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The influence of thyroid function disorders on pregnant women on the Apgar scale and psychomotor development of the child in the first 18 months of life

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ABSTRACT

Introduction. In the prenatal period, there are many exogenous and endogenous factors, which adversely affect the normal development of the fetus and may affect the further development of the child. The impaired reference level of thyroid hormones pregnant woman may entail a number of complications, especially in the first trimester of pregnancy, wherein the process takes place organogenesis and the formation of the nervous system.

Goal. The overall objective of the work is to verify the correlation between hypothyroidism and child developmental problems in the first eighteen months of life and the Apgar scale.

Materials and methods. The study included 200 pregnant women aged 17 to 40 years of age. The research tool was an online, proprietary questionnaire, which has been placed in social groups, which included pregnant women struggling with hypothyroidism.

Conclusions. Developmental disorders up to 18 months of children age occurred in 45% of women with thyroid dysfunction, of which 43% related to symptoms of neurological problems including 56% of impaired muscle tone. The present study demonstrates that the final outcome Apgar does not forecast problems in the course of further development of the

child up to 18 months of age. Significant further research, which will help establish the presence of mechanisms adverse impact on offspring and pregnancy outcomes.

Keywords: hypothyroidism; pregnancy; Apgar; physiotherapy; child development; dysfunction of the child.

INTRODUCTION

One of the common problems among pregnant women in the area of thyrology is hypothyroidism, which occurs at a frequency of 0.5% to 3.5% of the population[1]. Hypothyroidism is divided into full hypothyroidism (referred to as elevated levels of thyroid-stimulating hormone [TSH] and decreased concentration of hormone thyroxine [FT4], or TSH > 10mIU / 1 FT4 reference range) subclinical hypothyroidism (defined as the TSH concentration above the upper limit FT4 within the reference range) and insulated hypothyroidism (referred to as FT4 decreased concentration of hormone and TSH hormone concentration within the reference range)[2,3,4]. The main causes of hypothyroidism in pregnant women pertain to iodine deficiency and chronic lymphocytic Hashimoto's thyroiditis. Underlying hypothyroidism is also thyroidectomy, subtotal thyroidectomy, congenital hypothyroidism[2,5]. In the prenatal period, the function of thyroid is essentially modified. Physiological changes are related to increased by 50% production of thyroxine (T4) and triiodothyronine (T3), an increase of blood levels globulin (TBG), the occurrence of human chorionic gonadotropin (hCG), modification of the metabolism of iodine and a decrease of the immune readiness. All of the compensation of an organism is necessary to maintain a euthyreosis. If the thyroid pregnant woman is not able to adapt to the physiological changes in question, it is possible to emerge of hypothyroidism. Due to physiological changes in the secretion of hormones, the importance of the determination reference range for different trimesters and different from the rest of the population is shown[6,7]. Diagnosis of hypothyroidism in pregnant women includes determination of the level of TSH. According to the Minister of Health Regulation on the organizational standard of perinatal care, a pregnant woman must have the designated TSH up to the 10th week or up to the first doctor's consultation[8]. If a pregnant woman is detected with an elevated level of TSH the next step is the determination of FT4 and antibodies against thyroid peroxidase (anti-TPO). The term anti-TPO is crucial because their detection may increase the risk of hypothyroidism in pregnant women with euthyreosis and evidence of chronic lymphocytic Hashimoto' thyroiditis[9]. Hashimoto is one of the autoimmune diseases and relates to 2-17% of pregnant women, according to the ATA[3]. Along with the presence of anti-TPO antibodies, it is more likely to experience problems related to miscarriages, deliveries before 38 weeks and isolated occurrence of hypothyroidism in pregnant women, which remain in euthyreosis[10].

Recommendations made to treat hypothyroidism in pregnant women are different in different types. Thyroid hormones and TSH of a pregnant woman are an essential element in the proper course of pregnancy and normal fetal development. They have a primary role in the formation of neural tissue, differentiation of nerve cells, neural migration, metabolic regulation. Additionally involved in cellular homeostasis and to allow a proper neuromuscular maturation of bone and other tissues of the body[9,10,11,12]. Thyroid hormones play an essential role in the first trimester of pregnancy, and in this period there is a process of

organogenesis and the formation of the nervous system. Another important aspect is the relation of pregnant's fetal hormone from 16 to 20 weeks of pregnancy. After 20 weeks the thyroid of a fetus produces its own hormones but axis - hypothalamic-pituitary-thyroid is unable to fully cover all the requirements for hormones and the fetus continues to use hormones of pregnant's thyroid but to a lesser extent. The hypothalamic-pituitary axis of the thyroid gland of the fetus is fully functioning after birth[3,13,14].

One of the permanent, analyzed up to the present day, elements in the field of science is the Apgar scale. It is one of the most widely used screening treatment in newborns, soon after birth. Developed in 1952 by Dr. Virginia Apgar. The study is to determine the numerical result, predetermined time, 1-5-10 minutes of life. The doctor or midwife gives points to the newborn from 0 to 2 for each value of the evaluation parameter. Evaluated are heart rate, breathing rate, muscle tone, reflexes-in reaction to the stimuli, the color layers of the skin. Based on received results disorders are determined, which include cyanosis, hypoperfusion, bradycardia, hypotension, respiratory depression or apnea. For the correct score of the newborn is adopted from 8 to 10, scoring from 4 to 7 is average, however, the score from 0 to 3 is bad[15].

Objectives

The main aim of the work is to verify the correlation between the diagnosis of the type of hypothyroidism in pregnancy and result in the Apgar scale and also the occurrence of dysfunction of a child's development up to 18 months of age.

The specific objectives are analyzed by the relationship between:

- diagnosed chronic lymphocytic Hashimoto's thyroiditis of a pregnant woman, and problems in child development up to 18 months of age, the results of the Apgar score, birth weight, birth week,
- the final result of the Apgar score, and problems in child development up to 18 months of age.
- a specific type of pregnant women's hypothyroidism, and the occurrence of problems during the development of the child up to 18 months of age, the results of the Apgar score, birth weight.

Materials and methods

The study included 200 pregnant women from June to October 2019. The research tool was an online, proprietary questionnaire, which has been placed in social groups, which included pregnant struggling with hypothyroidism. The questionnaire consists of 17 questions, including 7 open-ended and 10 closed-ended (single or multiple choice). The questions in the questionnaire concern pregnant women's (body weight and age at the time of becoming pregnant) and newborn's (birth weight, birth week, Apgar score) basic data, as well as the type of hypothyroidism, the time of its diagnosis and treatment. Additionally, questions were asked about the reported objections by the pediatrician on psychomotor development of the child in the first 18-hundred months of age and the need to use the services of a physiotherapist children. pregnant, reported that in a survey of miscarriage or results not remember the Apgar score were not included in the study. Due to lack of sufficient data to conduct a statistical analysis (one person only as indicated Apgar score of 0 to 3 which

consequently is not allowed to perform the analysis) score of 0 to 3 was excluded from these studies.

Results questionnaires collected were subjected to statistical analysis. Test was used U Mann-Whitney, the Kruskal-Wallis and test chi². The analysis was performed using PQStat Software Version: 1.6.8 P7909081214. P-value <0.05 was considered statistically significant value.

Results

Basic data on the examined pregnant women and their children are shown in Table 1.

Data metric	Min.	Max.	M	Me
Age at time of becoming pregnant	17	40	29,24	29
Weight at the time becoming pregnant	41	117	66.84	65
Week of birth	29	42	39.18	39
Birth weight of a child	1190	5000	3,467.85	3460
The Apgar score (final result)	3 (6)	10	9.63	10

Table 1. Basic data metric of a surveyed pregnant women and newborns.

Figure 1 shows a percentage classification of the test group by the Apgar score. From all of the respondents, the largest number of (97.5%) indicated a score of 7 to 10 according to the Apgar score (in good condition).

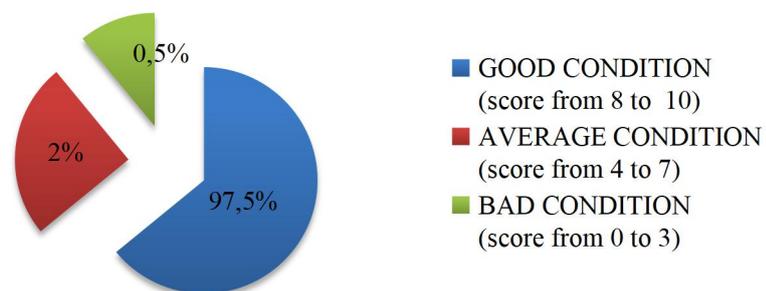


Figure 1. The division of the group by the Apgar score.

Using figure 2, a percentage breakdown of the studied group according to the general occurrence of problems during development to eighteen months of age was presented. The largest amount of the surveyed women (55%) has not confirmed any dysfunction of a child up to 18 months of age. The percentage layout of health problems in various fields of medicine is presented using figures 3. Given that most health problems have been reported in the field of neurology, figure 4 illustrates the percentage distribution of neurological problems.

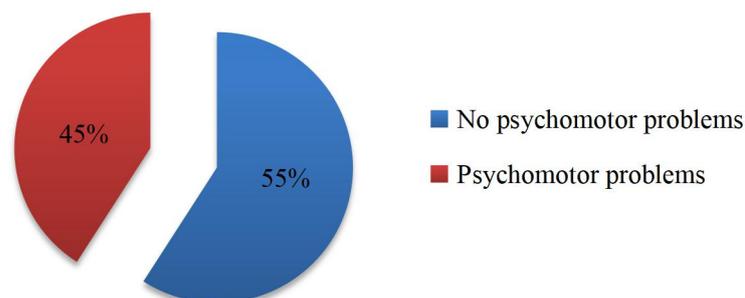


Figure 2. Layout of the studied group according to the general problems of psychomotor up to 18 months of age.

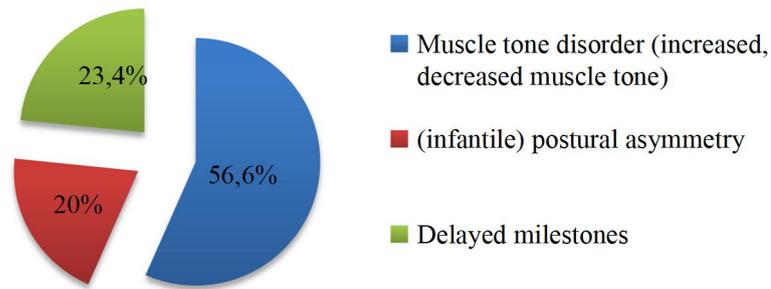


Figure 3. Percentage layout of health problems in particular medical fields.

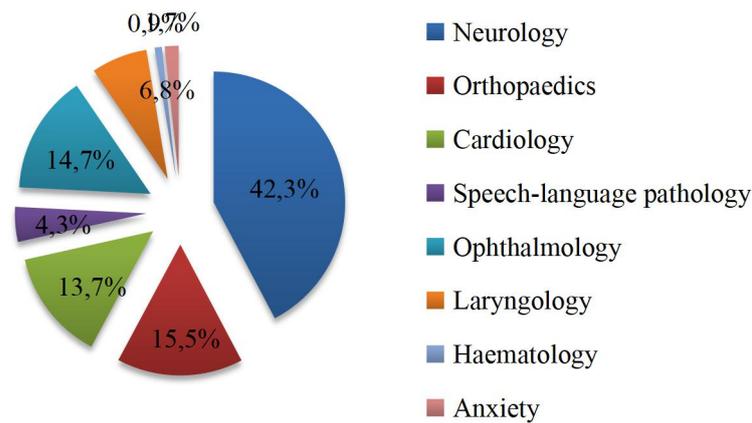


Figure 4. Development problems division of the health in the field of neurology.

The analysis carried out between the results obtained from the Apgar score, and the occurrence of problems in children during development to eighteen months of age showed no statistical significance (Table 2).

The occurrence of developmental problems of the child up to 18 months of age	The child's condition in the Apgar scale				The significance level $p > 0.05$
	Good condition		Average condition		
	n	% from the group	n	% from the group	
Yes	87	45	3	43	p = 0.908
No	106	55	4	57	

Table 2. The correlation between the Apgar score, and the occurrence of developmental problems of the child up to 18 months of age.

The percentage layout of the tested groups according to their diagnosed Hashimoto is represented by figure 5. The greatest number of respondents diagnosed is a group with diagnosed chronic lymphocytic Hashimoto's thyroiditis (63.5%). Tables 3,4,5,6 are showing the results of the statistical analysis between Hashimoto and selected parameters. Statistical significance was demonstrated between the diagnosis of Hashimoto and the age of the pregnant woman at the time of becoming pregnant. With age, the risk of Hashimoto's accession is increasing.

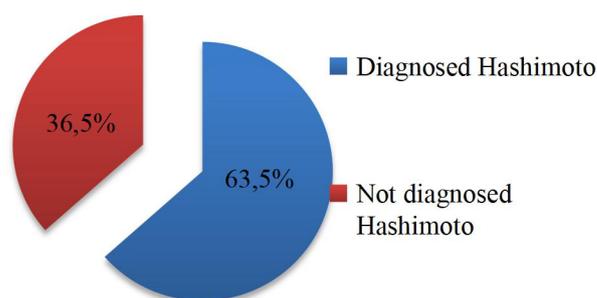


Figure 5. Distribution group in terms diagnosed Hashimoto.

In Table 3, a significance during the analysis of the statistical significance diagnosed or absence Hashimoto, and the age of the pregnant at the time of pregnancy ($p = 0.001$) was obtained. Along with age, there is a greater likeability of Hashimoto's occurrence. Parameters such as the week of birth and birth weight of a child did not differ significantly between women with not diagnosed and diagnosed Hashimoto.

	Diagnosed Hashimoto						The level of statistical significance $p > 0.05$
	Yes			No			
	M	Me	SD	M	Me	SD	
Week of birth	39.14	39	2.8	39.23	40	2.25	$p = 0.701$
Pregnant woman's age at the time of becoming pregnant	31,54	31.5	4.07	27,22	27	4.90	$p = 0.001$
Birth weight of a child	3,471.99	3450	555.87	3,460.66	3470	640.26	$p = 0.890$

Table 3. The occurrence of Hashimoto, and the basic metrics.

Table 4 is showing the relationship between the diagnosis of Hashimoto, and the occurrence of problems psychomotor up to 18 months of age. No statistical significance was obtained ($p = 0.220$). The largest group of whom offspring had psychomotor problems were women without diagnosed Hashimoto's thyroiditis (74 women). The number of women with diagnosed Hashimoto and developmental problems of children has a score of $n = 53$. The smallest number ($n = 36$) of women with not diagnosed Hashimoto and their offspring, in this group disorders during development did not occur. Comparable results ($n = 37$) occurred in the group of women diagnosed with the lack of Hashimoto, whose offspring experienced problems during the development.

Diagnosed Hashimoto	The occurrence of problems psychomotor up to 18 months of age				The level of statistical significance $p > 0.05$
	Yes		No		
	n	% from the group	n	% from the group	
Yes	53	59	74	57	p = 0.220
No	37	41	36	33	

Table 4. The relationship between the diagnosis of Hashimoto's thyroiditis, and the occurrence of problems in the child's development.

Diagnosed Hashimoto	The child's condition in the Apgar scale				The level of statistical significance $p > 0.05$
	Good condition		Average condition		
	n	% from the group	n	% from the group	
Yes	122	63	5	71	p = 0.657
No	71	37	2	29	

Table 5. The relationship between the diagnosis of Hashimoto's thyroiditis, and the results in the Apgar scale.

In Table 5 the relationship between the diagnosis of Hashimoto and the condition of the child in the Apgar scale is shown. The greatest amount were women (n = 122) who were diagnosed with Hashimoto, and the Apgar scale of their offspring was interpreted as a good condition. The lowest group were women (n = 2) diagnosed with Hashimoto, and their children obtained average condition by the Apgar scale.

Table 6 is showing a significant relationship between the time of diagnosis of hypothyroidism and the results of the newborn Apgar score. A decrease has been shown of Apgar score with an increasing time in which thyroid dysfunction is diagnosed.

Results in the Apgar scale	Time diagnosis of Hashimoto						The level of statistical significance of $p > 0.05$
	I trimester		II trimester		III trimester		
	n	% from the group	n	% from the group	n	% from the group	
Average condition	0	0	0	0	1	12.5	p = 0.044
Good condition	37	100	12	100	7	87.5	

Table 6. The relationship between the time of diagnosis of Hashimoto's thyroiditis, and the results of the Apgar scale.

The diagnosis of hypothyroidism before pregnancy affected 71.5% of women. And the minimum amount (4%) were women who were diagnosed in the third trimester of hypothyroidism.

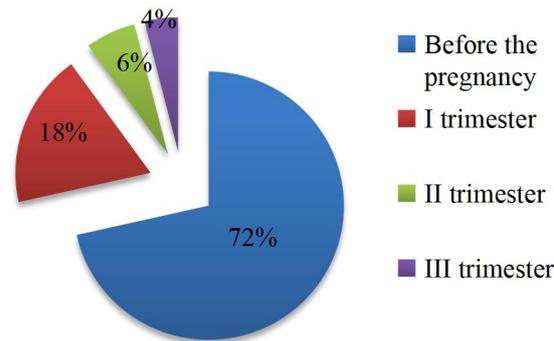


Figure 6. The time of diagnosis of hypothyroidism among women.

Another aspect analyzed in this study was the influence of the time of diagnosis of hypothyroidism in pregnancy to further problems in the child's development up to 18 months of age, birth weight, birth week, Apgar scale.

Table 7 is showing the relationship between the time of diagnosis of hypothyroidism, results in the Apgar scale, not depending on the time of diagnosis of hypothyroidism in the offspring of women with a predominance of the state of the average received good condition by the Apgar scale.

Results on the Apgar scale	The time of diagnosis of hypothyroidism								The level of statistical significance $p > 0.05$
	Before the pregnancy		I trimester		II trimester		III trimester		
	n	% from the group	n	% from the group	n	% from the group	n	% from the group	
Good condition	137	96	37	100	12	100	7	87.5	p = 0.272
Average condition	6	4	0	0	0	0	1	12.5	

Table 7. The time of diagnosis of hypothyroidism, and Apgar scores.

Table 8 demonstrated that irrespective of the time of diagnosis of hypothyroidism, lack of problems and their occurrence in the development of the child was not differing significantly in numbers

The occurrence of problems in the development of the child up to 18 months of age	The time of diagnosis of hypothyroidism								The level of statistical significance of $p > 0.05$
	Before the pregnancy		I trimester		II trimester		III trimester		
	n	% from the group	n	% from the group	n	% from the group	n	% from the group	
Yes	65	45.5	15	41	5	42	5	62.5	p = 0.717
No	78	55	22	69	7	58	3	37.5	

Table 8. The time of diagnosis of hypothyroidism, and speech development problems of the child to his 18-month.

In table 9 it is shown that the moment of diagnosis of hypothyroidism, does not affect the week of the delivery and birth weight of the child. The highest mean of birth weight of the child obtained in the second trimester, and the lowest in the third trimester of the pregnancy.

	The time of diagnosis of hypothyroidism												The level of statistical significance
	Before the pregnancy			I trimester			II trimester			III trimester			
	M	Me	SD	M	Me	SD	M	Me	SD	M	Me	SD	
Birth weight of a child	3455.5	3470	623.2	3495.9	3450	423.9	3680.8	3530	526.5	3240	3335	575.7	p = 0,613
Week of birth	39.09	39	2.3	39.6	39	1.3	39.7	40	1.1	39.3	40	2.8	p = 0.570

Table 9. The relationship between the time of diagnosis of hypothyroidism, and selected parameters.

The relationship between various types of hypothyroidism in pregnancy, and parameters such as birth weight, birth week, problems in the child's development, results in the Apgar scale are shown in Tables from 10 to 12.

In table 10 it is shown that regardless of the type of hypothyroidism, the mean of the above parameters does not affect a significant difference.

	Types of hypothyroidism									The level of statistical significance p> 00.5
	Subclinical			Isolated			Full			
	M	Me	SD	M	Me	SD	M	Me	SD	
Birth weight of a child [gram]	3488.2	3500	355	3410	3450	397.2	3463.9	3430	588.2	p = 0.618
Week of birth	38.89	39	2.38	39.6	40	1.54	39.3	40	2.05	p = 0.570
Age of a pregnant woman	27.63	28	4.93	27.3	28	4.10	29.66	thirty	5.02	p = 0.349
Weight of a pregnant woman	63.05	63	12.27	62,33	62	2.05	68,6	64	15,95	p = 0,670

Table 10. The relationship between certain types of hypothyroidism and the mean of basics parameters.

The occurrence of problems in the development of the child up to 18 months of age	Types of hypothyroidism						The level of statistical significance p> 0.05
	Subclinical		Full		Isolated		
	n	% from the group	n	% from the group	n	% from the group	
Yes	27	41	56	47	7	47	p = 0.718
No	39	59	63	53	8	53	

Table 11. The relationship between the different types of hypothyroidism, and further development problems.

Table 11 is showing that regardless of the type of hypothyroidism the presence or absence of faults during the development does not affect a significant difference. While Table 12 is showing that the type of hypothyroidism does not affect the child's scale worse condition on the Apgar scale.

Results on the Apgar scale	Types of hypothyroidism						The level of statistical significance $p > 0.05$
	Subclinical		Full		Isolated		
	n	% from Group	n	% from Group	n	% from Group	
Average condition	3	1.5	4	3	0	0	p = 0.682
Good condition	63	31.5	115	97	15	100	

Table 12. The relationship between the different types of hypothyroidism, and the results in the Apgar scale.

Discussion

In the presented study, the compound between the malfunctioning of a thyroid dysfunctions and the Apgar score, and in the development of the child to 18 months of age was analyzed. Statistical significance was achieved between the diagnosis of chronic lymphocytic Hashimoto's thyroiditis and the age of women. It has been shown that the probability of occurrence of Hashimoto's disease increases with the age of women. A similar result was obtained by Andersen SL, et al. in a population-based study of Danish mothers. They showed that all significant risk factor for thyroid disease is age > 30 [14]. One of the American Thyroid Association guidelines from 2017 was to perform screening of TSH levels in women over > 30 years of age[3,16]. Personal research and Eshkoli et al. show that the incidence of congenital hypothyroidism in children of studied women with Hashimoto's thyroiditis is rare. In this study, the dysfunction is concerned only in two children (1%)[17]. This result is consistent with the common knowledge that the problem of impaired thyroid function in children of women with Hashimoto's thyroiditis applies only to 2.5%. It is therefore considered that the screening tests are sufficient after the delivery without the need for further diagnosis[4,9].

From the analysis of the collected material statistical significance in analyzing the impact of Hashimoto on the week of birth, child's birth weight, Apgar score or problems in a child's development up to 18 months of age is not achieved. The same conclusion presented was presented by Zubkiewicz-Kucharska et al. The authors in their study have examined 367 children, of which, up to 94% of the children received a good Apgar score (8 to 10)[4]. Similar to the results of their research have been obtained by Plowden, who also did not show that Hashimoto affects premature labor and complications in children. Additionally, the authors found no increased likeability of gestational diabetes[18]. Different results were obtained by Korevaar, according to which there is a correlation between the presence of anti-TPO antibodies in pregnancy, and the incidence of premature births. In my research, it has been shown that pregnant women with anti-TPO antibodies, lower level of FT4 concentration compared to hCG have an increased risk of premature delivery[19].

Statistical significance in these studies has been compared to different trimesters, in which the diagnosis was hypothyroidism, and the results were on the Apgar scale. It has been shown that the decrease of Apgar score with increasing time in which thyroid dysfunction was diagnosed. To confirm the reliability of the result, it is necessary to repeat the test. It is not clear why the result was obtained. While performing the re-examination, the question on the

performed screening of TSH and the question on the frequency of TSH testing in pregnancy should be taken into account.

One of the priority objectives of the study is to demonstrate the relationship between the hypothyroid of a pregnant woman, and the occurrence of problems in the development of the child up to the 18-month life. As it is clear from the research, problems are related to 45% of children in the first 18 months of life. Fan et al. in their publication compared with each other six studies and thereby included an analysis of 4449 children of pregnant women with subclinical and overt hypothyroidism. They showed lower scores of intelligence and motor compared with patients with an intact euthyroid. The conclusion of their publication concerned the adverse effects of hypothyroidism on the psychomotor development of the child[20]. The same proposal for isolated adverse effects of hypothyroidism was received by Lazarus et al.[21]. The author Andersen presented in her publication that overt hypothyroidism is a risk factor for epilepsy in the offspring of mothers who struggled with hypothyroidism during gestation[22]. While Grattan et al. in their studies have shown that hypothyroidism of pregnant women increases the risk of developing congenital heart disease (CDH)[23]. Author Chen has not stated the deficit in the psychomotor development of the offspring at the age of 24 months[24]. Based on the above and as a result, the percentage of publications in their studies did not doubt that hypothyroidism is a risk factor for problems during the development of a child.

In accordance with current knowledge resulting from many studies, it is believed that overt hypothyroidism compared with subclinical possesses a greater likeability of irregularities related to lower IQ test results in children, gestational diabetes, premature delivery, problems in the development of a child[25]. To subclinical hypothyroidism discussion of the results of pregnancy and psychomotor of a child is still carried. In hypothyroidism, by ATA guidelines, an increase or reduction of FT4 causes colder gray matter based on the magnetic resonance study[3]. Own study showed no significant correlation between the types of hypothyroidism and the occurrence of problems in child development or results on the Apgar scale. The average prevalence of dysfunction development was close in different types of hypothyroidism. It is important to emphasize at this point that each of the surveyed women was treated, and 13% of pregnant women have failed to regulate hormones during pregnancy. A similar analysis was performed by Li P et al. which compared the results of pregnant women with elevated TSH to pregnant women with proper TSH (<2.5 mIU / L) in the first trimester of pregnancy. It did not reveal any relationship between the concentration of the hormone, and Apgar score, week of birth, birth weight[26]. An astonishing fact is that each respondent was treated, even if she had been diagnosed with hypothyroidism insulated. According to the ATA is not recommended for the treatment of pregnant women with hypothyroidism. Casey et al. have demonstrated that the initiation of treatment and subclinical hypothyroidism insulated between 8 and 20 weeks did not take effect in better psychomotor results, birth weight, week of birth and Apgar score than a group that was not subject of treatment[27]. Stagnaro-Green shows no increase in IQ and Apgar scores and no evidence by treating subclinical and overt hypothyroidism[25].

One of the main objectives of this study was to verify whether the underactive thyroid is a factor affecting the results of the Apgar score and whether the results of the Apgar score impinge further on the problems in the child's development. The Apgar score is commonly

used to assess the health status of a newborn specific minutes after birth. In their research, Zubkiewicz-Kucharska showed no effect on pregnant hypothyroidism on the Apgar scale[4]. No significant correlation was shown between the results of the Apgar score and developmental disabilities in children in the future. The same result was achieved by Trumpff et al. who studied the psychomotor development of 284 children in 4-6 years of age[28]. A different result is described by Razaz in his publication, who showed a significant correlation between the results of Apgar in children, without birth defects, born more than 37 weeks of gestation, and further health problems. According to the results enclosed in his publication, a reduced ratio of 7, 8 and 9 after 1, 5 and 10 minutes was a risk factor for the morbidity of the child, as compared to the children whose score was 10 after 1, 5 and 10 minutes[15]. Razaz in his analysis obtained a result that the decrease of results in 1 and 5 minutes, increases the risk of problems in the development of the child[29]. However, Persson established an increase in the risk of epilepsy and cerebral palsy with the decrease of the score at 5 and 10 minutes[30].

Conclusions

1. The relevance between diagnosed with static chronic lymphocytic Hashimoto's thyroiditis in pregnancy and problems in child development up to 18 months of age, the results of the Apgar score, birth weight, the birth week was not demonstrated. However, a large percentage (45%) of children who experience health problems informs us that pregnant hypothyroidism may entail some negative consequences for the fetus.
2. With age the risk of chronic lymphocytic thyroiditis Hashimoto increases ($p = 0.001$).
3. The final score of the Apgar scale does not forecast problems in the child's development up to 18 months of age. It is important to take into account the results of the Apgar in individual minutes during the retest.
4. Statistical significance between a particular type of hypothyroidism of a pregnant woman, and the occurrence of problems during the development of a child up to 18 months of age, the results of the Apgar score, birth weight, is not demonstrated.
5. Problems, during the development, were had by 45% of children of surveyed women of which 43% were related to symptoms of neurological problems including 56% of impaired muscle tone.

With the collected study material, analyzes and comparisons of the results of other authors, it can be concluded that the dysfunction of which is hypothyroidism during the pregnancy may increase the risk of problems in child development. Still no clear results. Further research, which will help to establish the presence of mechanisms adverse impact on offspring and pregnancy outcomes is significant.

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