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Characteristics and correction of the course of pregnancy and childbirth in women infected with Giardia

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ABSTRACT

of the dissertation submitted for the Doctor of Philosophy degree

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GENERAL CHARACTERISTICS OF THE WORK

Relevance of the topic and degree of development. Prevention and treatment of infectious and parasitic diseases remains one of the priority tasks not only of the sanitary-epidemiological service, but also of public health. Ensuring the satisfactory progress of pregnancy and childbirth is considered as one of the urgent medical and social problems for most countries of the world in modern times.[1,2] Almost all causative agents of parasitic diseases manifest themselves in the body with general pathological effects such as allergy and immunosuppression. Modern studies convincingly prove that disruption of the normal course of pregnancy and intrauterine development of the fetus depends not only on the presence of infection, but also on the severity of changes in the mother's immune homeostasis and the direction of the infection. Based on the results of the research, the majority of pregnant women with protozoan infections develop a symptom complex similar to early toxicosis of pregnancy. Vegetotropic effect of parasites causes continuous arterial hypotonia throughout pregnancy.[3,4]

Symptoms of intoxication, dyspeptic disorders, irritable bowel syndrome, hypochromic anemia, allergic reactions from the skin and respiratory organs, and hypovitaminosis are often recorded in infected pregnant women. In women suffering from giardiasis, habitual pregnancy losses, the risk of miscarriage, spontaneous abortions or premature births in the early period of pregnancy, as well as numerous diseases of newborns can be observed.[5]

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Allergic reactions are typical for protozoan infections. It was determined that perinatal pathologies are 1.6 times more common in children born to women with giardiasis.[6]

Despite the widespread prevalence of parasitic infections among pregnant women, and the fact that they have a negative impact on the clinical course of pregnancy, this problem has not been sufficiently studied.[7,8] The relationship between allergic reactions during pregnancy and the incidence of giardiasis, as well as the effect of giardiasis on the immunological status of a woman during pregnancy, is poorly covered in the literature.[9,10]

The object and subject of the research

The basis of the study was 137 Giardia-infected women aged 18 to 40 (average age 28.42±4.8 years) in the 16-40 weeks of pregnancy. Pregnant women from the main group are divided among themselves into the following groups: The 1st main group consisted of 56 women (40.9±4.2%). In these women, the pregnancy lasted against the background of primary infection with giardia (acute giardiasis) and ended with the birth of live children. The 2nd main group consisted of 81 women (59.1±4.2%), whose pregnancy was complicated by giardiasis with a long, relapsing course (chronic giardiasis) and ended with the birth of live children. As a control group, 45 pregnant women aged 18 to 45 (average age 25.42±0.8 years) with no history of protozoan infestation and clinical symptoms were taken.

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The purpose of the study

Comprehensive assessment of clinical and laboratory characteristics of pregnancy in women with giardiasis, improvement of prenatal preparation and delivery.

Tasks of the research work

1. Study of the level of giardiasis and risk factors of pregnant women in Baku;

2. Complex analysis of the characteristics of the clinical course of pregnancy and the results of clinical laboratory examination in pregnant women with giardiasis;

3. Study of the effect of giardiasis on the course and results of pregnancy, on the condition of the fetus and newborn;

4. Assessment of the somatic status of pregnant women with giardiasis, study of the pathogenetically based interaction between intestinal and genital microbiota;

5. Development of an algorithm for early diagnosis and prevention of giardiasis in pregnant women.

Methods of research work

A number of complex modern examination methods were used in the conducted research, including: clinical, epidemiological, parasitological, immunological, statistical, etc. methods.

The main provisions defended:

- Pregnancy and childbirth in women with giardiasis are characterized by an honest increase in complications for both the mother and the fetus.

- The spectrum of aggravating effects of giardiasis on the course of pregnancy and its satisfactory outcome.

- Modern approaches to diagnosis, therapy and prevention of giardiasis among pregnant women.

Scientific novelty of the research

1. In the study, the level of giardiasis infection and risk factors of pregnant women living in Baku were determined. The course of pregnancy was assessed, and the aggravating effect of giardiasis on the course and outcomes of pregnancy was studied. The frequency of pregnancy complications was investigated depending on the severity of giardiasis;

2. Early diagnosis and prediction of hemodynamic indicators in the fetoplacental system during giardiasis, as well as pathological conditions occurring during pregnancy, allows to reduce pregnancy complications, perinatal morbidity and mortality;

3. In the research work, it was shown that a complex approach is necessary in the diagnosis of giardiasis: clinical-laboratory, functional examinations, as well as evaluation of the hormonal function of the fetoplacental system;

4. On the basis of the obtained results, a complex examination algorithm of pregnant women with giardiasis, effective tactics of pregnancy and childbirth were developed.

Practical significance of research

Based on the data obtained during the examination of pregnant women with giardiasis, an effective examination program of women was proposed, which allowed to correctly assess the course of the disease. The differential diagnostic features of the disease were distinguished, and a combined effective treatment tactic was proposed to eliminate the negative impact of giardiasis on the course and outcome of pregnancy.

The study of the changes in the production and activity of cortisol, insulin-like growth factor-1 and interleukin-2 in the pre-clinical stage allowed predicting the occurrence of pregnancy complications in women with giardiasis. It was considered appropriate to determine the level of the mentioned factors in the blood serum and amniotic fluid of pregnant women. On the basis of the obtained data, methods of early diagnosis of giardiasis, as well as a set of measures aimed at the prevention of gestation period pathologies in pregnant women with giardiasis were developed.

On the basis of pathogenetic factors, during the development of the clinical picture of giardiasis, it was possible to assess the severity of the disease, control the effectiveness of therapy and choose effective obstetrical tactics. Application of the mentioned set of prognostic and diagnostic measures allows to reduce pregnancy and childbirth pathologies, perinatal morbidity and mortality.

Approval and application of the dissertation: The main provisions of the dissertation, materials of the scientific-practical

conference Current Problems of Medicine, Baku-2018; Materials of the scientific conference dedicated to the 80th anniversary of the birth of Honored Scientist Professor Abbas Ahmed Akhundbeyli, Baku-2018; Black Sea 2nd International Congress of Applied Sciences, Rize, August 23-25, 2019; Materials of the Scientific Conference dedicated to the 75th anniversary of the birth of Dr. Azam Tayyar Aghayev, Baku, 2019; Journal of Theoretical Clinical and Experimental Morphology, Volume 1, No. 3-4, 2019 was presented at scientific conferences.

The initial defense of the dissertation was held at the extended meeting of the II Department of Obstetrics and Gynecology of the Azerbaijan Medical University (16.03.2022, protocol No. 05) and at the meeting of the Discussion Council holding scientific seminars on the specialty 3215.01 - "Obstetrics and Gynecology" (13.06.2022, protocol No. 15) was discussed.

The name of the organization where the dissertation work was performed: Department of Obstetrics and Gynecology II of Azerbaijan Medical University.

Publication of the provisions and results of the case. 11 scientific articles and theses were published on the main provisions of the work. Among them, 3 articles and 4 theses were published in local press, 2 articles and 2 theses were published in foreign press.

Structure and scope of the dissertation. The dissertation is printed on a computer on 168 pages (215242 characters) with comments, "Contents", "Introduction" (9 pages, volume: 15267 characters), "Results" (2 pages, volume: 5552 characters), "Practical recommendations" (1 page, volume: 1022 characters) and "List of used literature" (22 pages) sections.

The main content of the dissertation is divided into 5 chapters. Chapter I "Literature review" (30 pages, volume: 57469 marks), Chapter II "Materials and methods of research" (10 pages, volume: 17722 marks), Chapter III "Research results" (29 pages, volume: 35674 marks) , Chapter IV (25 pages, volume: 23550 marks), Chapter V (19 pages, volume: 24445 marks), Discussion of results (18 pages, volume: 34541 marks).

204 literary sources were used in the writing of the dissertation, of which 2 Azerbaijani, 40 Russian and 162 foreign scientists' works were cited. The dissertation work is illustrated with 53 tables, 1 picture and 12 graphs.

Materials and methods of research

Based on clinical-laboratory criteria developed to achieve the goal set in the research work 137 giardia-infected pregnant women aged 18 to 45 years (average age 28.42±4.8) and 16-40 weeks pregnant were examined in 2015-2017. 652 pregnant women were examined to determine the prevalence of giardiasis among women of reproductive age. Among them, giardiasis was found in 137 women (21.0±3.5%). Depending on the characteristics of the course of pregnancy, pregnant women from the main group in different clinical forms of giardiasis are divided into the following subgroups:

- the 1st main group consisted of 56 women (40.9±4.2%), whose pregnancy was carried out against the background of primary infection with giardia (acute giardiasis) and ended with the birth of live children;

- The 2nd main group consisted of 81 women (59.1±4.2%), whose pregnancy was complicated by chronic giardiasis with a long, relapsing course and ended with the birth of live children.

As a control group, 45 pregnant women aged 18 to 45 years (average age 25.42±0.8) with no history of protozoan infestation and no clinical symptoms were taken. All pregnant women underwent parasitological screening to detect giardiasis.

Extragenital and gynecological diseases of women, the number and outcome of previous pregnancies, and obstetric complications were studied based on the analysis of medical histories. Data on termination of pregnancy included analysis of methods of delivery, evaluation of termination of delivery, analysis of the course of the postpartum period, as well as analysis of neonatal morbidity in the early neonatal period. In order to study the features of the effect of giardiasis on the course and results of pregnancy, classic obstetric methods and clinical-laboratory examinations, as well as methods of determining the allergic status and diagnosing giardiasis, were applied

to the examined pregnant women. During the anamnesis collection, special attention was paid to the signs of allergy of the pregnant woman's body and the prevalence of important risk factors of infection with giardiasis.

In order to detect protozoan invasion, parasitological examination of pregnant women with routine coprological methods, as well as examination with specific serological diagnostic methods was carried out. Search for cysts of Giardia was carried out by staining a thin smear of stool in Lugol's solution by the standard microscopy method. In addition, in order to increase the probability of detection of invasion, women were examined using a Burroughs preservative (to preserve invasion factors in the studied material). Statistical analysis of the obtained data was carried out with the help of software tools and Statistica 8.0 for Windows 9.0 package.

The following application software package was used in the research work: MS Office Excel 2010 for the organization and formation of the data matrix, the preparation of graphs and charts. Descriptive statistics methods were used to evaluate the arithmetic mean (M), error of the mean (m) and mean square deviation (σ) for normally distributed traits, and the integrity of the differences between groups was determined using the Student's (t) test. When comparing frequencies in 2 or more groups, the χ^2-Pearson test was used. Correlation analysis was used in some cases to evaluate the statistical relationships between the signs. Spearman's order (rank) correlation coefficient (using the rs-criterion) and Pearson's coefficient were used to measure correlation dependence. Correlations and differences were considered statistically significant when $p < 0.05$. Absolute and relative risks were calculated using propensity tables to compare groups on binary characteristics.

RESEARCH RESULTS AND THEIR DISCUSSION

During the study, all examined patients were included in prospective examinations. 76 (55.6±4.2%) pregnant women were examined in the first trimester of pregnancy, 44 pregnant women (32.1±3.9%) in the second trimester, and 17 (12.3±2.8%) pregnant women in the third

trimester. The characteristics of patients by age are presented in table 1.

Table 1.

Characteristics of pregnant women according to age

Age Groups	18 – 20		21 – 35		36 - 45	
	Ratio	%	Ratio	%	Ratio	%
Main group (n=137)	11	8,0±2,4	92	67,1±4,1	34	24,8±3,7
Control group (n=45)	4	8,9±4,2	29	64,4 ±7,1	12	26,7±6,7

It was found that the number of births was higher among women aged 21-35. It was found out that the numerical preference was among pregnant women aged 21-35. Thus, there were 92 people in the main group, which was 67.1±4.1%. In the control group, this indicator was 29 pregnant women aged 21-35 (64.4±7.1%). First and second births at the age of 36-45 (34 people in the main group, 12 people in the control group) were 24.8±3.7% and 26.7±6.7%, respectively. Pregnancy was observed in 11 (8.0±2.4%) and 4 (8.9±4.2%) people, respectively, among 18-20-year-old women ($p>0.05$). During the study of the social status of the examined women, it was determined that among 182 patients in 3 clinical groups, 117 (64.3±3.5%) women worked in professional activities, of which, according to the groups with mental labor: In group I (n=50) 55.4±6.6% pregnant women, in group II (n=81) 54.3±5.5% pregnant women, in the control group (n=45) 62.3±4.1% of pregnant women were employed. According to physical work in groups: 5.3±3.1% (n=3), 4.9±2.4% (n=4) and 8.9±4.2% (n=4) of pregnant women were employed. Housewives by groups, respectively: in group I 39.3±6.5% (n=22), in group II 40.8±5.5% (n=33), in the control group, 28.8±6.7% (n=10) were pregnant women. 182 patients in 3 clinical groups were analyzed according to their educational level. 132 (71.4±3.4%) had higher education, 29 (15.9±2.7%) secondary special education, 21 (12.7±2.5%) secondary education.

The obstetric anamnesis of the women in the comparison groups was studied in detail. It was performed artificial abortions in group I 16 (28.6±6.1%), in 17 (20.9±4.5%) women in the II group and 7 (15.5±3.1%) women in the control group until the 12th week of pregnancy. Spontaneous miscarriages in the anamnesis in 7 (12.5±4.5%) women in group I, 8 (9.9±3.3%) in group II, 3 (6.67%) in control group; undeveloped pregnancy was recorded in 6 (10.7±4.2%) women in group I, 4 (4.93%) in group II, and 2 (4.44%) in control group ($p<0.05$). In the anamnesis, 45 (80.4±4.6%) women in group I, 69 (85.2±3.9%) in group II, and 44 (97.8±2.1%) women in the control group were registered. Cesarean section births occurred in 6 (10.7±4.2%) women in group I, 8 (9.9±3.3%) in group II, and 2 (4.44%) in control group. Gynecological diseases were observed in all women with giardiasis. In patients with giardiasis, the number of endometrial polyps was 16.1±4.9% in group I and 20.9±4.5% in group II. However, simple endometrial hyperplasia is 12.5±4.5% and 9.9±3.3%, respectively; recurrent non-specific vaginitis was frequently found in the anamnesis of 26.8%±5.9% and 29.6±5.1% of women with giardiasis.

Asthenovegetative complaints are more common in the group of patients with giardiasis. These complaints were noted with the following frequency according to the groups: weakness 33.9±6.3% in group I, 18.5±4.5% in group II, extreme fatigue 32.1±6.2% in women of the main group, respectively and 39.5±5.4%; headaches 28.6±6.1% and 27.2±4.9%; irritability 26.8±5.2% and 13.4±3.9%; sleep disturbance 14.3±4.6% and 18.5±4.5%. Similar complaints were practically not found in the group of healthy women, they were recorded only in 8.9±4.2%, 6.7%, 17.7±5.7%, 15.5±3.6%, 4.4% of women, respectively. The high frequency of gastroenterological complaints in examined women attracts attention. All gastroenterological complaints were statistically significantly more common in patients with giardiasis. Gastroenterological complaints were more frequent in both subgroups of the main group, especially in group I (table 2).

Table 2.

Gastroenterological complaints in examined women

Complaints	I group (n=56)		II group (n=81)		Control group (n=45)		P
	Ratio	%	Ratio	%	Ratio	%	
Pain in the epigastric region	31	55,4±6,6	23	28,4±5,0	2	4,4	<0,05
Right subcostal pains	48	85,7±4,9	61	75,3±4,8	0	0	<0,05
Pain in the hypogastric region	35	62,5±6,5	32	39,5±5,5	0	0	<0,05
Nausea	23	41,1±6,6	31	38,3±5,4	4	8,9±4,2	<0,05
Bitterness in the mouth	19	33,9±6,3	22	27,2±4,9	2	4,4	<0,05
Swelling in the stomach	8	14,3±3,9	10	12,5±3,8	2	4,4	<0,05
Meteorism	38	67,9±6,2	16	19,7±4,4	3	6,7±	<0,05
Constipation	11	19,6±5,3	12	14,8±3,9	4	8,9±4,2	<0,05
Diarrhea	22	39,8±6,5	26	32,1±5,2	0	0	<0,05

So that, pains in the right subcostal region attracted attention in 85.7±4.9% in group I and 75.3±4.8% in group II, $p<0.05$, pain in the hypogastric region (62.5±6.5% and 39.5±5.5%, respectively, $p<0.05$), related to pain in the epigastric region (55.4±6.6% and 28.4±5 .0%, $p<0.05$)

Some syndromes, for example, intestinal dyspepsia (flatulence, change in stool consistency); functional dyspepsia (nausea); biliary dyspepsia (bitterness in the mouth) was also significantly more common in pregnant women in the main group ($p<0.05$).

Thus, these indicators for groups I and II were as follows: nausea 41.1±6.6% and 38.3±5.4%, bitterness in the mouth 33.9±6.3% and 27.2±4, 9%, flatulence 67.9±6.2% and 19.7±4.4%, diarrhea 39.8±6.5% and 32.1±5.2%.Gastric bloating and constipation were less frequent.

According in the main group, the level of ALT was 0.59±0.02nmol/l according to the level of the unit, in the control group it was 0.27±0.02 units, level of AST, it was 0.77±0.03 units and 0.42±0.03 ($p<0.05$).

According in the level of gamma-glutamyltranspeptidose (GGT) was 18.27±0.39 units in the main group, 12.39±1.21 units in the control group, and the level of alkaline phosphatase (QF), it was 362.23±56.40 units and 163.50±48.31 measurement units ($p<0.05$).

Although there was a statistically significant difference between the similar indicators in the comparison groups, hyperfermentemia was not detected in any patient. The average level of amylase in blood serum of women with giardiasis was higher than that of the comparison group. In women with giardiasis, against the background of concomitant gastroenterological pathologies, the glycemic profile and fat metabolism are disturbed.

Predominance of pathology of the hepatopancreatobiliary system during giardiasis in examined women was confirmed by USM of abdominal organs (table 3). Symptoms of atopic dermatitis were recorded in 26.8±5.9% and 27.2±4.9% of patients with giardiasis, respectively.

Clinical signs of gastroenterological diseases were fairly frequent in both groups of patients with giardiasis: coating of the tongue in the majority of patients (55.4±6.6% and 39.5±5.4%), pain in the epigastric area during palpation (55.4±6.6% and 28.4±5.0%, respectively), pains in the pyloroduodenal zone (77.35% and 33.33%), pains in the right subcostal area (85.7±4.9% and 75.3±4.8%) and pains in the hypogastric area (62.5±6 .5% and 39.5±5.5%), hepatomegaly (14.3±4.6% and 11.1±3.5%). The detected changes were determined by disturbances of the intestinal microbiota and damage to the mucosa of the MBT.

Table 3.

Information on USM in examined patients

Signs	Main group (n=137)		Control group (n=45)		p
	Müt	%	müt	%	
Hepatomegaly	22	16,1±3,1		2,22	<0,05
Symptoms of hepatosteatosis	21	15,3±3,1	2	4,44	<0,05
Changing the shape of the gallbladder	74	54,0±4,3	10	28,8±6,7	<0,05
Enlargement of the gallbladder	19	13,9±2,9	2	4,44	<0,05
Thickening of the walls of the gallbladder	34	24,8±3,7	2	4,44	<0,05
Stagnation in the gall bladder	49	35,8±4,1	3	6,67	<0,05
Stones in the gall bladder	9	6,57	1	2,22	>0,05
Cholecystectomy	5	3,65	0	0	>0,05
Changes in the echogenicity of the pancreas	17	12,4±2,8	7	15,5±3,1	>0,05
Changes in the echostructure of the pancreas	5	3,65	0	0	<0,05
Splenomegaly	3	2,18	0	0	>0,05

Hypochromic microcytic anemia was found in 3 women with giardiasis during clinical blood examination. The clinical examination of urine was within normal limits in all those examined. In addition, against the background of the predominance of gastroenterological complaints in women with giardiasis, coprological signs of digestive disorders were often detected: bile deficit syndrome

(28.6±6.1% and 27.2±4.9%, $p<0.05$) , pancreatic coprological syndrome (14.3±4.6% and 11.1±3.5%, $p<0.05$). Most of the examined patients were infected with Heliobacter pylori. In the group of women with giardiasis, the frequency of infection (38.7±4.2%) was significantly higher than the control group (8.8±4.2%) ($p<0.05$).

The condition of the newborns was assessed. Fetal outcome and early neonatal course were analyzed in 137 children born to mothers with giardiasis. All children born to mothers with giardiasis were divided into 2 groups: group I consisted of 56 newborns born to mothers in the main group I of pregnant women we examined, group II consisted of 81 newborns born to mothers in the main group II of pregnant women with giardiasis. 105 of the newborns (76.6±3.6%) were born on time and only 32 (23.4±3.6%) were born prematurely. Newborns were born between the 32nd and 40th week of gestation. Body weights of newborns in the presented groups did not undergo significant changes. This indicator in group I was 3143.31±460.63 grams, in group II it was 3192.7±414.45 grams. No statistically significant difference was found between groups I and II, as well as the control group ($p>0.05$). A similar picture was revealed in the anthropometric indicators of newborns. This indicator was 49.91 ± 1.84 cm in group I newborns, and 50.1 ± 1.74 cm in group II. No honest differences were found in the height indicators of newborn mice between the presented groups ($p>0.05$). The indicators obtained when assessing the condition of newborns born to mothers with giardiasis with the Apgar scale have attracted attention. Thus, in the first minute of life of newborns in group I, this indicator was 6.81±1.24 points and in the 5th minute, it was 7.1±0.97 points. These indicators are honestly lower compared to similar indicators in the control group: In newborns born to mothers from group II, the Apgar score at the 5th minute was honestly lower than the similar indicator of the control group ($p<0.05$). In newborns from group I, both indicators of the Apgar scale (6.81±1.24 points and 7.1±0.97 points) were higher than the analogous indicators of the control group (7.38±0.53 points and 7.6±0.47 points) was statistically significantly lower ($p<0.05$). Although the analogous indicators in group II newborns are relatively lower than those of the control group, only Apgar scale assessment of 7.51±0.58

points from the 5th minute was considered statistically significant ($p<0.05$).

Newborns with a score of 7-10 were considered good or optimal (requiring routine care). During the assessment according to the interval from 4 to 6 points, the health condition was considered satisfactory, in which case only some resuscitation measures are needed. Emergency resuscitation was required if the Apgar score was below 4 points.

The optimal condition of newborns in groups I and II was as follows: 7 points - 41 (73.21%) cases in group I and 48 (59.3%) cases in group II. In the control group, 2 (4.44%) newborns were born with intrauterine growth retardation (IUGR). The indicator of the presence of a large fetus was also observed in the same number of 2 (4.44%) below 7 points, the condition of these newborns was evaluated by the Apgar scale above 7 points. 2 (3.57%) of the newborns scored 6 points at the 1st minute and 3 (5.35%) at the 5th minute. In group II, BDIL was recorded in 1 case (2.47%). The frequency of BDIL was higher in women with giardiasis. This was due to the adverse effect of the hypertensive condition in pregnant women on the intrauterine development of the fetus. The duration of the dry period after premature discharge of amniotic fluid was higher in groups I (10.59±2.07 hours) and II (9.3±1.91 hours). This indicator was 1.54±0.68 hours in the Control group. Such a prolonged period of dehydration leads to infection of the fetus, serious changes in the immune status in the already existing dysbiosis conditions, and leads to perinatal complications.

The level of cortisol, interleukin-2 and insulin-like growth factor-1 in blood serum and amniotic fluid of pregnant women was studied. The data obtained in the main groups were compared with the data in the control group (table 4).

Table 4.

The dynamics of changes in the amount of cortisol in the blood serum and amniotic fluid of pregnant women in the control groups

Inspection object	Cortisol amount		
	Control group (n=45)	I group (n=56)	II group (n=81)
Blood serum (nmol/l)	1166,0±128,7	1147,1±150,1	1037,5±165,5
	-	p>0,4	p>0,4
Amniotic fluid (nmol/l)	147,7±21,3	424,2±65,1	227,0±29,0
	-	p<0,005	p>0,05
Amount of insulin-like growth factor-1			
Blood serum (nmol/l)	277,2±61,7	313,4±72,5	153,1±26,2
	-	p>0,4	p>0,4
Amniotic fluid (nmol/l)	118,0±31,2	160,43±74,0	151,45±41,0
	-	p <0,005	p>0,05
The quantity of IL -2			
Blood serum (nmol/l)	20,1±1,4	18,5±1,7	18,1±1,6
	-	p>0,4	p>0,4
Amniotic fluid (nmol/l)	23,3±3,1	33,1±2,7	25,73±4,0
	-	p>0,05	p>0,05

Note: p is the coefficient of honesty of indicators of group I, II in relation to indicators in the control group.

The amount of cortisol in the blood serum of pregnant women changed slightly: 11.47±150.1 nmol/l in group I, 1037.5±165.5 nmol/l in group II, 1166.0±128.7nmol/l in the control group. At this time, honest changes were not determined (p>0.05). During the study of the characteristics of changes in the level of cortisol in the cerebrospinal fluid, a different picture was noticed. Thus, the amount of hormone in the control group was 147.7±21.3nmol/l, and in women with giardiasis it increased to 424.2±65.1nmol/l. In group I, the indicator increased almost 3 times (p<0.005). The level of IL-2 in the blood serum of pregnant

women underwent slight changes. Its maximum amount was found to be 20.1±1.4 pg/ml in the control group. The minimum level was 18.1±1.6 pg/ml in women in group II. Therefore, no statistical difference was found in the determination of IL-2 in blood serum in pregnant women of either group I or II compared to the indicators of the control group ($p>0.05$). However, honest differences in these indicators were not determined in our research ($p>0.05$). Different results were obtained during the determination of the amount of IL-2 in the amniotic fluid. The level of IL-2 in pregnant women in group I (33.1±2.7 pg/ml) was higher than the similar indicator in the control group (23.3±3.1 pg/ml). Thus, the study of the characteristics of IL-2 level changes gives reason to think that its level in the blood serum of pregnant women does not depend on accompanying pathologies. A significant increase in amniotic fluid levels in women with giardiasis was associated with protozoan invasion.

Maximum levels of insulin-like growth factor-1 (IBA-1) were also recorded in the blood serum of pregnant women in group I (313.4±72.5 ng/ml). The minimum level was 153.1 ± 26.2 ng/ml and was found in pregnant women of the II group. Although the increase of this indicator was noticeable in group I, and its decrease in group II, there was a reliably honest difference when comparing the results with the control group. That is, the presence of giardia was accompanied by a slight change in the amount of IBA-1. The study of IBA-1 in amniotic fluid shows that in the amniotic fluid of women from group I, this indicator was statistically significantly higher ($p>0.05$) compared to the indicator of the control group, although the indicators in the II group were higher compared to the control group, they were not statistically significant ($p>0.05$). Thus, there was a similar indicator in different groups: from 118.0±31.2 ng/ml in the control group, 160.43±74.0 ng/ml in group I, 151.45±41 ng/ml in group II; it was not done only in group I ($p>0.05$).

3 factors mainly affect the frequency of forms of invasion. 1. Repetition of previous treatment. For example, the frequency of the severe form decreases from 24.6±3.7% to 4.7±1.8% with an increase in the frequency of therapy from 1 to 5 ($\gamma=-0.86+0.11$), that is, unspecialized treatment leads to the transition of the disease to a chronic, sluggish state, even if the clinical symptoms disappear (graphs 1 and 2).

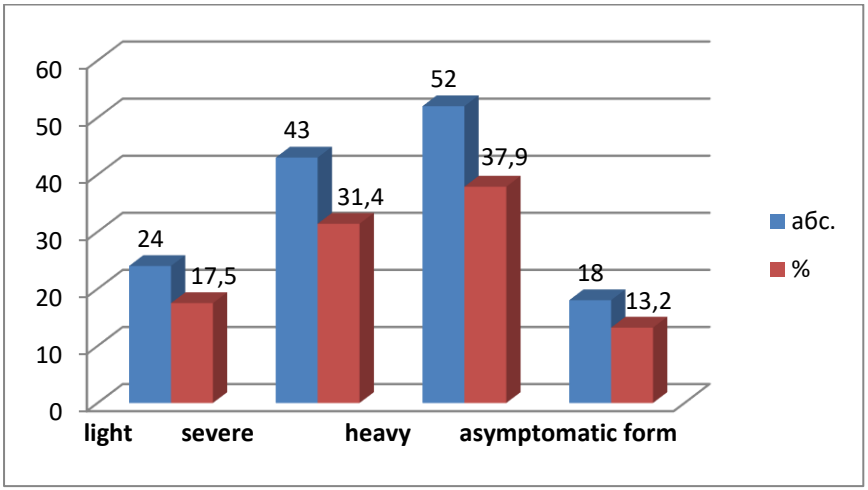
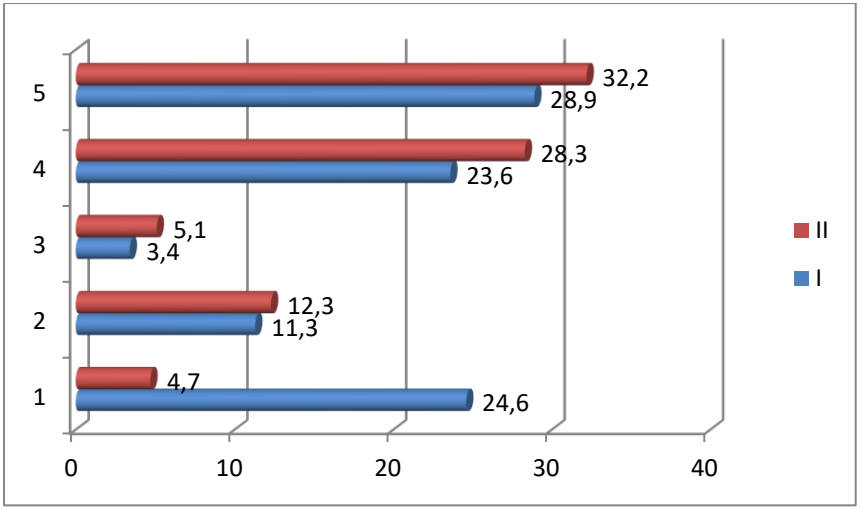


Chart 1. Forms of the clinical course of giardiasis



Graph 2. The influence of leading factors on the frequency of forms of invasion

1. Repetition of previous treatment; 2. Associations of ШPF during secondary form; 3. Associations of PF during severe form; 4. Associations with pathogenic microflora, chlamydia and

trichomonads in the middle form; 5. Associations with pathogenic microflora, chlamydia and trichomonads during the severe form I – once; II- many times.

2. Accompanying microflora. Giardiasis has independent clinical symptoms, but when pathogenic microflora, chlamydia and trichomonas join, its severity increases and the frequency of more severe forms of the disease increases. Most likely, the degree of pathogenicity of each pathogenic factor is cumulative. All these associated infections aggravate the clinical course of giardiasis.

The amount of bifidobacteria (In group I - 1742 kl/g x105, in group II - 2367 kl/g x105) and lactobacilli (In group I – 1218 kl/g x105, in group II – 2114 kl/g x105) was lower than normal values in both examination groups (bifidobacteria 5062 kl/g x105, lactobacilli 4334 kl/g x105). However, the amount of lactobacilli in the group of women with giardiasis was significantly lower ($p<0.05$). In the comparison group, their amount was within the norm (3.73±1.60 KEV/g and 8.17±1.63 KEV/g, respectively). In group I, compared to group II, an increase in the level of CSF: Gardnerella vag., Streptococcus sp., Enterococcus sp., Candida albicans was noted.

Not only the positive clinical dynamics of blood biochemical tests, but also positive changes were observed in all studied groups during the treatment process: a decrease in the level of QF, which is considered an indicator of intrahepatic cholestasis, and a decrease in the level of amylase, against the background of a decrease in the frequency of hepatomegaly. In the group of patients receiving prebiotic and complex therapy, a positive dynamic of indicators of carbohydrate and lipid metabolism was noticed.

In the group of patients receiving prebiotic and complex treatment, the frequency of lactobacilli cultivation increased significantly; only in the group receiving antibacterial therapy, while the frequency of lactobacilli did not change, the decrease in the frequency of CSF was predominant. The dynamics of detection frequency of various representatives of the uterine microbiota in patients with concomitant pathologies of giardiasis and MBT against the background of the therapy is presented in table 6.

Table 6

The dynamics of the detection frequency of the most important representatives of the uterine microbiota in patients with concomitant pathologies of giardiasis and MBT against the background of the therapy (%)

Bakterial ştamlar	1st group (n=37)		2nd group (n=29)	
	Before treatment	After treatment	Before treatment	After treatment
Lactobacillus	25,2	88,2**	21,4	28,6
Gardnerella vag.	23,5	0*	17,8	7,1
Escherichia coli	58,8	33,3*	46,4	21,4*
Streptococcus spp.	64,7	41,1*	67,8	25**
Staphylococcus aur.	29,4	17,6*	32,1	10,7*
Corynebacterium sp.	76,4	47*	64,2	35,7**
Enterococcus sp.	52,9	17,6**	50	21,4*
Streptococcus B	33,3	23,5	53,5	17,8**
Klebsiella spp.	47	29,4*	57,1	14,2**
Staphylococcus epid.	41,1	23,5*	35,7	7,1**
Candida albicans	17,6	5,8*	10,7	3,5*

Note: * - differences before treatment and after treatment are honest ($p<0.05$);

**- pre-treatment and post-treatment differences are honest ($p<0.01$).

Against the background of the restoration of the microecology of the uterus, during the examination of the patients, hyperemia and swelling of the vulva and uterus disappeared, and at the end of the treatment, the discharge became transparent and mucous; the pH of the uterus is close to normal (pH=4.0-4.5).

During the examination of the patients 4 weeks after the start of the treatment, they noted a significant improvement in the somatic status of all women. Against the background of the therapy in both groups, the overgrowth of many SPF decreased, in the group receiving

"Eubikor" the overgrowth of normoflora in the uterine cavity decreased.

In the observation group, 182 (100%) births occurred, of which 171 (93.9±1.8%) were on time, 11 (6.1±1.8%) were premature, no delayed births were recorded. In 149 women (81.9±2.8%), births occurred spontaneously and in 33 (18.1±2.8%) they were performed surgically (caesarean section). The average duration of childbirth in women from all groups did not differ: it was 8.4+0.6 hours in the first group, 8.6±0.3 hours in the second group, and 8.1±0.3 hours in the control group. The dry period was 5.8 ± 0.4 hours in all groups. No more than 400 ml of satisfaction was observed after spontaneous births in the examined groups. In most cases, the content was up to 220 ml.

During the study of the quantitative composition of the microflora of the uterus, a clear decrease in the normal level of lactobacilli was noticed in the main group, while their amount was within the normal range in the comparison group. At this time, in group I compared to group II, an increase in the level of CSF: Gardnerella vag., Streptococcus sp., Enterococcus sp., Candida albicans was noted.

BV and non-specific vaginitis are often found during giardiasis. In the material taken from the cervical canal and uterine cavity in women with giardiasis has been revealed a lot to Ureaplasma urealyticum - 47 (34.0±4.1%) and 3 (6.7%) pregnant women ($p<0.05$), Chlamydia trachomatis - 41 (29.9±3.9%) and 2 (4 .4%) in pregnant women ($p>0.05$) and Mycoplasma hominis - 22 (16.1±3.1%) and 4 (8.9%) pregnant women ($p>0.05$). Neisseria gonorrhea was not detected in any of the examined women.

66 patients with a history of giardiasis and relevant gastro-enterological pathology, and various degrees of intestinal and genital microbiota changes were examined in order to determine ways of correcting the changes in intestinal and genital tract microbiota.

The 1st group consisted of women (n=37) who received 2 packets of "Eubikor" in the amount of 18 grams per day before meals for 4 weeks as part of complex therapy (carried out with antiparasitic, antibacterial, spasmolytic, secretolytic and enzyme preparations).

The 2nd group (comparison group) consisted of those patients (n=29) who were treated only with antiparasitic, antibacterial, spasmolytic, secretolytic and enzyme preparations without using prebiotics.

It was found that the treatment of patients from group 1 was more effective, compared to the group that did not receive prebiotics, the following symptoms were already reduced: pain syndrome (pain in the right subcostal area up to 75.7%, pain in the epigastric area - up to 29.7%, pain in the hypogastric area - up to 40.6%), nausea (up to 40.5%) , bitterness in the mouth (up to 32.4%), flatulence (up to 54.1%), constipation (up to 32.4%), diarrhea (up to 18.9%), asthenic complaints - 43 up to .3%. Disappearance of pain was observed after 4.5±0.5 days of treatment in group 1 and 10.2±0.8 days after treatment in group 2 ($p<0.05$). Dyspeptic cases were prevented by 5.2±0.7 days of treatment in group 1 and 12.2±0.5 days of treatment in group 2 ($p<0.05$). Compared to the group that did not receive prebiotics, the following symptoms decreased more: pain in the right subcostal area during palpation - 72.9%, pain in the epigastric area during palpation - 75.7%, hypogastric pain during palpation - 78.4%, liver enlargement - up to 18.9%. The period of reduction of pain during palpation was found within 7-8 days in the 1st group and 11-13 days in the second group ($p1.2<0.05$).

4 weeks after the treatment in patients receiving prebiotic and complex treatment with "Eubikor", the deficit of bifidobacteria and lactobacilli was eliminated in 35 out of 37 (94.6±4.5%) patients in the first group. In the control group, against the background of the application of antibacterial therapy only, the situation worsened in the direction of a gradual decrease of both lactobacilli and bifidobacteria. A significant (6-fold) decrease in the level of Staphylococcus sp., Staphylococcus int., Streptococcus mut and Clostridium difficile was noted against the background of taking "Eubikor", which was not observed in the control group.

Based on the results of the research, it can be said that giardiasis in pregnant women leads to disruption of the functioning and interaction of the microbiota of different biotopes of the body, which leads to the development of complications in the gestation

process. The data of the research suggests the need to develop new algorithms for the diagnosis of parasitosis in pregnant women, which allows predicting the course of pregnancy, identifying risk factors and preventing possible complications.

RESULTS

1. Giardiasis was detected in 21.0±3.5% of pregnant women during the epidemiological observation conducted in Baku. Complicated heredity for gastrointestinal tract pathologies (OR=1,296), past acute intestinal infections (OR=1,334), history of repeated abortions (OR=1,492), recurrent non-specific vaginitis of gynecological pathologies (OR=1,581), hyperplastic processes of the endometrium and so on was related to the risk factors of development of giardiasis among pregnant women. Giardiasis was found in 67.2±4.0% of pregnant women aged 21-35 years. Non-observance of personal hygiene rules in close contact with children (24.1±3.6%) (48.2±4.3%) non-observance of apartment hygiene and the presence of low socio-economic conditions (27.7±3.8%) were considered the leading risk factors of giardiasis infection among pregnant women.

2. The most common clinical symptoms of giardiasis in pregnant women in the main group are diarrhea (85.7±4.9% in acute giardiasis, 75.3±4.8% in chronic giardiasis); frequent stools with an unpleasant odor (78.6±5.4% and 53.1±5.5%, respectively, $p<0.001$); abdominal pain (67.9±6.2% and 54.3±5.5%, $p>0.05$); allergic symptoms (62.5±6.5% and 27.2±4.9%, $p<0.001$); flatulence (55.4±6.6% and 28.4±5.0%, $p>0.05$), weight loss (26.8±5.9% and 39.5±5.4%, $p> 0.05$); excessive fatigue (33.9±6.3% and 18.5±4.5%, $p<0.01$) and others. In pregnant women with giardiasis, the unit of gypsy enzymes ALT (0.59±0.02 IU/L) AST (0.77±0.03) QQTP (18.27±0.39 IU/L) QF (362.23±56.4 IU/L) level was statistically significantly higher than the similar indicators of the control group ($p<0.05$).

3. During the analysis of the gestational period in pregnant women with giardiasis, the risk of disruption of pregnancy in the first trimester is 28.6±6.1% in acute giardiasis, 32.1±5.2% in chronic giardiasis; pathological conditions in the first half of pregnancy were

32.1±6.2% and 38.3±5.6%, respectively; anemia 41.1±6.6% and 62.9±5.4%; 14.3±4.6% in acute giardiasis, 19.8±4.4% in chronic giardiasis; amniotic fluid prematurity 25.0±5.8% and 19.7±4.4%, respectively; anomalies of birth activity 14.3±3.8% and 17.6±4.6%, partial close union of the couple 8.9±3.8% and 12.3±3.8%; acute and chronic hypoxia of the fetus occurred with a frequency of 19.6±5.3% and 9.7±3.2%. When assessing the condition of newborns with the Apgar scale, this indicator was 6.81 ± 1.24 points and 7.1 ± 0.97 points, respectively, in the 1st and 5th minutes after birth of children born to mothers with acute giardiasis, both indicators were statistically significantly lower than the similar indicators of the control group ($p<0.05$).

4. Astheno-vegetative syndrome, intestinal dyspepsia, functional dyspepsia, right subcostal syndrome in pregnant women with giardiasis: steatosis of the liver, violation of somatic status as initial symptoms of gallstone disease, as well as upper respiratory tract and urinary tract diseases, childhood and adolescent infections, acute intestinal infections prevailed. In pregnant women with giardiasis, an excessive increase of conventional pathogenic flora was observed both against the background of the deficit of the entire microbiota of the intestine, and against the background of the deficit of only lactobacilli and bifidobacteria. In pregnant women with giardiasis, in addition to intestinal microbiota disturbance, sharp changes in the uterine microflora, both quantitatively and qualitatively, were noted.

5. Including prebiotics in the treatment complex of women with giardiasis and chronic diseases of the digestive organs accompanied by changes in the intestinal and genital microbiota led to positive dynamics in the somatic status, improvement of the clinical picture of diseases of the digestive organs and bacterial vaginosis, normalization of the microecology of the intestine and urogenital tract, improvement of the quality of life of patients. The set of examinations made it possible to propose an algorithm for the implementation of effective measures for the treatment and prevention of giardiasis among pregnant women.

PRACTICAL RECOMMENDATIONS

1. In coprological diagnosis of giardiasis, the 8-12-day phenomenon of "intermittent cyst secretion" does not allow identification of the parasite quickly and within a few days. In case of suspicion of giardiasis, it is recommended to carry out stool examination 3-4 times with an interval of 1 week (min. 3-5 days) within 3-4 weeks.

2. Detection of different classes of antibodies against giardia antigens in blood serum is considered an indirect method of laboratory diagnosis of giardiasis and can be used as an additional diagnostic method.

3. Treatment with metronidazole in pregnant women with giardiasis significantly lowers pro-inflammatory cytokine IL-8. This result can be evaluated as a prognostic criterion.

4. Treatment with antiparasitic drugs during giardiasis; determination of immunostimulating drugs, pro- and prebiotics against the background of basic therapy; improving the quality of life; it is recommended to implement a complex of measures such as hygienic and dietary regime, prescribing phytopreparations.

List of Scientific Works Published on the Dissertation Topic

1. Gasimova G.M. Algorithm for early diagnosis of giardiasis in pregnant women // Materials of the practical conference "Current Problems of Medicine", Baku-2018, p. 43

2. Gasimova G.M. Bagirova Kh.F. Features of the course of pregnancy and childbirth in women infected with Giardia // “Healthy Women” scientific and practical journal, No. 4 (130), 2018, pp. 48-51

3. Gasimova G.M. The state of the fetoplacental complex in pregnant women with giardiasis infection // Materials of the scientific conference dedicated to the 80th anniversary of the birth of Honored Scientist, Professor Abbas Ahmed oglu Akhundbeyli, Baku-2018, pp. 131-133

4. Gasimova G.M. Differential-diagnostic features of the clinical course of giardiasis in pregnant women // "Health" - scientific and practical journal, No. 1, Baku-2019, p. 71-75
5. Gasimova G.M. Cytokine profile changes during giardiasis in pregnant women // "Health" - scientific and practical journal, No. 4, Baku-2019, p. 197-201.
6. Gasimova G.M. Risk factors for the development of giardiasis in pregnant women// Black Sea 2nd International Congress of Applied Sciences, Rize, August 23-25, 2019, p. 23
7. Gasimova G.M. Ultrasound characteristics of invasion by Lyamlia in pregnant women// Modern Achievements of Azerbaijan Medicine eimi-practical journal, No. 2, 2019, p. 170-174.
8. Quality of life in pregnant women with Giardiasis
9. Gasimova G.M. Behavioral characteristics among pregnant women with giardiasis // "Theoretical clinical and experimental morphology" journal, volume 1, N3-4, 2019. P.154-155
Gasimova G.M. Differential diagnostic features of the clinical course of giardiasis in pregnant women in Baku // “Medical News” magazine, Minsk, No. 12(303) 2019 p.55-57
11. Gasymova G.M. On the role of giardiasis in reproductive pathology in pregnant women in Baku // Ministry of Health of the Republic of Uzbekistan, Fergana Medical Institute of Public Health Collection of the International Scientific and Practical Conference “Current Problems of the Epidemiology of Infectious and Non-Infectious Diseases”, April 12, 2022, p.60-62.

Conventional Abbreviations

alt -Alaninaminetransferase
aspartate aminotransferase
dbil - retardation of intrauterine development of the fetus
iba-1 - insulin-like growth factor
shpf - conditionally pathogenic microflora
qqtp - gamma-glutamyltranspeptidase
qf -alkaline phosphatase

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