinical data in tests were excluded from the study. For sampling, Cochran's sampling formula with limited population size was used, according to a similar study and considering the number of statistical populations in Ardabil city, which is equal to 400 people, and with a confidence level of 95%, the number of sample was calculated to be 195 people. To collect data from a checklist including the variables of mother's age, baby's weight and height, family history of thyroid disease, hypothyroidism and hyperthyroidism of the mother, TSH, free T4, anti-TPO, gestational age, pregnancy grade, gestational diabetes, gestational blood pressure and control thyroid, gestational age at the time of birth and sex of the baby were completed by checking the files of the studied samples. Collected data were analyzed by t-test to compare the mean of quantitative variables between two groups, and Pearson's correlation coefficient to check the correlation of quantitative variables in statistical package for the social sciences (SPSS) version 21. The significant level was set as $p<0.05$.

RESULTS

In this study, 56.9% of the samples were from Ardabil city. 25.6% of parents of babies had a family relationship. A history of thyroid disease was observed in 19.5%, a history of diabetes in 1.5%, and a history of hypertension in 6.2% of mothers. The average age of the study mothers was 28.72 years with a standard deviation (SD) of 5.47 years (Table 1).

Table 1: Distribution of demographic variables of the study.

Qualitative variable	Number	Percent
Residence place		
Ardabil	111	56.9
Other cities	84	43.1
Family relationship of parents		
Yes	50	25.6
No	145	74.4
Pregnancy turn		
First	78	40.0
Second	69	35.4
Third	40	20.5
Fourth	5	2.6
Fifth	3	1.5
Number of children		
1	79	40.5
2	80	41.5
3	34	17.4
4	2	1.0
Mother's underlying disease		
Thyroid	38	19.5
Diabetes	3	1.5
High blood pressure	12	6.2
History of drug treatment of mother's thyroid disease		
Hyperthyroidism	4	1.2
Hypothyroidism	34	17.4
No	157	80.5
Family history of maternal thyroid disease		
Yes	41	21.0
No	154	79.0
Gender of the baby		
Boy	115	59.0
Girl	80	41.0
Variable (quantity)	**Mean**	**SD**
Mother's age	28.22	5.47
Height of the baby	48.23	3.75
Baby's weight	3041.65	683.69

According to Pearson's correlation test, there was no statistically significant relationship between mothers' age and newborn's TSH. There was no significant relationship between the mother's history of hypothyroidism and the mother's hypothyroidism (during the tests) with the baby's TSH level. There was a direct and significant relationship between mother's TSH level and mother's free T4 level. There was no statistically significant relationship between the level of TSH of the newborn and the level of TSH and Free T4 of the mother. According to the t-test, no significant difference was seen in the TSH level of the baby according to the anti-TPO status of the mother. According to the t-test, there was no significant relationship between the mother's history of diabetes and the mother's history of high blood pressure with the baby's TSH level. According to the analysis of variance (ANOVA) test, no significant difference was seen in the TSH level of the baby according to the mother's thyroid status.

DISCUSSION

From early pregnancy, the fetus needs thyroid hormone for many developmental processes. Optimal thyroid hormone levels are achieved through an engaging partnership between mother and developing child. It has been shown that maternal thyroid hormone passes through the placenta during pregnancy.[8-10]

In addition, the fetal thyroid gland produces small amounts of thyroid hormone from about 10 to 11 weeks of gestation. However, only after the activation of the fetal hypothalamic-pituitary-thyroid (HPT) axis does fetal thyroid hormone production increase several weeks later-around 20 weeks of gestation. Until then, the fetus is dependent on small amounts of the mother's thyroid hormone, which is obtained through the placenta.[11,12] There is considerable evidence that low as well as high maternal plasma thyroid hormone concentrations in early pregnancy, possibly leading to abnormal fetal thyroid hormone levels, are associated with neurocognitive dysfunction in offspring.[13,14] Furthermore, abnormal fetal plasma thyroid hormone concentrations during pregnancy may alter postnatal HPT axis function not only during the neonatal period but also long after.[15-17] Low or high concentrations of maternal plasma thyroid hormone are mainly caused by maternal thyroid dysfunction, which leads to transfer of thyroid hormone through the placenta. Maternal thyroid dysfunction can be hypothyroidism or hyperthyroidism. In addition to disease-related abnormal maternal thyroid hormone concentrations affecting fetal thyroid hormone levels, thyroid function and fetal and neonatal thyroid hormone levels can be impaired by maternal thyroid autoantibodies, and by antithyroid drugs used by the mother to treat hyperthyroidism. Because of the significant complications and even fatal outcome, fetal and neonatal hyperthyroidism are considered serious conditions, even though well-designed observational studies on their clinical and developmental outcomes are lacking.[18-20] This study was conducted with the aim of investigating the relationship between neonatal hypothyroidism and maternal thyroid disease in Ardabil city. A study that had not been conducted in this area, and other studies had not reported the same and aligned results, and the recommendation of previous researchers was to conduct more studies in order to achieve definitive results. In the present study, there was no correlation between the history of maternal thyroid disease and neonatal hypothyroidism. Further investigations even showed the existence of an inverse relationship between the mother's TSH and the baby's TSH, although this comparison was not significant. Therefore, it can be concluded that neonatal hypothyroidism is a multi-factorial disease and the history of congenital thyroid disease as an independent factor has no effect on the severity of this disorder at birth. Medda and her colleagues, who investigated the risk factors of congenital hypothyroidism, have pointed out the existence of a very small and insignificant relationship between the existence of a family history of thyroid disease and the occurrence of neonatal hypothyroidism.[21] At the end of the study, they found many risk factors involved in the etiology of neonatal hypothyroidism and genetic and environmental factors involved in the occurrence of this disorder. On the other hand, in the studies that found a connection between the occurrence of congenital hypothyroidism and maternal thyroid disorder (including maternal antithyroid drugs, iodine deficiency or excessive iodine), this disorder was mostly attributed to transient hypothyroidism. In the study of Ismail Nesab and his colleagues under the title of investigating the risk factors of congenital hypothyroidism in babies born in Kurdistan province, as in the present study, no significant relationship was found between the history of thyroid disease in the mother and the incidence of hypothyroidism in the newborn.[22] But the interesting point was that in the above study, a significant relationship was found between the history of thyroid disease in the family (mother, father, first degree relatives) and the severity and incidence of hypothyroid disease in newborns, which according to this result; It can be considered necessary to investigate this relationship in Ardabil province in the future. Anyway, it seems that the existence of such a history in the family can be caused by genetic issues as well as the amount of iodine intake. Therefore, the history of thyroid diseases in other family members can probably be one of the risk factors of congenital hypothyroidism and its severity. As discussed earlier, genetics is one of the effective factors in this disease, and the mere presence of this disease in the mother of the baby will not determine the rate of its occurrence in the baby, but this history should be taken into account with genetic issues, including the presence of this disease in the baby check other family members. In any case; If there is a strong history of thyroid disease, and not just the presence of this disease in the mother herself, more follow-up should be done on the pregnant mother. The role of genetic diseases affecting hypothyroidism such as dyshormonogenesis with recessive autosomal transmission has been determined.[23] Also, the presence of history of thyroid disorders in first degree family members of hypothyroid babies has been shown in other studies.[24,25] Considering that Iran is known as a country free from

iodine disorder; The role of genetic and family factors can be considered more than environmental factors such as deficiency or excess of iodine.[26] Of course, it is necessary to investigate more in terms of the effect of iodine on the occurrence of this disorder in Ardabil province in order to express a more precise opinion. In the present study; No significant correlation was found between maternal anti-TPO level and the occurrence of congenital hypothyroidism. In the study of Ozdemir et al, they showed that maternal TPO levels, especially high titers, are transmitted to infants and are clinically relevant. Also, in this study, the average level of TSH was significantly higher in the mothers of hypothyroid infants, which indicates that the disease was not properly controlled in the mothers of the above study. While in the present study, this rate was not significant, which is probably due to the good screening and control of this disease in the mothers of Ardabil.[27]

In the present study, there was no significant relationship between maternal age, history of hypertension and maternal diabetes, and TSH level of hypothyroid infants. This is while Zhou et al found a significant relationship between the presence of these variables in the mother and the incidence of hypothyroidism in the newborn.[28] Therefore, considering the present study as a supplement to the mentioned study; It can be said that the existence of these risk factors are effective in the occurrence of hypothyroidism in infants, but among infants with this disease; From a statistical point of view, there is no significant difference between the TSH levels of babies and mothers with and without diabetes and high blood pressure, as well as the age of the mothers. The results of this study showed that out of 195 patients with congenital hypothyroidism, 115 (59.0%) were boys and 80 (41.0%) girls. Considering that the sex ratio of people born in Ardabil (according to the census of 2015) is 51 to 49, therefore it is expected that the sex ratio of the affected people is also in the same range, while the percentage of male patients was significantly higher than that of female patients. In most of the studies conducted in the field of investigating the risk factors of congenital hypothyroidism, the female gender has been introduced as a risk factor. Among the studies conducted in Italy, white race, female sex, twin pregnancy and genetics have been introduced as risk factors for congenital hypothyroidism.[29] In another study conducted in the United States of America, the incidence of this disease was reported to be higher in females than in males.[30] In another study conducted in 2010 in America, the increase in the incidence of congenital hypothyroidism in recent years was the same in both sexes, and only in a study conducted in Texas, similar to our study, this rate increased more among boys.[31] The frequency of patients shows that boys are more at risk of neonatal hypothyroidism in our region, and contrary to the global trend that has introduced female sex as a risk factor for hypothyroidism, this is not the case in Ardabil. The cause of this problem is unclear and needs more studies. Lack of cooperation and follow-up of some patients for testing and also some errors and problems in data are some limitations of this study.

CONCLUSION

Based on the results of the present study, no significant relationship was found between neonatal hypothyroidism and the presence of thyroid disease in mothers. It is suggested to conduct a study on iodine levels in children with neonatal hypothyroidism and their mothers. It is also recommended to carry out a study by investigating the presence of thyroid disease in family members and first degree relatives in infants with neonatal hypothyroidism. It is also recommended to conduct a similar study in other provinces of the country and compare the results.

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