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Iodine deficiency in pregnant women through neonatal tsh assessment study retrospective of neonatal screening in Romania

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Abstract

Iodine is an essential micro-nutrient for the human being taking in account its role in the synthesis of thyroid hormone.

In pregnancy it is an increased iodine requirement according to the high metabolic rate and if the iodine requirement is not covered by an adequate intake the pregnant women and the fetus are at risk of iodine deficiency consequences

This paper work aims to evaluate neonatal TSH as a marker of iodine status of women in pregnancy, which in pregnant women include, abortion, premature birth, low birth weight, increased perinatal mortality and in newborn impaired brain development and low IQ.

Currently, iodine deficiency prevention in Romania is implemented by law 586 /2002 and 1904/2004 which indicate the mandatory iodization of table salt and the mandatory use of iodized salt in the bakery.

The neonatal TSH was retrospectively analyzed from MEDILOG neonatal screening registry Romania. The individual TSH values were rated against a threshold of 5 mIU/L from 317449 children enrolled in the screening program for congenital hypothyroidism in 2017, 2018, 2019, 2020 and 2023.

In Romania 23.5% of neonates have TSH values above the previous mentioned threshold, fact which enrolls the population as moderate iodide deficient (according to UNICEF, WHO norms). There are differences at different couny level with a iodide deficiency ranking from mild to moderate. There are no differences between endemic and non-endemic areas.

The results of this study are discussed in the context of similar works at the national and international level.

Keywords: pneonatal TSH, iodine status, pregnancy, Romania

INTRODUCTION

Iodine is a micronutrient that takes part in the synthesis of thyroid hormones, which are indispensable for the metabolic activity, growth and development of the body and of the brain, beginning with the fetal life.

Iodine is found in the soil and water and enters the human body through food (vegetable and animal origin).

The iodine requirement of the human being is related to age and physiological condition of the body.

According to the WHO standards the iodine requirements are

- 90 mcg for children aged 0-5 years,
- 120 mcg for a child 6-12 years old,
- 150 mcg for a child over 12 years old and for an adult.
- 250 mcg in pregnancy and breastfeeding women [1]

A low iodine intake causes so-called iodine deficiency disorders, which in children include impaired brain

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development and low IQ, deafness, dwarfism, hypothyroidism and in pregnant women, abortion, premature birth, low birth weight, increased perinatal mortality [2,3].

In pregnancy it is an increased iodine requirement according to the high metabolic rate and if the iodine requirement is not covered by an adequate intake the pregnant women and the fetus are at risk of iodine deficiency consequences.

Over the past 25 years, it has become widely recognized that the consequences of iodine deficiency, including impaired brain development and low IQ in children, and nodules and hyperthyroidism in adults, can occur in the absence of clinical manifestations, such as cretinism and goiter.

Taking in account the fact that "iodine deficiency is considered the most common cause of preventable mental impairment throughout the world" in countries affected by iodine deficiency, its sustainable elimination was a strategic goal worldwide. This goal was achieved in many regions through the universal salt iodization [4].

Thus, in 2018, the prevalence of the population consuming iodized salt worldwide is 88%, followed by an adequate intake of iodine in 118 countries in 2020 compared to 67 in 2003 [4].

Romania is known as a country with iodine deficiency, with endemic areas of goiter. Early in the 50's Romania introduced public health policies for the elimination of iodine deficiency disorders trough salt iodization [5,6].

Currently, iodine deficiency prevention in Romania is implemented by law 586 /2002 and 1904/2004 which indicate the mandatory iodization of table salt and the mandatory use of iodized salt in the bakery.

To order to monitor the results and efficiency of a iodine deficiency prevention program in a population there are used several methods: urinary iodide concentration, thyroid volume determination, thyroglobulin analysis, neonatal TSH determination

The policy for iodine deficiency prevention ensures an adequate iodine intake at the population level proved by the median urinary iodide concentration of schoolchildren in several studies [7,8].

In the countries where neonatal screening is implemented, the determination of the neonatal TSH value is increasingly used as a method to identify iodine deficiency [9-15].

The present study highlights the value of neonatal TSH to monitor the iodine status of pregnant women in the context of other iodine deficit assessments of the population of Romania.

MATERIALS AND METHODS

Our study aims to assess the iodine status of the neonate and indirect of the pregnant women, through the analysis of the neonatal TSH, provided by the national screening program for congenital hypothyroidism database.

The neonatal TSH values of children born in Romania registered in the MEDILOG registry for neonatal screening management (administrated by NIMCH in the frame of the National Health Program XIII) were analyzed retrospectively over a period of 5 years (2017, 2019, 2020, 2022, 2023).

Dry spot collection storage, transport and laboratory tests are in accordance with the national standards. The dry spot sample was collected from heels on filter paper at maternity, 2-5 days after birth. The samples were processed at the Medical Analysis Laboratory of NIMCH Department of Pediatrics – reference laboratory for neonatal screening of the Bucharest Regional Center. The FEIA immunoenzymatic method was used for processing TSH test and cut off of 20 mIU/L of TSH was considered positive for hypothyroidism.

In order to assess iodine status the frequency of neonatal TSH values above the TSH reference threshold of 5 mIU / L was considered.

It was assessed also the severity of iodine deficiency according the international standards, on the percentage of neonatal TSH values above 5 mIU/l

- below 3% of TSH defines the adequate iodine status, between 3 and 19.9% light iodine deficiency, between 20-30.9% a moderate deficiency, over 40% a severe deficiency.

Neonates with prematurity and birth weight below 2500 and those with TSH values above 20 mIU/L which were considered hypothyroid were excluded from the study.

The data was analyzed global and grouped by counties, areas with endemic iodine deficiency and year of birth.

Statistical analysis, descriptive methods, frequencies, chi square test were performed using SPSS software version 23.

RESULTS

The initial study sample consists of 317,449 newborn, 48.6% girls and 51.4 % boys born in 2017, 2018, 2019, 2020, 2023 and coming from 42 counties. After exclusion of premature, low birth weight, newborn and children with TSH value above 20 mIU/L, the study sample was reduced to 299583 newborns, 89% of the initial group.

DISCUSSION

TSH is a pituitary hormone which regulates thyroid function through negative feedback, which means that a decrease in thyroid hormones generates subsequent an increase of the pituitary TSH secretion.

The thyroid of the newborn has a very low storage capacity for iodine and consequently is very sensitive to iodine deficiency. In order to maintain the homeostasis of the thyroid hormones, iodine deficiency increases TSH secretion of the fetus and the subsequent iodine turnover.

Consequently an increase of neonatal TSH at birth defines an inadequate iodine intake in pregnancy and presume negative effect on fetal brain development

In order to evaluate the iodine status, neonatal TSH values above 5 IU/L on dry spot which are collected 3-5 day after birth are considered marker of iodine deficiency in pregnancy.

The clinician should be aware that during the first 6 h of life after birth, a physiologic TSH surge occurs, and the concentration of TSH may remain above 10 mU/L during the first 24 to 48 h of life. Babies with dry spot collection before 24 h of life and values of TSH in the limits of mild iodine deficiency could have normal values at a new test.

The prevalence of neonates with neonatal TSH values above the 5 mIU/L threshold is proportional to the degree of iodine deficiency in pregnancy and defines its severity.

TABLE 1. *Prevalence of neonatal TSH values according the threshold of 5 mIU*

TSH of neonates > 2500 g	N	% of Total N
<5	229243	76,5%
>=5	70340	23,5%
Total	299583	100,0%

Determination of neonatal TSH is considered one of the methods used to define and monitor iodine deficiency in pregnancy. It is recommended to be done in communities were screening for neonatal hypothyroidism is performed.

Taking in account the neonatal TSH values, 23.5 % of the newborns, coming from 42 counties in Romania born in the reference years 2017, 2018, 2019, 2020, 2023 have a neonatal TSH value above 5 IU/L which include our sample in a population with a moderate deficit. The moderate deficit is maintained in 4 years 2018, 2019, 2020, 2023 excepting year 2017 when a slight deficit (17%) was found. The most severe deficit was found in 2020 (28%), the year of Covid 19 pandemic.

TABLE 2. *Prevalence of neonatal TSH threshold according to the endemic status of the residence area*

TSH of neonates	Nonendemic counties	Endemic counties	Total
Nr. of TSH of neonates <5	114179	115064	229243
% of TSH of neonates <5	75,9%	77,2%	76,5%
Nr. of TSH of neonates ≥5	36347	33993	70340
% of TSH of neonates ≥5	24,1%	22,8%	23,5%
Total (Nr.)	150526	149057	299583
Total (%)	100,0%	100,0%	100,0%

The analysis of neonatal TSH in each county indicates values which point out a mildy iodine deficit of neonates in 12/42 counties and Bucharest Municipality and a moderate deficit in 30/42 counties.

Differences don't exist between the prevalence of neonates with neonatal TSH above 5 mg in counties grouped as endemic and nonendemic areas.

Iodine deficiency is higher in winter compared to the reference value for the country (26.6; 23.5). Seasonal variations are mentioned in scientific literature with results depending on the study under discussion.

Based on iodide of schoolchildren, Romania is considered now a country with an adequate iodine status of the population.

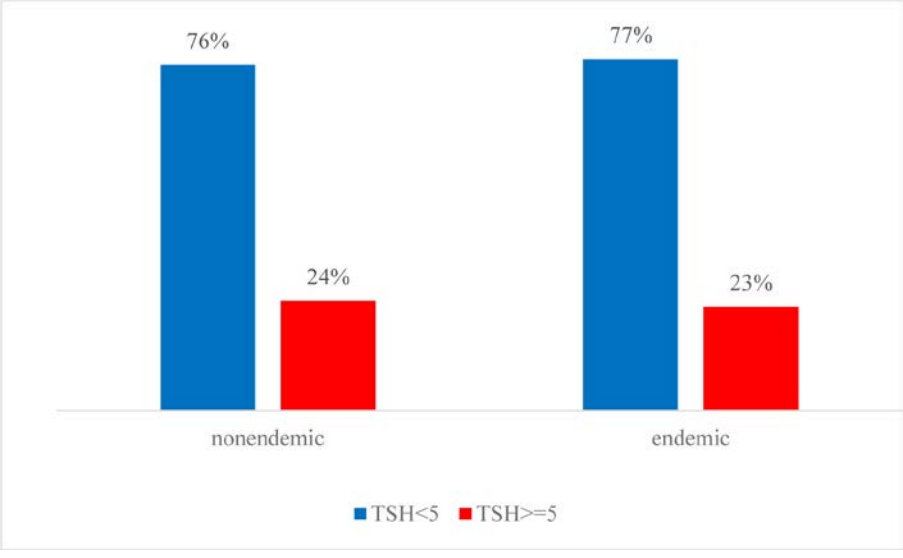

FIGURE 1. *Prevalence of neonatal TSH threshold according to the endemic status of the residence area*

TABLE 3. *Prevalence of neonatal TSH threshold according to the year of birth of the neonates*

TSH of neonates	2017	2018	2019	2020	2023	Total
Nr. of TSH of neonates <5	37754	53137	46030	46024	46298	229243
% of TSH of neonates <5	76,3%	82,7%	77,2%	71,7%	74,6%	76,5%
Nr. of TSH of neonates ≥5	11739	11112	13568	18195	15726	70340
% of TSH of neonates ≥5	23,7%	17,3%	22,8%	28,3%	25,4%	23,5%
Total (nr.)	49493	64249	59598	64219	62024	299583
Total (%)	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

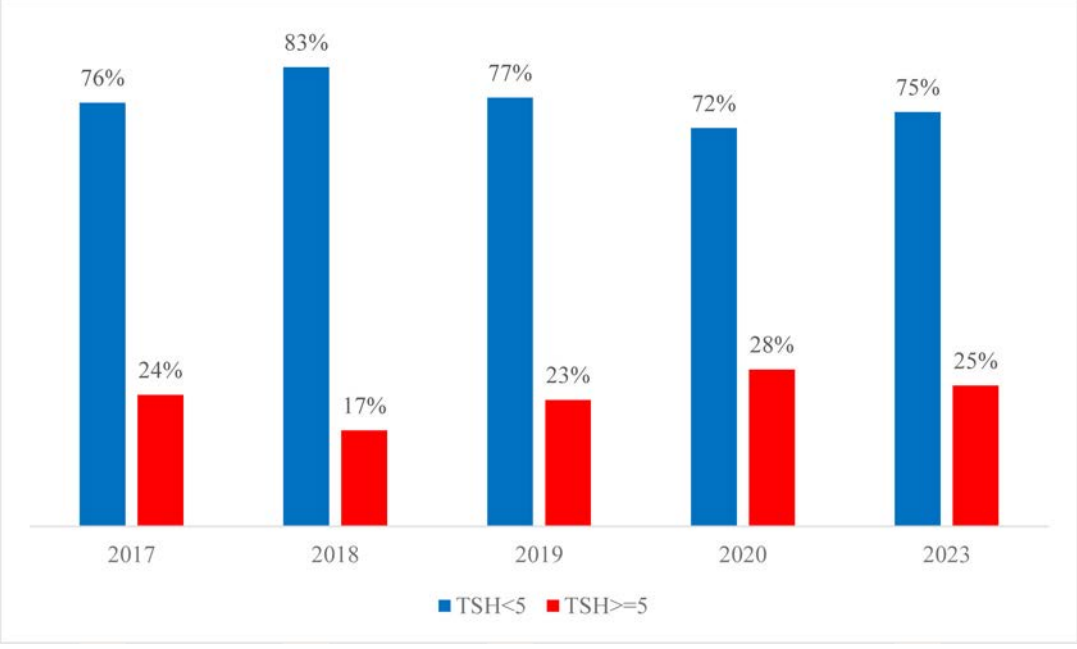

FIGURE 2. *The prevalence of neonatal TSH threshold according to the year of birth of the neonate*

The differences between the above mentioned situations are linked to the population tackled for the study of iodine deficit: pregnant women for TSH and schoolchildren for iodide. Despite an adequate iodine status of the population proven by urinary iodide of schoolchildren, pregnant women still remain a vulnerable group to iodine deficiency [17-22].

Additional factors could increase iodine deficiency in pregnancy:

- low salt intake to prevent hypertension
- reduction of bread consumptions to prevent overweight
- low consumption of food with a high iodine content milk, eggs, fish
- assumption of fake news not to use iodized salt for its negative effects
- loss of iodine of salt which is added during cooking, boiling of food

A special mention must be granted to the increased frequency of iodine deficit, marked by increased neonatal TSH in 2020, time of Covid pandemic. This fact can be related to the restriction of food including iodized salt circulation, production, storage and lifestyle changes at individual and population level.

At the individual level it is known that the use of antiseptics with iodine in the treatment of the perineum during delivery can generate an increase in neonatal TSH level and influence the prevalence of elevated TSH values.

CONCLUSION

Neonatal TSH reveals in Romania a moderate iodine deficiency in pregnant women, although Romania is currently considered a country with an adequate iodine status, proven by median iodide in schoolchildren.

The status on iodine deficiency, is similar and within the limits mentioned above in 2024, 2019, 2016, 2024.

Evaluation of neonatal TSH must be done in complementarity with the results of other iodine deficit as-

TABLE 4. *Prevalence of neonates according to the neonatal TSH threshold and county of residence*

County	Nr./%	TSH <5	TSH ≥5	Total
Alba	Nr.	6519	1388	7907
Alba	%	82,4%	17,6%	100,0%
Arad	Nr.	9958	2077	12035
Arad	%	82,7%	17,3%	100,0%
Bacau	Nr.	253	95	348
Bacau	%	72,7%	27,3%	100,0%
Bihor	Nr.	57	15	72
Bihor	%	79,2%	20,8%	100,0%
Bistrita-Nasaud	Nr.	137	10	147
Bistrita-Nasaud	%	93,2%	6,8%	100,0%
Botosani	Nr.	41	23	64
Botosani	%	64,1%	35,9%	100,0%
Braila	Nr.	4564	1651	6215
Braila	%	73,4%	26,6%	100,0%
Brasov	Nr.	13311	7401	20712
Brasov	%	64,3%	35,7%	100,0%
Bucuresti	Nr.	35284	13686	48970
Bucuresti	%	72,1%	27,9%	100,0%
Buzau	Nr.	6231	2129	8360
Buzau	%	74,5%	25,5%	100,0%
Calarasi	Nr.	4738	1546	6284
Calarasi	%	75,4%	24,6%	100,0%
Caras-Severin	Nr.	307	99	406
Caras-Severin	%	75,6%	24,4%	100,0%
Cluj	Nr.	90	22	112
Cluj	%	80,4%	19,6%	100,0%
Constanta	Nr.	15950	4951	20901
Constanta	%	76,3%	23,7%	100,0%
Covasna	Nr.	5228	1882	7110
Covasna	%	73,5%	26,5%	100,0%
Dambovita	Nr.	9510	2499	12009
Dambovita	%	79,2%	20,8%	100,0%
Dolj	Nr.	12777	1078	13855
Dolj	%	92,2%	7,8%	100,0%
Galati	Nr.	10855	2565	13420
Galati	%	80,9%	19,1%	100,0%
Giurgiu	Nr.	5725	1660	7385
Giurgiu	%	77,5%	22,5%	100,0%
Gorj	Nr.	4407	891	5298
Gorj	%	83,2%	16,8%	100,0%
Harghita	Nr.	75	35	110
Harghita	%	68,2%	31,8%	100,0%
Hunedoara	Nr.	5264	1903	7167
Hunedoara	%	73,4%	26,6%	100,0%
Ialomita	Nr.	5485	1486	6971
Ialomita	%	78,7%	21,3%	100,0%
Iasi	Nr.	104	50	154
Iasi	%	67,5%	32,5%	100,0%
Ilfov	Nr.	11936	4664	16600
Ilfov	%	71,9%	28,1%	100,0%
Maramures	Nr.	37	10	47
Maramures	%	78,7%	21,3%	100,0%
Mehedinti	Nr.	4593	735	5328
Mehedinti	%	86,2%	13,8%	100,0%
Mures	Nr.	138	57	195
Mures	%	70,8%	29,2%	100,0%
Neamt	Nr.	85	39	124
Neamt	%	68,5%	31,5%	100,0%
Olt	Nr.	5959	1413	7372
Olt	%	80,8%	19,2%	100,0%
Prahova	Nr.	15315	5065	20380
Prahova	%	75,1%	24,9%	100,0%
Salaj	Nr.	40	8	48
Salaj	%	83,3%	16,7%	100,0%
Satu Mare	Nr.	20	9	29
Satu Mare	%	69,0%	31,0%	100,0%
Sibiu	Nr.	183	72	255
Sibiu	%	71,8%	28,2%	100,0%
Suceava	Nr.	73	27	100
Suceava	%	73,0%	27,0%	100,0%
Teleorman	Nr.	5349	1262	6611
Teleorman	%	80,9%	19,1%	100,0%
Timis	Nr.	204	62	266
Timis	%	76,7%	23,3%	100,0%
Tulcea	Nr.	4278	784	5062
Tulcea	%	84,5%	15,5%	100,0%
Unknown region	Nr.	10	6	16
Unknown region	%	62,5%	37,5%	100,0%
Valcea	Nr.	5803	1868	7671
Valcea	%	75,6%	24,4%	100,0%
Vaslui	Nr.	138	62	200
Vaslui	%	69,0%	31,0%	100,0%
Vrancea	Nr.	5403	1581	6984
Vrancea	%	77,4%	22,6%	100,0%
Total	Nr.	229243	70340	299583
Total	%	76,5%	23,5%	100,0%

sessments in order to mirror the specificity of iodine deficit at different levels and population.

Dynamics of neonatal TSH by country and region provide an added value to the study of the implementation in time of the iodine deficiency prevention program using iodized salt.

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Conceptualization, Michaela Nanu
Project administration, Michaela Nanu
Supervision, Michaela Nanu

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