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Research Article

Folate Deficiency Prevalence and Correlation with Neural Tube Defects Formation in Georgia

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Abstract

Several assessments of nutritional status have been done in the recent past in Georgia, but they did not contribute substantially to the estimation of nationwide prevalence rates of nutritional outcomes. In fact, until 2015 there was not any effective surveillance system in Georgia, which could provide with reliable data for developing national strategy of micronutrient deficiency elimination and improving the nutritional status of population. For nutrition surveillance system had been used sentinel surveillance approach, selecting 4 regions and 1 sentinel site for pregnant in each Region (pregnant health facilities).

Methodology: Iron deficiency and folate deficiency was studded in pregnant women. Iron deficiency was measured using ferritin concentration in plasma with cut-off points of < 15 μg/l. Below 3.0 ng/ml was considered as a cut-off point of Folate (in plasma) deficiency in pregnant (1st trimester). For anemia detection has been used Hb cut-off points of < 11 g/dl.

Findings: Blood laboratory studies on micronutrient deficiencies indicate that more than half of studded pregnant women (n = 1203) are iron deficient (57%), almost a third have folate deficiency (28%), and one-fifth already have severe anemia (20%). The rate of neural tube defects per 1000 births averages 3.7 (data are taken only from the sentinel sites involved in the study).

Conclusion: Study results show that iron deficiency is high prevalent and folate deficiency was quite common during the 1st trimester of pregnancy in Georgia. And the rate of neural tube defects per 1000 births is about 7 times high (3.7) compering with WHO references (must not be more than 0.5 per 1000 births).

Keywords: NTDs; Nutrition; Georgia

Introduction

Most congenital malformations (BDs) develop during the first 3 months of pregnancy. 1 in 33 babies are born with a birth defect in the United States. Most of them are caused by a combination of many factors: 1. Genetic. 1.1 One or more genes undergo a change and, in some defects, one or all of the genes are absent. 1.2 Chromosomal factor. In some cases, a chromosome or part of a chromosome may not be present (e.g., Turner syndrome). In other cases, the child has an extra chromosome (e.g., Down syndrome). 2. Exposure to medicines, chemicals or other toxic substances. E.g., harmful alcohol consumption may lead to FASD (fetal alcohol spectrum disorders), and 3. Lack of some nutrients. For example, insufficient intake of folate (folic acid) during the pre-pregnancy and 1st trimester of pregnancy is more likely to lead to neural tube defects (NTDs). Numerous studies confirm that if a woman's body receives the required amount of folic acid, the risk of developing fetal neural tube defects is reduced by 50 - 70%. Nerve tube defects develop during the first 28 days of pregnancy - usually before a woman learns she is pregnant. About 50% of pregnancies in the world are unplanned. Thus, every woman who is even planning a pregnancy should take folate (folic acid).

Every year, more than 300,000 babies are born with neural tube defects, the main cause of which, according to many studies, is folate deficiency. The prevalence of neural tube defects (NTDs) in Europe is 1.3 - 35.9 (per 10,000 live births). In Southeast Asia it reaches 66.2.

The most common forms of neural tube defects are a) "Spina bifida" (spinal cord hernia) - the fetal spine cannot completely cover the spinal cord, resulting in impaired spinal cord function. Children born with spinal cord hernias have lifelong problems and require multiple surgical interventions. B) Anencephaly - underdevelopment or incomplete development of the brain. Babies with anencephaly die before birth or soon after birth. C) Cerebral hernia (encephalocele) - protrusion of brain tissue due to the openness of the skull.

In 2009, a national nutrition survey was conducted in Georgia under the auspices of the United Nations Children's Fund (UNICEF). The study showed a fairly high rate (36.6%) of folate deficiency in pregnant women.

Folate deficiency is common where meat is not used for food at all and vegetables are processed thermally for a long time (it is thermolabile). To avoid deficiency, it is necessary to eat raw vegetables and fruits. Humans receive folate through food, or as a result of its synthesis by small amounts of intestinal microflora. It is included in both plant and animal products. It should be noted that female and cow's milk contain approximately equal amounts of folate (50 ng/g), while goat's milk contains about 8 times less. Absorption of folic acid occurs in the duodenum and proximal part of the small intestine. Transmembrane transport and accumulation in the cell is carried out with the help of vitamin B12. Scientific research has shown that people consume less folate than they need. Because of this, food fortification laws have been passed in many countries since the late 20th century. Folate deficiency can lead to other complications, such as leukopenia, thrombocytopenia, megaloblastic anemia, premature birth, stunted growth and delayed puberty in children, etc. Every woman planning a pregnancy should take 400 mcg of folic acid a day for up to 12 weeks of pregnancy. Women who have given birth to children with a pathology of the nervous system from a previous pregnancy should take much more folic acid (5 mg per day). Folic acid is also prescribed for anemia caused by folate deficiency before normalization of erythrocyte counts. Folic acid is an essential cofactor in DNA synthesis.

Common causes of folate deficiency are: 1. Decreased intake of food (e.g., chronic malnutrition, excessive alcohol consumption, restriction of protein intake in food), 2. Absorption disorders (achlorhydria, celiac disease, zinc deficiency, excessive increase in bacterial microflora) and 3. Increase in bacterial microflora. Demand (infancy, pregnancy, lactation, malignancies). 4. Patients with vitamin B12 deficiency may experience enhanced excretion of folic acid by the kidneys. Rarely, hypothyroidism and congenital deficiency of enzymes can also disrupt folic acid metabolism.

Iron deficiency is also one of the most important problems for pregnant women and fetuses, as well as young children. Which is mostly manifested by the development of anemia. According to the World Health Organization, an average of 40% of the population has anemia. It is known that about 2/3 of all cases of anemia are due to iron deficiency anemia (RDA). It is most commonly found in women of reproductive age, among pregnant and lactating women, as well as in children of early and pubertal age. Megaloblastic anemia (folate deficiency anemia), which is caused by folate deficiency, also plays an important role in the development of anemia. Thus, it is also important to consider the study of anemias in folate deficiency studies to determine the proportion of folate-deficient anemias in common anemias.

Based on the experience of many countries around the world, based on the scale of its consumption, it is advisable to develop and implement a national strategy for fortification of bread flour (iron and folic acid). An economic analysis conducted in the US showed that the cost-effectiveness ratio was 40: 1 in the case of fortification of flour with folic acid (i.e., $ 1 invested gives $ 40 in savings), and 36: 1 in the case of iron fortification. The prevalence of neural tube defects (NTDs) has been significantly reduced as a result of the introduction of a fortification strategy. For example, by 2006, the prevalence of neural tube defects in the United States had decreased by 37%, in Canada by 46%. In general, since the beginning of fortification, countries have confirmed an average reduction of NTDs of 30 - 50%.

The aim of the research

Study of correlation between folate deficiency and neural tube defects (NTDs) in Georgia and based on the results elaboration of recommendations for plening effective preventive measures.

The targets of the research

- Pregnant women, and
- Fetus

Study design

The sentinel approach was used, and 5 sentinel sites (health facilities) in 4 Regions of Georgia (Achara/Batumi, Samegrelo/Martvili, Tbilisi, and Kakheti/Lagodekhi) were selected for this study.

Data collection

Three types of data collection were used: 1. extracting data from selected health facilities (sentinel sites), 2. Laboratory results of blood, and 3. Information from special questionnaires used in this study.

Laboratory testing

Laboratory testing of blood (Venous) samples were used.

Data analysis

The Statistic Package for the Social Sciences (SPSS) was used for Data Analysis.

Laboratory testing was realized by the following study scheme: 1. Hemoglobin/in pregnant (1st trimester) visiting sentinel site 2. Iron and folate deficiencies (laboratory testing) were studded in pregnant (1st trimester). Laboratory testings on iron and folate deficiencies were conducted in Tbilisi reference Laboratory.

Research Methodology

- Pregnancy (1st trimester) blood tests were performed on ferritin and folate to detect Iron and folate deficiency.
- Ultrasound examination of the fetus (during pregnancy) was performed within the capabilities of the clinic.
- According to the results of the Folate study, pregnant women were followed up to detect further formation of neural tube defects (NTDs).
- The nutritional characteristics and actual nutrition of pregnant women were studied using the 24-hour recall method, using a structured closed questionnaire that was filled out on all pregnant women from whom blood was taken for folate testing.
- An additional questionnaire was completed for pregnant women whose fetuses were exposed to NTDs.
- Hemoglobin was determined in pregnant women (using a venous blood testing by multiannalizer) to detect anemia.
- A unified coding system for pregnant women was used (one ID for all studies of one pregnant woman).
- In parallel with the laboratory examination of the blood contingent (pregnant women) for the study of folate deficiency, information was obtained from maternity clinics about cases of neural tube defects in the fetus and newborn. The results of ultrasound examination of pregnant women (including cases of neural tube defects, cases of abortion) as well as cases of birth of children with neural tube defects were studied.
- Information was found on cases of congenital anomalies observed in the clinics selected for the study in the last 3 years, including on congenital anomalies in pregnant women in consanguineous marriages.
- The case-control epidemiological research method was used. Was examined the prehistory of each NTD case with a nutritional profile questionnaire and a review of laboratory test data. It was considered “case” to be pregnant with a diagnosis of fetal NTD. “Controlled” - pregnant - without NTD. The methods and tools of (Follow up) and (Time trend), “Face to Face” interviews were also used.

The questionnaire used to study actual nutrition included information on the consumption of folate-rich staple foods, with pregnant women noting that the information they provided was not just about one day, but about almost daily nutrition. Thus, by analyzing the information obtained from the questionnaires, we can judge about their actual nutrition, which determines their nutritional status [1-12].

The questionnaire included the main foods rich in folate: dark green leafy vegetables, citrus, meat, liver (beef, lamb, and pork, chicken), legumes, cereals, cereals, etc.

The following Cut off points were used:

- Anemia - < 110 g/L (Hemoglobin)
    - Severe anemia - < 70 g/L
- Iron deficiency - ferritin < 15.0 μg/L
- Folate deficiency - folate (in plasma) < 3.0 ng/mL

The data were processed through the statistical research computer program - SPSS.

Limitations

Only those pregnant women who were taking folic acid before taking blood (before registering a pregnancy) for our study were excluded from the study (blood test), although this category of pregnant women was also included in the study as pregnant women taking folic acid before conception.

Study Results

The study in pregnant women showed about 20% prevalence of anaemia of the 1203 pregnant enrolling in study.

The age of the subjects ranged from 17 to 48 years. Most of the surveyed pregnancies (64.4%) were present in 21 - 30 years. On the 17 - 20 years age group was 6.6%, the age group of 31 - 40 years was 27.7% and the age group of 40 - 48 years was 1.3% of pregnant women. The average age of the examined pregnant women is 28 years.

Age groups (years)	% Of studded pregnant
17 - 20	6.6
21 - 30	64.4
31 - 40	27.7
41 - 48	1.3
Total	100% (n = 1203)

Table 1: Anemia was detected in 20% (n = 240) of the examined contingen.

	# Of studded pregnant	Anemia (Hb < 110g/L)	Severe anemia (Hb < 70g/L)
Total	1203	20%	0.0%

Table 2: The hemoglobin concentration in pregnant women ranged from 71 to 150g/l.

Hb (g/L)	%
71 - 109	20
110 - 119	28.2
120 - 139	50.3
140 - 150	1.5
Total	100% (n = 1203)

Table 3: Cases of anemia were distributed so, according to age groups.

Age groups (years)	% Of anemic pregnant
17 - 20	16
21 - 30	24
31 - 40	18
41 - 48	7
Total	20%

Table 4

Descriptive				
Hemoglobin			Statistic	Std. Error
Fol	Mean		118.28	.336
	95% Confidence Interval for Mean	Lower Bound	117.62	
		Upper Bound	118.94	
	5% Trimmed Mean		118.82	
	Median		120.00	
	Std. Deviation		11.651	
	Minimum		71	
	Maximum		150	
	Range		79	

Table 5: Iron deficiency was detected in 57% (n = 686) of the examined contingent.

	# Of studded pregnant	Ferritin < 15.0 µg/L
Total	1203	57%

Table 6: Ferritin concentrations in pregnant women ranged from 0.01 to 235.6 µg/L.

Ferritin (µg/L)	%
0.01 - 5.0	14
5.1 - 15.0	43
15.1 - 20.0	12
20.1 - 30.0	12
30.1 - 40.0	6
40.1 - 50.0	5
> 50	8
Total	100% (n = 1203)

Table 7: Cases of iron deficiency were distributed so, according to age groups.

Age groups (years)	% Of pregnant with Iron deficiency
17 - 20	38
21 - 30	70
31 - 40	49
41 - 48	62
Total	57%

Table 8

Descriptive				
Ferritin			Statistic	Std. Error
Fol	Mean		20.0062	.59567
	95% Confidence Interval for Mean	Lower Bound	18.8375	
		Upper Bound	21.1748	
	5% Trimmed Mean		17.3939	
	Median		14.4000	
	Std. Deviation		20.66046	
	Minimum		.01	
	Maximum		235.60	
	Range		235.59	

Table 9

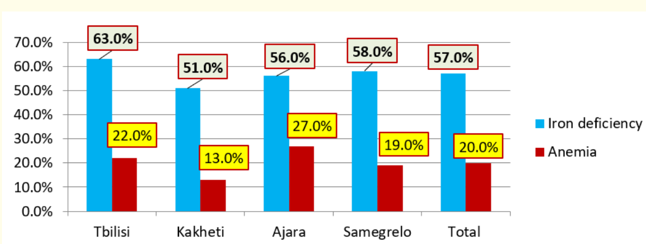

Figure 1: Iron deficiency and Anaemia prevalence (percentage) by regions.

Severe anaemia cases were not identified in pregnant women.

Folate deficiency

Folate deficiency was detected in 28% of the investigated contingent (n = 337). The prevalence of folate deficiency in studded contingent is much higher (approximately 1.5 times) in the regions of western Georgia (Achara, Samegrelo) than in the east (Kakheti, Tbilisi). The reason for this difference, most likely, lies in the eating habits of the population, which has traditional characteristics for the regions.

	# Of studded pregnant	Blood serum folate < 3.0 ng/mL
Total	1203	28%

Table 10: Folate deficiency.

Folate (ng/mL)	%
0.01 - 3.0	28
3.01 - 10.0	29.6
10.01 - 20.0	21.2
20.1 - 30.0	17.6
30.1 - 48.0	3.6
Total	100% (n = 1203)

Table 11: Cases of folate deficiency were distributed so, according to age groups.

Age group (years)	% Of pregnant with folate deficiency
17 - 20	23
21 - 30	27
31 - 40	32
41 - 48	25
Total	28%

Table 12

Descriptive				
Folate			Statistic	Std. Error
Fol	Mean		10.7675	.29664
	95% Confidence Interval for Mean	Lower Bound	10.1856	
		Upper Bound	11.3495	
	5% Trimmed Mean		9.7562	
	Median		6.8200	
	Std. Deviation		10.28874	
	Minimum		.09	
	Maximum		76.50	
	Range		76.41	

Table 13

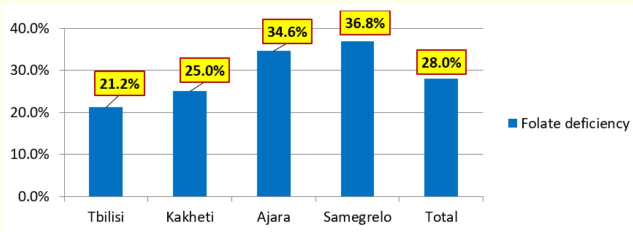

Figure 2: Folate deficiency prevalence (percentage) by regions.

Folate concentrations ranged from 0.01 to 48.0 ng / ml.

Reviewing regional profiles for Iron deficiency, showed that prevalence in studied four regions is almost the same, and that all regions have a high prevalence.

Neural tube defects

The rate of neural tube defects per 1000 births averages 3.7 (Table # 4). Data are taken only from the sentinel institutions involved in the study.

Iron deficiency - anemia

A blood test for the ferritin component was used to detect iron deficiency. The results were grouped according to the rates of anemia (< 110 g/l) (including severe anemia/< 70 g/l)) and non-anemia. The results were grouped according to iron deficiency (< 15 μg/L) and non-deficiency.

	# Birth	# NTDs	NTDs/1000 Birth
Total	15115	56	3.7

Table 14: NTDs.

Regions	# Births (in study period)	NTDs		
		total	Spina Bifida	Anencephaly/ encephalocele
Tbilisi sentinel	11346	31	20	11 (4/7)
Kakheti sentinel	1286	7	4	3 (2/1)
Achara sentinel	1846	14	10	4 (2/2)
Samegrelo sentinel	637	4	3	1 (1/0)
Total	15115	56	37	19 (9/10)

Table 15: NTDs by the Regions/sentinels.

A 2X2 table was used for statistical analysis, according to which calculations were made to determine the risk/relative risk (RR) and odds ratio (OR) ratios (iron deficiency anemia/iron nondeficiency anemia), as well as Chi-squire and P value statistical reliability. These calculations revealed a “strong positive correlation” between iron deficiency and anemia (RR - 4.4; OR - 6.3).

	Anemic	Nonanemic	Total	
With Iron deficiency	a/214	b/468	682	R1 = 214/682*100 = 31.4%
Without iron deficiency	c/35	d/486	521	R2 = 35/521*100 = 7.2%
Total	249	954	1203	

Table a: RR(R1/R2) -4.4; OR (ad/bc) - 6.3.

Chi-squire - 109.4; P< 0.05 (0.00001).

Folate deficiency - anemia

A blood test for folate was used to detect folate deficiency. The results were grouped according to folate deficiency (< 3.0) and non-deficiency (> 3.0) data. The overall percentage of folate deficiency was determined in the total cohort examined, and an analysis was performed to determine the correlation between (or nonexistent) folate deficiency and anemia. A 2X2 table was used for the analysis, according to which the current ratio of risk/relative risk (RR) and odds ratio (OR) (folate deficiency anemia/folate nondeficiency anemia) as well as Chi-squire and P value statistical reliability indices were used. These calculations revealed a “positive correlation” between iron deficiency and anemia (RR - 2.3; OR - 2.6). Percentage calculations for anemia show that folate deficiency accounts for approximately 46.8% of anemia cases (Table b).

Folate deficiency detected in anemic pregnant women/a/(a+c)/46.8% (How many folate deficiency patients had anemia)

	Anemic	Non-anemic	Total	
Folate deficiency	a/126	b/210	336	R1 = 37.5%
Not folate deficiency	c/ 143	d/724	867	R2 = 18.7%
Total	269	934	1203	

Table b: RR(R1/R2) - 2.3; OR (ad/bc) -2.6.
Chi-squire - 61.5; $P < 0.05$ (0.00001).

However, further filtration revealed that folate deficiency was observed in 14% of the non-iron deficient and anemic contingent. This figure also indicates the fact that a certain percentage of anemia is caused directly by folate deficiency (megaloblastic anemia).

Age(years)	15 - 29	30 - 39	40 - 49
%	71	27.7	1.3

Table 16: Pregnant women by age groups.

Duration (weeks)	4 - 6	7 - 8	9 - 10	11 - 12
%	13	34	20	33

Table 17: Duration of pregnancy for registration moment.

Nutrition - folate deficiency

Folate-rich products consumption - Folate intake

mcg/day	% Pregnant
< 100	8%
100 - 400	22%
400 - 600	54%
600 - 1000	14%
> 1000	2%

Table 18: Folate daily intake.

Folate deficiency (ng/mL)	Pregnant %	NTDs
< 3.0 (deficiency)	28%	40
3 - 5	18%	8
5 - 10	17%	5
10 - 20	22%	3
> 20	15%	0
Total	100%	56

Table 19: NTDs - Folate deficiency.

Folate deficiency - NTDs

A 2X2 table was used to determine the cause-and-effect relationship between folate deficiency and neural tube defects. See also Chi-squire and P value statistical reliability indicators. These calculations revealed a "very strong positive correlation" between Folate deficiency deficiency and NTDs (RR - 7.2; OR - 8.2).

	NTDs	Not- NTDs	total	
Folate deficiency	a/40	b/269	309	R1 = 13%
Not folate deficiency	c/16	d/878	894	R2 = 1.8%
Total	56	1147	1203	

Table c: RR(R1/R2) - 7.2; OR (ad/bc) - 8.2.
Chi-squire - 64.3; $P < 0.05$ (0.00001).

Share of folate deficiency in total NTDs - a/(a + c) = 71%/(How many had folate deficiency in pregnant women with fetal NTDs)

Figure 3: Folate intake – folate deficiency (in plasma).
Less than norm- < 400 mcg/day
In normal range- < 400-1000 mcg/day
High enough - < 1000 mcg/day.

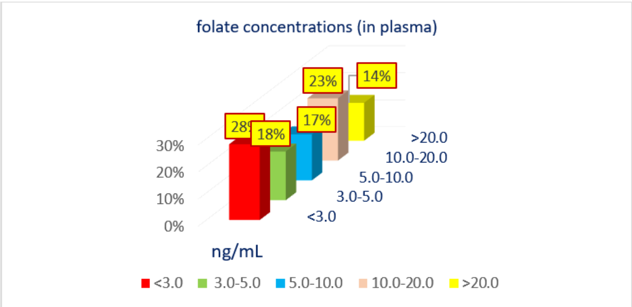

Figure 4: Folate concentrations.
Less than cut off point - < 3.0 ng/ml
In normal range - < 3.0 -20.0 ng/ml
High enough - < 20.0 ng/ml.

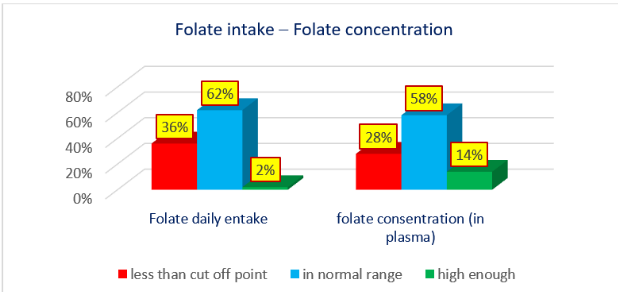

Figure 5: Folate intake - Folate concentration.

Figure 6: Co-foundings.

Folate deficiency occurred in 52% of anemic pregnancies and 22% of non-anemic pregnancies. In addition, folate deficiency was observed in 14% of anemic pregnancies who did not have iron deficiency. Iron deficiency was reported in 86% of anemic pregnancies, and 49% in non-anemic pregnancies.

The fact that folate deficiency is relatively high in both anemic and iron-deficient pregnancies in general suggests only that the amount of both iron and folate-rich (rich) products in the daily diet of pregnant women is lower. Drawing a parallel between iron deficiency and iron deficiency provides a clearer picture of nutritional status and actual nutrition. Which allows accurate and highly effective planning of nutritional interventions.

An in-depth analysis of the data revealed that iron deficiency contributed the most to the development of anemia, and a certain causal percentage came from folate deficiency, most likely from melatoblastic anemia caused by folate deficiency.

In parallel with the blood test, information was obtained about the extent to which pregnant women were informed about the need to take folate (folic acid) and its effect on health. Only, about 25% (22% - 30%) had information, and it was incomplete, about this, and in some cases a woman was taking folic acid (12%) before pregnancy was identified. Particularly low data were observed in women of first pregnancy (22%), while in the case of recurrent pregnancies this rate was relatively high (about 30%). Such pregnant women, according to the study protocol, could no longer participate in the subsequent study.

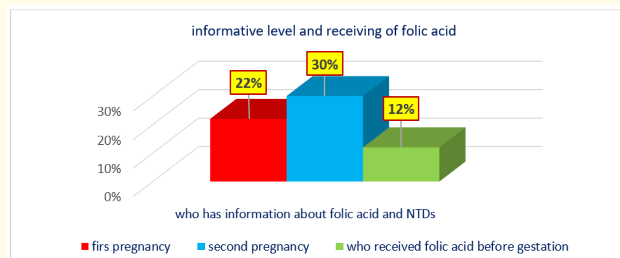

Figure 7: Informative level and receiving of folic acid.

A relatively high percentage of folate deficiency was observed in pregnant women in the 40 - 49 age group compared to other age groups, albeit slightly.

Age (years)	15 - 29	30 - 39	40 - 49
Tested pregnant (%)	71%	27.7%	1.3%
Folate deficiency (%)	27%	29%	32%

Table 20: Folate deficiency by age groups.

An analysis was made of how many pregnancies predominated in the cohort of pregnant women examined, and whether there was any association with the facts of the development of neural tube defects as to how many pregnancies a woman had.

	1st pregnancy	**2nd pregnancy**	**3rd pregnancy**	**4th pregnancy**	**5th pregnancy**
Pregnancy %	34.6%	32.9%	23.7%	7.3%	1.5%
NTDs % (from the total NTDs)	57%	37.5%	5.5%	-	-

Table 21: Pregnancy - NTDs.

The table shows that the vast majority of cases of neural tube defects occur in 1st (57%) and 2nd pregnancies (37.5%). From these facts we can conclude that during the 1st pregnancy there is a huge information deficit regarding the positive medical effects of folate intake, as a result of further recommendations made by the doctor this percentage decreases in pregnant women (due to self-dissemination of information in the population), which is more pronounced in subsequent pregnancies. And this will eventually affect the prevalence of NTDs as well. Graphically, these facts look like this:

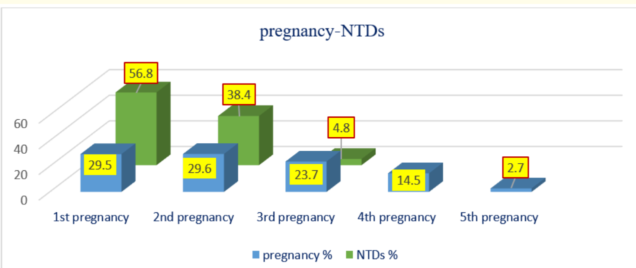

Figure 8: Pregnancy-NTDs.

The probable contributing factors to the development of NTDs cases were studied. Behavioral risk factors, the presence of which may to some extent lead to the formation of NTDs. In particular, I found information about tobacco use by a pregnant woman, as well as alcohol consumption. According to WHO references, one and the other significantly affect the health of the fetus. These factors were reported in 300 pregnant women (in all four sentinels), and it was found that only 12% of pregnant women (n = 36) reported tobacco use and 5% (n = 15) alcohol consumption, and that it was "in moderation." Among those whose fetuses developed NMD (n = 56), only 3.6% (n = 2) consumed tobacco and 1.8% (n = 1) alcohol. Due to low statistical reliability, it is impossible to consider these factors as the leading causes of NTDs.

One Sentinel base (Pineo Medical Ecosystem) also provided information on cases of neural tube defects and possible links between blood relatives. During the last 18 months (06.2019 - 12.2020) 5 cases of NTDs were observed in the clinic (spina bifida-1; anencephaly-2; encephalocele-2). Relative marriages were not observed in any of the cases.

Recommendations

- It is recommended that women of reproductive age, adolescents (girls), and pregnant women be provided with information on healthy and wholesome nutrition. To this end, the development of government and municipal programs should be promoted, as well as the active involvement of non-governmental organizations and the population itself in awareness-raising activities.
- It is recommended that a woman should start taking folic acid at a dose of 400 mcg per day at least 2 months before pregnancy and continue for up to 12 weeks of pregnancy. (Source: Prevention of neural tube defects/WHO).
- It is recommended to promote the implementation of the strategy of targeted fortification of food (including women of reproductive age) in Georgia with folic acid and iron. In addition, anemic pregnancies with iron supplements should be continued according to the doctor's decision.
- As the study showed a high prevalence of fetal neural tube defects, it is recommended to add a variable - "neural tube defect" to the abortion section of the birth registry system to reflect NTDs in medical statistics that resulted in abortion based on medical indications.
- It is recommended that trainings be conducted for physicians on the issues of complete nutrition of women, taking folic acid (supplements), and prevention of neural tube defects.
- It is recommended that the state take action to promote family planning, and therefore the likelihood of receiving folic acid before pregnancy increase significantly.
- It is recommended that a woman of reproductive age receive information about the positive preventive effects of folic acid when purchasing a pregnancy test or other medical services. For this, pharmacies and medical institutions should be provided with appropriate information and educational materials.
- Information-educational campaigns for women of reproductive age should be carried out in order to increase the rate of early registration of pregnant women in the country, in terms of timely start of antenatal care.
- It is recommended to put on the packaging of various products (including medical) a label (slogan) that will focus the buyer on the health of the fetus (e.g., "folic acid protects the health of the fetus, etc.")

- a) it is recommended to make appropriate changes and additions to the existing legislative acts:
- The Law of Georgia on Prevention of Diseases Caused by Deficiency of Iodine, Other Micronutrients and Vitamins should be included in the Law on Voluntary Fortification of Food with Iron and Folic Acid; b) in the state programs for maternal and child health, should be added a note - "Providing free access to folic acid and iron supplements for women of reproductive age".

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