

**THE REPUBLIC OF AZERBAIJAN**

**Manuscript copyright**

**FACTORS NEGATIVELY IMPACTING ON FETUS  
FORMATION, THEIR PREVENTION AND PATHOGENESIS**

Speciality: 3215.01 – Obstetrics and gynaecology

Field of science “Medicine”

Doctoral candidate: **Konul Galib Garayeva**

**ABSTRACT**

**of the dissertation applied in order to take  
Doctor of Medicine academic degree**

**BAKU – 2021**

The dissertation work has conducted out at the Scientific Research Institute of Obstetrics and Gynecology of the Ministry of Health of the Republic of Azerbaijan and the Scientific Research Center of the Azerbaijan Medical University.

**Scinetific advisors:** doctor of medical sciences, professor  
**Jamila Fazil Gurbanova**

Honored Scientist, Doctor of Medical Sciences, professor **Sabir Cahan Aliyev**

**Offical opponents:** doctor of medical sciences, professor  
**Leyla Musa Rzaquluyeva**

Honored Scientist, Doctor of Medical Sciences, professor **Hicran Firudin Bağırova**

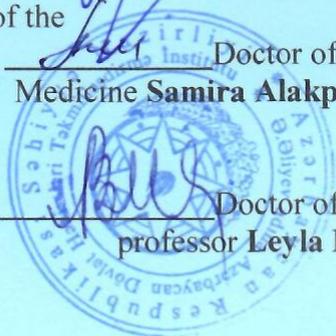
Doctor of medical sciences, professor  
**İslam Sharif Mahalov**

Dissertation Council BED 2.11 of the Supreme Attestation Commission under the President of the Republic of Azerbaijan operating under the Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev.

Charirman of the dissertation council: \_\_\_\_\_ Doctor of Medical Sciences, professor **Nazim Akif Gasimov**

Scientific secretary of the dissertation council: \_\_\_\_\_ Doctor of Philosophy in Medicine **Samira Alakpar qızı Akparbeyova**

Chairman of the scientific workshop: \_\_\_\_\_ Doctor of Medical Sciences, professor **Leyla Musa Rzaquluyeva**



**Rationale:** Rapid migration of the population nowadays, resulted in a number of infections unknown in our country, as well bad habits that easily infect the society. Besides a number of genital and non-genital infections among the women, they tended towards smoking, alcohol use and drug addiction and this tendency was rapidly increased. Therefore, perinatal complications created new problems in the obstetrics by disrupting normal course of the pregnancy (V.V.Sinitskiy et al. 2008; A.V.Skalniy et al. 2009). On the other hand, the treatment of extragenital diseases among the women became serious obstacle to the development of the pregnancy because of negative impact on perinatal fetal development during the use of the medicines (Babenko O.P. 2013; Askarova Z.F., et al. 2014; Tyazhelkov A.P. 2014).

Of course, these factors result in developmental delay of the fetus, rapid increase in the number of non-developing pregnancies and defective children.

- 
1. Sinitskiy V.V., Solovyov A.G., Solovyov G.N. et al. Indicators of endogenous intoxication of the mothers addicted to nicotine and their newborns. // Human ecology, 2008, № 8, p. 3-6.
  2. Skalniy A.V., Kin K.L. Chambers K.D. et al. Zinc metabolism disturbance in perinatal impact of alcohol // Materials of the I Russian national narcological congress, Moscow, November 2009. M, p. 18-19.
  3. Babenko O.P. The course of the pregnancy of the women in exacerbation of chronic cytomegalovirus infection // Respiration physiology and pathology report 2013, Issue 47, p. 82-86.
  4. Askarova Z.F., Mardanoca A.K., Askarov R.A. et al. Congenital birth defects of the children in the Republic of Bashkortostan (according to the monitoring data for 2007-2012). //Russian paediatric journal 2014, № 2, p. 4-9.
  5. Tyazhelkov A.P. Congenital hand defects with insufficient development of constituent elements //Healthcare of the Far East 2014, № 4, p. 65-72.

As mentioned in the World Health Organization (WHO) report for 2013, every year 10-20 million children are born with different defects. The illness frequency among them increases; and the number of those with mental and physical retardation is expressed in terms of high figures (Lee O.N. 2012; Prikhodko O.B., et al. 2013; Gorikov I.N. 2015).

As all over the world, as a result of abnormal course of intrauterine development, the number of the women with non-developing pregnancy, as well the children born with congenital birth defects is being increased in the Republic of Azerbaijan (Bunyatzada S.Z. 2011; Muradova Z.S., Aliyeva E.M. 2012. Naghdaliyev A.S. 2012).

- 
1. Lee O.N. Pregnancy and childbirth complications in the women with Anamnia //Bulletin of surgery of Kazakhstan 2012, № 2, p. 84-85.
  2. Gorikov I.N. The state of hepatobiliary system in moderate cerebral ischemia in carried newborns from the mothers with chronic cytomegalovirus infection in the second trimester of the pregnancy // **Respiration physiology and pathology**. 2015, Issue 55, p. 82-86.
  3. Prikhodko O.B., Babtseva A.F., Romantsova Y.B., et al. Lack of control over bronchial asthma during the pregnancy as a predictor of perinatal complications //Allergology and immunology. 2013, № 3. p. 188-189.
  4. Bunyatzada S.Z. The role of the risk factors in the formation of congenital birth defects //Health, 2011, № 5, p.107-111.
  5. Muradova Z.S., Aliyeva E.M. The course and perinatal features of the pregnancy in the women with threat of premature birth in the 29-33 weeks of the pregnancy //Health, 2012, № 2, p. 83-89.
  6. Naghdaliyev A.S. High-risk pregnancies, perinatal pathologies during the births, and loss levels //Health, 2012, № 2, p. 94-98.

Of course, these factors negatively impacting on the course of the pregnancy, make difficult to preserve the gene pool, which ensures the future of the people. Therefore, the preservation of reproductive health is in the spotlight, because it is not only medical, but also social problem.

In this regard, governmental and non-governmental organizations make the projects related to fetal development in the womb, ensuring the pregnancy with perfect birth and healthy growth of born children, as well implement different programs and the results got from them are discussed at scientific meetings of various level. One of these meetings was the II International Symposium took place in Beijing in 2005. At this symposium took place under the title of "Congenital defects all over the world", the researches made by the world scientists in this field were discussed and it was recognized that this problem is a priority area in the obstetrics.

**Object and subject of research.** From the first days of pregnancy to the end, 737 pregnant women were examined. 396 of them (54%) had extragenital diseases, 235 (32%) had pathology of the genitals and 106 (14%) had addiction to harmful substances. Factors that negatively affect the course of pregnancy have been studied as a subject of research.

**The main purpose of the research.** Investigate the factors that hinder the prenatal development of the fetus, clarify their mechanism of action on the fetus and based on it, develop preventive measures to ensure the normal course of pregnancy.

**Research task:**

1. Studying the impact of extragenital diseases on intrauterine fetal development.
2. Clarifying pathophysiological mechanism of negative impact of extragenital diseases on intrauterine fetal development.
3. Developing the prevention of negative impact of extragenital diseases on intrauterine fetal development.
4. Studying the impact of genitourinary diseases on intrauterine fetal development.
5. Clarifying pathogenesis of negative impact of genitourinary diseases on intrauterine fetal development.

6. Developing the prevention of the impact of genitourinary diseases on intrauterine fetal development.
7. Studying the impact of bad habits on intrauterine fetal development.
8. Clarifying pathogenesis of the impact of bad habits on intrauterine fetal development.
9. Developing the prevention of the impact of bad habits on intrauterine fetal development.
10. Studying the impact of organic diseases of uterus on intrauterine fetal development and preparation of preventive measures against its negative impact.
11. Studying the impact of general infections on intrauterine fetal development.
12. Studying pathogenesis of the impact of general infections on intrauterine fetal development.

**Research methods:**

In order to achieve the set goal, the period from embryonic development to birth in pregnant women with extragenital diseases, common infections, genital defects and infections was monitored. In this case, the complications of the perinatal period, intranatal period and postnatal period were identified and the factors that led to the termination of pregnancy and the structure of congenital malformations of newborns were analyzed. Based on the results obtained, pregnant women were divided into groups and prophylactic measures were developed. Experiments were performed on 80 white rats in accordance with bioethical norms and the pathogenesis of the negative effects of alcohol on development was clarified.

**The main provisions of the defense.**

1. From the 20th week of pregnancy, a decrease in the amount of total protein in the blood to 60-63 g/l, an increase in urea to 100-115 mg-dl may result in a spontaneous fall of the fetus. Decrease in total protein to 55-60 g/l in the 35-36 th week of pregnancy, increase in urine to 110-130 mg/dl is a risk factor for the prenatal period. Therefore, in order to predict spontaneous abortions and stillbirths, the amount of

total protein, urea and alkaline phosphatase in the blood should be determined during each trimester of pregnancy.

2. Pregnant women with amount the blood sugar level of more than 200 mg/dl are more likely to have a miscarriage or stunted embryo in the first trimester. In this regard, regardless of the type of diabetic plan pregnant women 0,86 units/kg in the I trimester, 1, 2 units/kg in the II trimester, 1,2 units/kg of blood sugar in the III trimester to reduce amount blood sugar, as well as spontaneous miscarriage 7%, stillbirth 5% reduces.
3. Thyroid dysfunction is a high risk factor for prenatal development of the fetus from the first week of pregnancy to the last week and has a negative impact on the prenatal development of the fetus in 71% of pregnant women. Treatment of pre-pregnancy thyroid disease ensures a smooth transition of the I and II trimesters of pregnancy and reduces the abnormal development of the fetus by 38%.
4. In pregnant women with non-infectious hepatitis there is a correlation between an increase in the concentration of markers that reflect the functional state of the liver and a defect in the prenatal development of the fetus (AST, ALT, alkaline phosphatase, total bilirubin). Fetal malformations are more common in alcoholic hepatitis where markers are higher than normal.
5. Prenatal development of the fetus in pregnant women with viral hepatitis depends on the functional status of the liver. In order to improve it giving heptal to pregnant women from beginning of the 1st trimester reduces the concentration of AST, ALT, alkaline phosphatase enzyme in the blood and amount of total bilirubin. This, the likelihood of developmental defects in the perinatal period of the fetus is significantly reduced.
6. Type 2 herpes simplex is a high risk factor for normal perinatal development of the fetus. Due to the increase in its blood titer, 12% of pregnant women had a miscarriage, 21% has a stillbirth and 9% has a malformed fetus. When taking

valsiklevir before pregnancy, the titer of type 2 herpes simplex in the blood drops and spontaneous miscarriage was reduced by 6%, stillbirth by 15% and the perinatal development of the fetus as a whole decreased from 70,5% to 44%.

7. Alcohol intake is a serious risk factor for pregnancy 46% of women who drank alcohol before pregnancy but eventually gave it up are at risk of pregnancy. 83-84% of pregnant women who continue to drink alcohol during pregnancy this pregnancy is complicated.
8. Pregnancy doesn't end in 67% of alcoholics, 78% of drug addicts and 35% of smokers due to serious complications in women addicted to harmful substances (alcoholism, drug addiction and smoking).

#### **Scientific novelty of research.**

1. There is correlation between the increase in creatinine in the blood and the intrauterine development of fetus. Elevated levels of creatinine in the blood have been found to be a high risk factor for spontaneous miscarriage and stillbirth.
2. It has been suggested that there is a correlation between impaired protein metabolism and hyperfermentic and fetal malformations.
3. In order to assess the perinatal development of the fetus during thyroid dysfunction, the determination of TSH, T<sub>3</sub>, T<sub>4</sub> hormones in the blood is of prognostic importance. It has been proven that the stabilization of the concentration of these hormones ensures the normal perinatal development of fetus.
4. During urogenital diseases, pathological changes of the hormonal system under the influence of toxic substances formed by the vital activity of the microflora have been revealed.
5. It has been determined that the reduction of energy balance of the pituitary gland and the intensification of

oxidative stress play an important role in the pathogenesis of the course of pregnancy.

6. There is correlation between the energy balance of the pituitary gland during pregnancy and the functional state of the ovaries.
7. The important role of strengthening the antioxidant defense system in the prevention of intrauterine growth defects has been proven.

### **Theoretical and practical significance of the research.**

1. There is correlation between the increase in creatinine in the blood and the intrauterine development of the fetus. It is known that an increase in blood creatinine is a high risk factor for spontaneous miscarriage and stillbirth.
2. Although 14% of pregnant women with extragenital diseases had congenital malformations, their number decreased to 6% as a result of preventive measures.
3. The blood sugar in the blood above 200 mg/dl are a high risk factor for spontaneous abortion and stillbirth.
4. Plasmapheresis in the first trimester in pregnant women with toxoplasmosis infection dramatically lowers the titer of toxoplasmosis in 88% of pregnant women and reduces the complications of intrauterine development of the fetus by 40%.
5. Decreasing the titer of mycoplasma in the blood before pregnancy does not prevent spontaneous abortion, but reduces congenital malformations by 19%, can prevent stillbirth, malformations and intrauterine complications.

### **Approbation and application of the dissertation:**

1. Family health in the XVI century. Papers of the XVI International Scientific Conference 27 April – 4 May, 2012, Budapest, Hungary, Part I.

2. European Science and Technology. Materials of the IX International research and practice conference Vol 1. December 24<sup>th</sup> – 25<sup>th</sup>, 2014, Munich, Germany.

3. Современные технологии: актуальные вопросы, достижения и инновации. Пенза, 27 февраль 2017.

4. V Всероссийская междисциплинарная научно-практическая конференция с международным участием. 30 октября-02 ноября 2018 года, Сочи 2018.

5. Mamalıq və ginekologiya üzrə XXII Dünya Konqresi Brzilya Rio 14-19 oktyabr. 2018.

6. Prenatal tibb üzrə XXVI Avropa Konqresi material. Sankt Peterburq. 2018.

7. Karadeniz I Uluslararası multidisiplinar çalışmalar kongresi. Sağlık bilimleri 15-17 mart 2019, Giresum, Türkiyə.

8. 6<sup>th</sup> International Conference on Innovations and Development Patterns in Techical and Natural Sciences 20<sup>th</sup> March, 2019, Vienna 2019.

9. Scientific Research of the sco countries: Synergy and integration. International Conference September 28, 2019, Beijing China 2019.

The results of the study where applied in the International clinic and Ege clinic.

Preliminary discussion of the dissertation case was held at a meeting with the participation of the employees at the Scientific Research Institute of Obstetrics and Gynecology. August 4, 2021.

It was held at the seminar BED 2.11 of the dissertation conusil organized under ASATİD after A. Aliyev. October 24, 2021. Protokol "1.

### **Application of results:**

The resulets obtained in the study are used in the treatment of pregnant women in Scienific Research Institute of Obstetrics and Gynecolgy and the "Ömür clinic".

### **Volume and structure of the dissertation:**

The dissertation is typed on a computer, commented on 316 pages (456267 characters) and consists of ections of nitroduction (17405 characters), main confent (387134 characters), conclusion (36870 characters), results (5358 characters), practical recommendations (3005 characters), list of used literature.

"The main content of the dissertation" is divided into 7 chapters: 1. Literary summary (44869), 2. "Materials an methods" (8797), 3. "Results of the research" (191792), 4. "Viral hepatitis (47678)", 5.

“Commar infections” (18739), 6. “Diseases of the genital organs” (30855), 7. “Harmful habits” (44399 characters).

The list of used literature covers 498 sources. 10 of them are in Azerbaijane, 307 in Russian and 181 in other language.

### **Research materials and methods.**

The research included 737 pregnant women who were under our supervision within the period from 2004 to 2014. 396 of them (54%) had extragenital diseases, 235 (32%) - pathology of genital organs, and 106 (14%) were addicted to bad habits.

Among pregnant women with extragenital diseases hypertension was found in 56 patients (14%), congenital heart defect in 20 patients (5%), chronic pulmonary disease in 15 patients (4%), digestive system diseases in 54 patients (14%), gallbladder and biliary tract disease in 25 patients (6%), hepatitis of viral origin in 78 patients (20%), hepatitis of different origin in 30 (8%) patients, diabetes in 55 patients (14%), thyroid diseases in 31 patients (8%), kidney diseases in 14 patients (3%), alcoholic psychosis (AP) in 18 patients (4%).

The patients with hypertension were divided based on the classification of European society of hypertension and cardiology and it was detected that 18 (32%) of them had prenatal hypertension, 21 (37,5%) - gestational hypertension, 8 (14%) - hypertension with concomitant proteinuria of significant degree, 9 (16%) - hypertension with concomitant prenatal hypertension.

High blood pressure was detected mainly in pregnant women over 30 years of age. They were periodically examined by the cardiologists and all the patients were advised to follow normal eating pattern, reduce salt and water intake, moderately increase physical load, 8-10 hours sleep in the evening and 1-2 hours sleep in the afternoon.

In order to calm central nervous system dopegyt was prescribed for 22 (39%) and nifedipine - for 34 pregnant women (61%). When it was impossible to lower high blood pressure in cases of concomitant diseases, 6.5 mg of Hypothiazid was applied. Pregnant women with a blood pressure of 160/100 mmHg were hospitalized. In this way, we were able to ensure the prevention of

the pre-eclampsia by regulating the level of the pressure of pregnant women with hypertension.

As a result of the treatment compiled based on the nephrologist recommendations along with cardiologist ones, in comparison with the 20<sup>th</sup> week of the pregnancy, the amount of protein in the urine in pregnant women with proteinuria in 35-36 weeks decreased by 12% and by 28% during the birth.

As a result of implemented preventive measure, positive dynamic was observed in perinatal fetal development. A miscarriage was detected in 5% of 56 pregnant women. As well the fetus was died in the same amount of the patients. Remaining 50 patients completed their pregnancy with a childbirth. The placenta was separated untimely during intranatal period in 8% of pregnant women. Congenital defect was detected in postnatal period in 12% of born children.

25 people among the patients who had taken our advice and had been treated in medical institutions with cardiological profile after postnatal period was registered at the hospital with repeated pregnancy. There was no gestational hypertension with concomitant proteinuria of significant degree and with concomitant prenatal hypertension among them. 1 Dopegyt tablet was applied before ??? to pregnant women with the blood pressure over 140/90 mmHg.

In addition to antihypertensive medications folic acid was prescribed for pregnant women in the I trimester, and Riboflavin (Vitamin B<sub>2</sub>) in the II trimester. In order to ensure the prevention of the miscarriages, Dydrogesterone was prescribed for pregnant women with low density of progesterone in the I trimester. After 1 week of application of the medication, the density of the progesterone in the blood gradually increased and reached normal level by the end of the 3<sup>rd</sup> week.

As a result of preventive measures implemented, the blood pressure was stable at all the stages of the pregnancy. There were no stillbirths and miscarriages detected. There was congenital birth defect found only in 12% of the newborns (in 3 newborns). 1 of them was with ventricular septal defect and 2 of them were with rectal atresia.

As a result of our research, we decided that the reason of complicated course of the pregnancy was a decrease in the level of progesterone in the blood due to constantly high blood pressure.

In order to prevent fetal development with any defect in pregnant women with the hypertension, they are to be treated taking the advice of cardiologist, nephrologist and, if necessary, ophthalmologist along with the advices of obstetrician-gynaecologist, and to stabilize their blood pressure. If there are stillbirth, habits or miscarriage in the anamnesis of pregnant woman it is necessary to determine the amount of the progesterone in her blood in the morning.

The heart defect was transferred inherently in 12 (60%) of 20 pregnant women with congenital heart defect. Induced abortion was implemented in 4 pregnant women (20%) due to the development of the heart defect. And 3 patients (15%) had a defect. 65% of pregnant women completed their pregnancy normally.

5 patients (25%) were treated before the next pregnancy and the pregnancy of all of them (100%) was without any defect.

15 pregnant women with chronic pulmonary disease was examined by pulmonologist, allergist and phthisiologist. Their recommendations were taken into consideration during the preparation of the pregnancy protocol. The consultation was repeated at the beginning of each trimester.

Based on the recommendations of allergist, agonist medications –  $\beta_2$ , sodium cromoglycate, symbicart were prescribed twice a day for 7 pregnant women with bronchial asthma.

Actovagin was applied for pregnant women with chronic pulmonary disease intramuscularly every other day within 7 days in each trimester. The aim was the elimination of hypoxia.

Among 4 patients with chronic bronchitis the pregnancy of 1 patient ended with the stillbirth, and pregnancy of 3 patients - with the birth of healthy child. The same was observed in 4 pregnant women with pulmonary tuberculosis.

The pregnancy of 1 patient among 7 pregnant women with bronchial asthma ended with the stillbirth, the pregnancy of 2 of

them ended with instillation abortion. The result of the pregnancy of 4 patients was physiological birth.

Thus, perinatal fetal development was unsatisfactory in 50% of pregnant women with pulmonary tuberculosis and in 43% of pregnant women with bronchial asthma.

Among 54 pregnant women with digestive system diseases, 22 patients (41%) had chronic constipation, 13 patients (24%) - irritable bowel syndrome, 9 patients (17%) - reflux esophagitis, 4 patients (7%) - peptic ulcer. After the consultation with the gastroenterologist, the medications were prescribed to pregnant women that did not have negative impact on the fetal development, as well corresponding diets were developed.

As a result of the measures taken, the fetus developed abnormally in 15 (28%) of 54 pregnant women with digestive system diseases. 32 patients among pregnant women who had taken our recommendations and had reasonably treated at a gastroenterologist after postnatal period applied to the hospital with repeated pregnancy. The number of the miscarriages among them decreased and included 9% of pregnant women (3 patients). There were no stillbirths observed. Spinal canal backwardness was detected during the ultrasonography and the pregnancy ended with instillation abortion only in 1 pregnant woman in the first week of the II trimester. The children from remaining 28 pregnant women were born without any defect. Thus, abnormal fetal development was observed after the treatment in 4 (12.5%) of 32 pregnant women.

There were gallbladder and biliary tract disease in 25 pregnant women examined by us. 10 (10%) of them were diagnosed with gallstone and 15 (60%) with chronic cholecystitis. In order to evaluate functional status of the liver during the pregnancy period, ultrasound was implemented and the density of AST, ALT, Alkaline phosphatase in the blood were determined at the beginning of each trimester.

The disease was worsened in 3 (20%) of 15 pregnant women diagnosed with the gallstone and the gallbladder was constrainedly removed by means of laparoscopic operation. In case with remaining pregnant women the disease development was regulated using

phytotherapy and medications without negative impact on fetal development. The disease dynamic was evaluated based on the changes in the density of AST, ALT, Alkaline phosphatase enzymes, the amount of total bilirubin and cholesterol in the blood. The results obtained in the II trimester of the pregnancy confirm that the longer the term of pregnancy, the deeper the changes in the functional status of the liver.

The fetus was retarded in 4 (16%) of pregnant women and the pregnancy of 2 of them ended with the stillbirth. The weight of 2 newborns was below the standard. In addition, Botallo's duct remained open in 1 newborn, and another one was transferred to the children's surgery department being diagnosed with pyloric stenosis. Thus, intrauterine fetal development was abnormal in 6 (24%) of 25 pregnant women.

Based on our recommendations 17 patients was treated after postnatal period at hospital conditions by the gastroenterologists. They were taken under the control of the polyclinic; and the treatment was continued. 10 patients (59%) among them became pregnant 1-3 years after the treatment and was repeatedly registered as pregnant women. Since the first days of the pregnancy, heptral was prescribed on special scheme to pregnant women in order to eliminate the spasm arisen in gallbladder and biliary tract, as well, to strengthen antioxidant protection system of the mothers. The liver biomarkers in the blood were determined, thus its functional status was kept under control. We found that reasonable treatment of the disease before the pregnancy, as well prevention of the stagnation able to be arisen in hepatobiliary system within the pregnancy period provided normal perinatal fetal development. Thus, the pregnancy was resulted in the stillbirth only in 1 (10%) of 10 pregnant women.

20 patients among pregnant women were diagnosed with the hepatitis of non-infectious origin. 5 (25%) of them had hepatitis of alcohol, 8 (40%) - of medication and 7 (35%) - of alimentary origin. In order to control the liver functioning, corresponding markers were determined in the blood at the beginning of each trimester. Heptral was prescribed to pregnant women starting from the I trimester. As a result of the effect of heptral, total bilirubin level and density of the

enzymes in the blood started to decrease starting from the end of the I trimester, however their level had still been higher than the standard.

Despite the treatment implemented, perinatal fetal development was inadequate in 80% of pregnant women with hepatitis of alcohol origin, 37,5% of pregnant women with hepatitis of medication origin and 29% of those with hepatitis of alimentary origin.

11 patients repeatedly became pregnant after reasonable treatment at the hepatologist based on our recommendation. 7 of them made recovery, the density of the liver markers was higher than the standard only in 4 pregnant women with the hepatitis of alcohol origin.

After registered pregnant women took heptral the density of the biomarkers in the blood tended towards normalize by the end of the I trimester. Average density of AST, ALT and Alkaline phosphatase decreased by 16%, 11% and 7% respectively, and total bilirubin level - by 15%. This positive dynamic also had positive effect on the course of the pregnancy. The pregnancy complicated only in 3 of them (27%). There was the miscarriage in 1 pregnant woman (9%) and the stillbirth in 2 patients (18%).

55 pregnant women was diagnosed with **diabetes**. 30 of them (55%) was diagnosed with type 2 **diabetes** before the pregnancy. They were registered at corresponding clinic and treated. The diabetes was determined during the registration related to the pregnancy in 25 patients (45%). They were diagnosed with gestational diabetes. Based on the fact that the diabetes had different complications, we examined pregnant women together with endocrinologist, nephrologist, hepatologist and angiologist. Pregnant women were repeatedly examined by the commission once a month based on especially drawn up schedule. In addition, the levels of sugar, cholesterol, triglycerides, high-density lipids and creatinine in the blood were determined at the beginning of each trimester.

Sugar level increased by 61%, total cholesterol level - by 41.5%, triglycerides level - by 57%, creatinine level - by 36.5% and high-density lipids level decreased by 11% in comparison with

standard in 28 pregnant women in the first weeks of the I trimester. In order to regulate increased blood sugar level 8 pregnant women used diabeton, 10 pregnant women - glikovash, 7 pregnant women simple amaril-2. And 3 pregnant women used different diets. However, based on the methods, compiled by us in my presence at the Research Institute of Obstetrician and Gynaecology in 2010 (A.Sh. Shahpalangov et al., 2010, Health № 1, p. 174-176), starting from 2011 we prescribed 2 metformin tablets during the day (day and night) to 19 pregnant women in order to decrease increased blood level. Main reason of prescribing metformin was the fact that along with the blood sugar level it regulated the triglycerides and sexual hormones imbalance.

14 patients among pregnant women with the diabetes used different medications for the treatment of the diabetes. It resulted in the miscarriage in 3 of them (21%) by the end of the I trimester. 2 of them did not come for the examination. The examination of 9 pregnant women demonstrated that the blood sugar level decreased by 15% and creatinine level - by 6%. However, there were no interesting changes in the lipid metabolism. It was determined that the risk of the miscarriage in pregnant women with the blood sugar level of more than 200 mg/l in the I trimester was higher. As a result of the research implemented, it was determined that, despite that simple amaril-2, glicovash and diabeton use decreased the blood sugar level to a certain degree, they were able to regulate neither sugar level, nor lipid metabolism.

19 pregnant women used metformin. When registering, in comparison with the standard, their blood sugar level was higher by 75%, total cholesterol level - by 41.5%, triglycerides level - by 57%, creatinine level - by 36.5%. And the level of high-density lipids decreased by 11%. After Metformin application (at the end of the I trimester) the blood sugar level decreased by 10%, total cholesterol level - by 6%, triglycerides level - by 4%, creatinine level - by 2%. And the level of high-density lipids increased by 1%.

Mentioned positive dynamic also had the impact on the course of the pregnancy. The miscarriage cases in pregnant women who used metformin in the I trimester was registered only in 5%.

This dynamic became more intensive at the end of the II trimester. The level of lipid metabolism markers and sugar in the blood was closer to the standard. Respectively, the miscarriage was registered in the II trimester in 7% of pregnant women (1 patient).

The level of the lipid metabolism markers in the blood of pregnant women with gestational diabetes was normal, so only the blood sugar level was checked. It was determined that when registering, in comparison with the standard, average blood sugar level was higher by 47,5%, at the end of the I trimester this value was higher by 51%, at the end of the II trimester - by 38%, and in the III - by 21%. Vice-versa, there was the miscarriage in 1 pregnant woman (4.5%) in the II trimester. As well there was the stillbirth in 1 pregnant woman. The stillbirth case was observed in another one pregnant woman in the III trimester.

It should be noted that miscarriage or stillbirth were observed in pregnant women with the blood sugar level more than 200 mg/dl. Therefore, we consider that an increase in the blood sugar level is the test of prognostic importance, so if it increases above 200 mg/dl, it become a risk factor not only for the miscarriage, but also for the stillbirth.

Thus, intrauterine fetal development was abnormal in 19 (34.5%) of 55 pregnant women. The pregnancy of 4 of them (7%) was disrupted because of the defect detected during ultrasound examination, including separation of the head from the body (1 patient), separation of one of lower extremities from the body (1 patient), open thorax (1 patient) and abdominal cavity situated outside in form of the bubble (1 patient). Besides, there was the miscarriage in 6 (11%) and the stillbirth in 5 pregnant women (9%).

Remaining 40 pregnant women (73%) complete their pregnancy with a childbirth. 4 of them (10%) was born with congenital defect. 1 of those born with the defect had acromegaly, another one - ureter atresia, 2 - patent ductus arteriosus.

After the pregnancy had been ended, we submitted to those who wanted to repeatedly become pregnant the recommendation sheet drawn up together with the endocrinologist and sent them to endocrinological clinic situated at their residence address. The

purpose of the submission of the recommendation sheet was the informing the patients about their lifestyles, food, medications use, the complications able to be arisen during the pregnancy related to mother and fetus.

25 (45%) among 55 pregnant women repeatedly became pregnant 1-5 years after the treatment based on the recommendation sheet. Together with the endocrinologist and based on the recommendation of Dedov I.I., Burmakulova F.F., published in 2015, we suspended the application by pregnant women of peroral medications for the treatment of the diabetes, regardless of the type of the diabetes, and preferred the insulin therapy. We prescribed 0.86 unit/kg of insulin in the I trimester, 1.2 unit/kg - in the II trimester and 1.2 unit/kg - in the III trimester. As a result, we managed to significantly reduce the blood sugar level. Thus, the blood sugar level decreased approximately to the standard in the I trimester (schedule 1).

#### Schedule 1.

Average blood sugar level in pregnant women with the diabetes who used insulin.

№	Statistical value	The I trimester mcmol/l	The II trimester mcmol/l	The III trimester mcmol/l
1	M±m	6.86±0.13	6.61±0.13	6.26±0.10
2	P	>0.05	>0.05	<0.001

Reducing the blood sugar level using insulin also had positive effect on the course of the pregnancy.

In comparison with the patients who had not used insulin, the amount of the miscarriages sharply decreased from 11% to 4%. 2 of the newborns (9%) had congenital defects (hydrocephalus and cleft lip). Thanks to the insulin use the pregnancy was abnormal only in 4

(16%) of 25 pregnant women. Despite the insulin use, the blood sugar level reached the value of 8.0 mmol/l in 2 pregnant women. There was the miscarriage in one of them and the stillbirth in another one. Thus, our research once again proved that the diabetes is a risk factor for complicated course of the pregnancy.

Therefore, we recommend to take pregnant women with the diabetes under strict control, to prescribe metformin to the patients, taking into consideration the blood sugar level during the pregnancy and to use the insulin only in severe cases.

41 patients among those who had been under our observation were diagnosed with the thyroid diseases. As soon as pregnant women were registered, the endocrinologist examination was organized and a protocol was drawn up on the course of the pregnancy taking into consideration the recommendations of the endocrinologist. Ultrasound was implemented and the density of TSH, free T<sub>3</sub> and T<sub>4</sub> hormones in the blood was determined. It was determined that there was hyperthyroidism in 15 (37%) of 41 pregnant women and hypothyroidism in 26 patients (63%) among the same number of pregnant women.

First of all, in order to balance the iodine deficiency of pregnant women, we decided to give them during the day iodised salt in amount of 150 mg per day and 200 mg potassium iodide preparation for oral use once per day. Besides, we prescribed 2 tablets (300-400 mg) of propyltiourasil 3-4 times per day and 30-40 mg of timazol 3 hours after it for the first 3 months of the pregnancy. The use of these preparations in accordance with this scheme was continued till the thyroid hormones reached standard level.

200 mg potassium iodide once per day was prescribed for the first days of the pregnancy to 26 pregnant women with the hypothyroidism.

At endocrinological clinic where they had been registered, they used 300-400 mg of propyltiourasil during the day (2 tablets 3-4 times per day) 3 months before the pregnancy, and 30-40 mg timazol during the day 3 months after the pregnancy. Prescribed treatment kept impaired function of the thyroid in the condition compensated to a certain degree till the end of the pregnancy. However, intrauterine

fetal development was abnormal in 42% of pregnant women (11 patients). In perinatal period the pregnancy was disrupted in form of the miscarriage in 4 (36%) and in form of the stillbirth in 2 pregnant women (18%). Instillation abortion was implemented in 1 patient (9%) because the head of the fetus was separated from the body.

In internatal period the birth activity was poor in 2 pregnant women (18%). There was uterine atony after the birth in 1 patient (9%).

And there was hydrocephalus in postnatal period in 1 newborn (9%).

And 15 pregnant women had the hyperthyroidism. 200 mkg potassium iodide during the day was prescribed to them. And in cases when the sizes of the thyroid were not reduced, 50-100 mkg L-trioksine were prescribed to them 30 minutes before the breakfast. As a result, the density of TSH hormone increased to average limit.

The results of our clinic observations demonstrated that replacement therapy of impaired function of the thyroid to pregnant women with the hyperthyroidism with the eliminating the iodine deficiency of the body occurred starting from the first days of the pregnancy kept the density of the thyroid hormones within certain limit. As a result, negative impact of the thyroid dysfunction on fetal development was partially eliminated, so the pregnancy in 10 (67%) of 15 pregnant women ended with physiological birth. Botallo's duct remained open in 1 of them.

The pregnancy in pregnant women with the hyperthyroidism was complicated. The complication in 6 (40%) of 15 pregnant women occurred in perinatal period. There was the miscarriage in 2 pregnant women, monstrous fetus in other 2 patients and the stillbirth in 1 patient.

Thus, perinatal development of 29 (71%) of 41 patients under our observation was complicated. When discharging from the hospital they were recommended to register at endocrinological clinic and undergo treatment for a long time before repeatedly become pregnant. Based on this recommendation, the strumectomy operation was implemented in 6 (40%) of 15 patients with the hyperthyroidism, because they had had thyroid nodule. After the

operation they stayed registered at the clinic and the replacement therapy was implemented. They were registered with the pregnancy 2-5 years after surgical operation. Their density of TSH was within normal limits, density of T<sub>3</sub> increased by 3% and density of T<sub>4</sub> - by 7% in comparison with normal limit. The thyroid hormones were within normal limits also during the pregnancy. As a result, intrauterine fetal development was abnormal in 2 (33%) of 6 patients, and the pregnancy ended with physiological birth in 4 patients (67%).

Thus, the results of our scientific research demonstrate that the complications that occur in the course of the pregnancy are caused by an imbalance of thyroid hormones; and the regulation of an imbalance of thyroid hormones during the pregnancy is faced with a number of the difficulties. Therefore, we consider that in case of the thyroid disease, it is necessary to implement the replacement therapy that compensates impaired function of the gland, to eliminate the iodine deficiency and to control the level of the thyroid hormones during the pregnancy before planning the pregnancy.

In order to solve this matter, the strumectomy operation was implemented in 6 patients (40%), because they had had thyroid nodule. After surgical operation they stayed registered at the clinic and the replacement therapy was implemented within this period.

14 pregnant women were received with the kidney diseases. 2 of them (14%) had polycystic kidney disease, 5 (36%) - pyelonephritis, 7 (50%) - chronic kidney failure.

When registering pregnant women, blood creatinine level increased by 213%, urea level - by 74%, residual nitrogen level - by 130% and urine protein level - by 198%. The treatment plan was drawn up together with the nephrologist. As a result of the treatment implemented, in comparison with the first days of the pregnancy, blood creatinine level decreased by 13%, urea level - by 10% at the end of the III trimester. And residual nitrogen level continued to increase.

In comparison with the first days of the pregnancy, total protein level in urine decreased by 44%. Despite positive changes obtained, the pregnancy results were unsatisfactory. There was the

miscarriage in 6 patients (43%) and the stillbirth in 1 patient (7%). 1 newborn (14%) was lightweight, 2 newborns (28%) were born with hydrocephalus and 1 newborn (14%) - with hypoxia.

Thus, intrauterine fetal development was abnormal in 11 (79%) of 14 pregnant women with the kidney pathology.

There were no pregnant women with the kidney pathology, applied to us in order to be registered with repeated pregnancy.

18 pregnant women was diagnosed with alcoholic psychosis. They were registered at the clinic at their residence address and treated under the control of the psychiatrist. This treatment continued during their pregnancy. It became necessary to prescribe the anti-depressant in 12 patients (78%) among pregnant women. Also, it was sufficient to prescribe weak sedative medications to 6 pregnant women (22%). Perinatal fetal development was complicated in 10 patients (83%) among pregnant women who had used psychotropic medications. Their pregnancy was disrupted as a result of miscarriage in 4 of them, stillbirth in 1 of them and monstrous fetus in another one. Each of the newborns (6 newborns) had, respectively, hydrocephalus, tetralogy of Fallot, urethral obliteration, increased intracranial pressure.

The pregnancy was disrupted in 2 of 6 pregnant women who had not used psychotropic medications. The reason of this in one of them was the miscarriage, in another one - the stillbirth. The auricle of 1 of 4 newborns was lower than usual position, and distal phalange of the 5<sup>th</sup> finger of right hand was subject to the displasy in another one.

Thus, perinatal fetal development was abnormal even in of 67% of 6 pregnant women who had not used psychotropic medications. In common, the pregnancy was complicated in 78% of pregnant women with alcoholic psychosis.

When analysing the impact of extragenital diseases on the course of the pregnancy it was determined that extragenital diseases listed by us are a risk factor for the miscarriage. The highest risk factors among these diseases are kidney pathology and alcoholic psychosis.

And the stillbirths are typical for pregnant women with heart defect and gastrointestinal system diseases. Thyroid diseases, heart defect, hepatitis of alimentary origin and pulmonary diseases are high risk factors for monstrous fetus.

Another one factor preventing the course of the pregnancy is the hepatitis of viral origin. The fact that this disease is widely spread among the women of reproductive age makes it the priority matter also for the obstetrician- gynaecologists. Since such questions as "Will the pregnancy in the patients with the hepatitis of viral origin be the successful or unsuccessful?", "Will the hepatitis of viral origin cause the contraindications related to the pregnancy?", "Will the delivery be performed in physiological way or using the caesarean section?" continue to be the discussion subject at scientific meetings of the obstetrician- gynaecologists. Therefore, we considered important to monitor the course of the pregnancy in the patients with the hepatitis of viral origin. In order to do it, the research covered 78 pregnant women. Hepatitis C was at the 1<sup>st</sup> place among pregnant women who took part in the research, Hepatitis B was at the 2<sup>nd</sup> place and Hepatitis A - at the 3<sup>rd</sup> place. Usually, the pregnancy of pregnant women with the hepatitis of viral origin is unsuccessful. On the one hand, main reason of this is the contraindication related to antiviral therapy during the pregnancy, on the other hand - absence of specific prevention in prenatal period.

When registering, all of 78 pregnant women were consulted with hepatologist and virologist. The pregnancy management protocol was drawn up after unanimous decision had been adopted.

In order to improve the liver functions during the pregnancy, heptral was used as the base medication. Heptral was prescribed for use twice per day (800 mg) in form of the tablet. When the liver tests sharply increased, 400 mg heptral was injected intravenously during the day. In order to maintain obtained results after the medication was applied during 2 weeks, heptral was used within 10 days in the dosage of 1 tablet per day.

8 patients (11%) among pregnant women were registered being diagnosed with hepatitis A virus. Before heptral was prescribed, in comparison with normal limits, the density of AST in

the blood increased by 272%, the density of ALT - by 294% and the density of Alkaline phosphatase - by 41%. Total bilirubin level characterizing toxic status of the liver increased by 111%. As a result of the effect of heptal, the density of the liver bioassays in the blood decreased proportionally during the pregnancy.

The course of the pregnancy became more moderate in connection with positive changes in the liver function as a result of the effect of heptal. There was miscarriage in 1 (12,5%) of 8 pregnant women, the newborns of 2 of them (25%) were lightweight, Botallo's duct of the newborn of 1 patient (12,5%) remained open. Thus, the pregnancy of 50% of all the pregnant women, infected with the Hepatitis A virus, was complicated.

19 patients among pregnant women, who took part in the research, were infected with the Hepatitis B virus. Before heptal was applied, the density of the enzymes in their blood was, respectively, 323%, 334% and 71% more than normal limit. And total bilirubin level was 167% more than normal limit. As we can see hereof, in comparison with A virus, B virus caused deeper functional changes in the liver. As a result of heptal use during the last week of the I trimester, the level of the markers reflecting functional status of the liver bioassays tended towards the decrease, and got more significant form at the end of the II trimester. Density of AST in the blood decreased by 15%, density of ALT - by 9%, density of Alkaline phosphatase - by 8%.

Despite the regulation of functional status of the liver as much as possible, there was no positive result obtained during the pregnancy.

There was stillbirth in 2 pregnant women (10,5%), monstrous fetus in 1 pregnant woman (5%) and miscarriage in 1 pregnant woman (5%). Hepatitis B virus was detected in all the newborns (100%). In addition, rectal atresia was detected in 3 (20%), esophageal atresia in 2, ventricular septal defect in 2 (13%) of them.

Thus, fetal development was with the defects in 11 patients (58%) among pregnant women infected with B virus.

23 patients among pregnant women were infected with the Hepatitis C virus. When registering density of AST in their blood

was 376%, density of ALT - 344%, density of Alkaline phosphatase - 76% and total bilirubin level - 219% more than normal limits. After heptal was applied (at the end of the II trimester), in comparison with the level measured before heptal was prescribed, density of AST in the blood decreased by 16%, density of ALT - by 13%, density of Alkaline phosphatase - by 8% and total bilirubin level - by 18%. Despite little positive dynamic in functional status of the liver, there were severe complications detected in pregnant women. There was stillbirth in 4 of them (17%) and miscarriage in 4 other ones. The pregnancy ended with instillation abortion in 2 pregnant women (9%) because of monstrous fetus. There was congenital defect detected in 3 newborns (23%). One of them had esophageal, another one - rectal, the third - auricular atresia.

Thus, perinatal fetal development was abnormal in 13 (56.5%) of pregnant women infected with the Hepatitis C virus.

20 patients among pregnant women who had been under our observation were infected with 2 virus types: Hepatitis A and B. When registering, in comparison with normal limits, density of AST in their blood increased by 331%, density of ALT - by 335%, density of Alkaline phosphatase - by 73% and total bilirubin level - by 181%.

Heptal use relatively improve functional status of the liver, so the density of the enzymes in the blood, reflecting it, tended towards the decrease. In comparison with the levels, measured before heptal application, the levels (or density) of AST, ALT and Alkaline phosphatase at the end of the II trimester decreased by 12%, 6% and 5% and total bilirubin level - by 26%. Thus, heptal application prevented the aggravation of the abnormalities occurred in functional status of the liver in pregnant women with Hepatitis caused by both viruses (A and B). Despite this fact, the course of the pregnancy was as follows. There was stillbirth in 3 (15%) of 20 pregnant women and miscarriage in 3 of them. There was congenital defect detected in 4 newborns (cleft lip, cleft palate, etralogy of Fallot, open Botallo's duct).

Thus, the course of the pregnancy was abnormal in 50% of pregnant women infected with A and B viruses who were under our observation.

Hepatitis B and C was detected in combined form in 31 pregnant women. In comparison with normal limits, density of AST in their blood increased by 432%, density of ALT - by 372%, density of Alkaline phosphatase - by 89% and total bilirubin level - by 271%.

As with other hepatitis of viral origin, positive impact of heptral was detected also on pregnant women with B and C viruses in combined form. Thus, starting from the end of the I trimester the density in the blood of the markers reflecting functional status of the liver tended towards the decrease and got more intensive form in the II trimester. Thus, the density of AST, ALT and Alkaline phosphatase decreased by 15%, 17% and 12% respectively, and total bilirubin level by 30%. However, despite all this positive dynamic, the course of the pregnancy was unsuccessful in 58% of pregnant women. There were stillbirths in 4 (13%), miscarriages in 2 of them (6,5%), and the pregnancy ended with instillation abortion in the same number of pregnant women because of severe defects of the fetus. The pregnancy ended with premature birth in 5 patients (22%) among pregnant women in intranatal period.

8 newborns (35%) were infected with B virus, 15 newborns (65%) - with C virus. 3 newborns (13%) were lightweight.

Thus, hepatitis of viral origin is a risk factor for severe pregnancy complications. Prenatal development in 53 (68%) of 78 pregnant women was with different complications.

Pregnant women had taken our recommendations when discharging and registered in territorial polyclinic. 58 patients (74%) among them underwent treatment at the hospital and managed to relatively stabilize the course of the disease. 32 of them (55%) repeatedly became pregnant 1-6 years later.

4 (12.5%) of 32 pregnant women were diagnosed with Hepatitis A, 7 patients (22%) - with B, 11 patients (34%) - with C and 10 patients (31%) - with Hepatitis caused jointly by B and C viruses.

When registering, density of AST in the blood was 141%, density of ALT - 132%, density of Alkaline phosphatase - 25% and density of total bilirubin - 43% more than normal limits. As we can see hereof, in comparison with the women who had become pregnant

without the treatment at the hospital, density of AST in the blood of the women who had become pregnant after the treatment at the hospital decreased by 34%, density of ALT - by 41%, density of Alkaline phosphatase - by 11.5%, total bilirubin level - by 32%. All the pregnant women used heptal. As a result of the effect of heptal, starting from the I trimester, the density of the markers reflecting functional status of the liver in the blood significantly decreased.

Maintaining functional status of the liver in a certain limit during the pregnancy also had positive impact on the course of the pregnancy. There was no complication in intrauterine fetal development of 50% of pregnant women, infected with the Hepatitis A virus. However, in comparison with the women who had become pregnant without the treatment, nobody was infected with A virus.

And as a result of the effect of heptal, in comparison with the level measured before heptal application, density of AST in the blood at the end of the I trimester decreased by 8%, density of ALT - by 18%, Alkaline phosphatase - by 4.5%, total bilirubin level - by 11.5% in pregnant women infected with the Hepatitis B. The level of these markers decreased more significantly at the end of the II trimester. This positive dynamic reduced a little the complications able to occur during the pregnancy. Thus, there were stillbirth in 1 patient (14%) among pregnant women, and miscarriage in another one. Premature birth was implemented in 1 patient. B virus was detected in the blood of 3 newborns (60%).

Thus, the pregnancy ended with the defect in 3 patients (43%) among pregnant women infected with B virus, included in the 2<sup>nd</sup> group.

11 patients among pregnant women were infected with Hepatitis C virus. Despite the treatment in specialized medical institutions before they had become pregnant, the level of the markers in their blood, reflecting functional status of the liver, was very different from standard. However, obtained results differed from the level achieved in the women who had become pregnant without specific treatment.

After the level of the markers, reflecting functional status of the liver in the blood, was detected heptal was prescribed to them.

At the end of the II trimester the density of AST and ALT in the blood decreased by 6%, density of Alkaline phosphatase - by 12%, density of total bilirubin - by 21%. Taking this into consideration, we can say that prescribing heptral to the women who became pregnant after the hepatitis treatment gives more effective results. However, despite all this positive dynamic, the level of the complications in the course of the pregnancy was high (64%). There was the stillbirth in 1 of them (9%) and the miscarriage in another one. The pregnancy of 3 patients (27%) among pregnant women ended with premature birth and the newborns of 2 patients (18%) were lightweight. However, in comparison with the 1<sup>st</sup> group, 67% of the newborns was not infected with the Hepatitis C.

10 patients (17%) among pregnant women, who took part in the research, were infected with both viruses (Hepatitis B and C).

Despite the level of the markers in their blood reflecting functional status of the liver was higher than standard when registering, it was significantly lower in comparison with the 1<sup>st</sup> group.

After heptral application at the end of the II trimester density of AST in the blood decreased by 9%, density of ALT - by 15%, density of Alkaline phosphatase - by 10%, density of total bilirubin - by 38%.

As a result of preventive measures implemented, the pregnancy was complicated in 50% of all the cases. The pregnancy was disrupted because of the stillbirth in 2 of them (20%) and the miscarriage in 1 patient (10%). 1 newborn (10%) was lightweight, and another one was born with rectal atresia.

The results of our observations demonstrate that the hepatitis of viral origin is a high risk factor for defective fetal development.

80 patients (11%) among pregnant women were infected with general infection. Toxoplasmosis was detected in 24 of them (30%), cytomegalovirus - in 36 patients (45%) and rubella in 20 patients (25%).

The I trimester of pregnant women infected with toxoplasmosis proceeded without any complication. In the II trimester the pregnancy ended with the miscarriage in 2 patients

(8%) and with the stillbirth in 3 patients (12,5%). Early in the III trimester there was the miscarriage in another 1 patient (4%), as well the stillbirth in one more patient. The pregnancy ended with instillation abortion in 2 patients (8%) because of severe defect.

A number of the complications occurred also in intranatal period. There was early rupture of the membranes in 1 patient among pregnant women and the pregnancy of 3 patients ended with premature birth. 3 newborns (16%) were lightweight, 1 newborn had cleft palate and another one - open Botallo's duct.

Thus, the pregnancy was complicated in 18 patients (75%) among 24 pregnant women, infected with the toxocosis.

14 patients among pregnant women who had treated after postnatal period repeatedly became pregnant. Toxoplasmosis titre was high in 6 of them. The toxocosis titre was lowered by applying in these pregnant women 1 plasmapheresis session at the initiative of the infectious disease doctor. Thus, the pregnancy continued with low toxoplasmosis titre in 10 (71%) of 14 pregnant women. As a result, by applying the plasmapheresis, it became possible to decrease the complications during the pregnancy from 75% to 35%. Based on scientific researches, implemented by us, we can say that the plasmapheresis implemented before the pregnancy and during the I trimester in case of the toxoplasmosis do not impact negatively on the embryo and significantly decrease the complications during the pregnancy.

36 patients (45%) among pregnant women were infected with the cytomegalovirus. The cytomegalovirus titre was high in all of them. There was miscarriage in 1 patient in the 33<sup>rd</sup> week of the I trimester and in 2 patients (5,5%) in the II trimester. There was stillbirth in 3 patients (8,5%) and the pregnancy of 2 patients (5,5%) ended with instillation abortion in the III trimester because monstrous fetus had been detected.

28 patients (78%) among pregnant women completed their pregnancy with a childbirth. Internatal period was also complicated. There was early rupture of the membranes in 3 patients (11%) among pregnant women and the pregnancy of 4 patients (14%) ended with premature birth. Rectal atresia was detected only in 1 patient (4%).

Thus, the pregnancy was complicated in 16 patients (44%) infected with the cytomegalovirus.

20 patients among pregnant women repeatedly became pregnant 1-4 years after the treatment at medical institutions specialized in infectious diseases and was registered in our clinic. The I trimester proceeded without any complication, but there was the miscarriage in 2 patients (10%) in the II trimester. And there was the stillbirth in 1 patient (5%) in the III trimester. 17 patients (85%) among pregnant women completed their pregnancy with a childbirth. The pregnancy of 1 of them (6%) ended with premature birth. There was congenital defect only in 1 newborn (6%). Thus, as a result of the decrease of the cytomegalovirus titre in pregnant women, the pregnancy of 6 patients (30%) was complicated.

Thus, the decrease of the cytomegalovirus titre in the blood before the pregnancy reduced the complications during the pregnancy by 16%.

20 patients (25%) among pregnant women were infected with the rubella. The I trimester of their pregnancy proceeded normal. However, there was the miscarriage in 2 patients (20%) and stillbirth in 1 patient (5%) in the II trimester. There was the stillbirth in 2 more patients in the III trimester. The pregnancy ended with a birth in 15 patients (75%). Intranatal period was also complicated. The pregnancy ended with premature birth in 3 patients (20%) among pregnant women, as well there was early rupture of the membranes in 1 patient (7%). Congenital defects were detected in 3 newborns (20%). Thus, the results of our scientific research show that there were different complications during the pregnancy of 60% of pregnant women infected with the rubella.

10 patients among pregnant women repeatedly became pregnant 1-3 years after the treatment at medical institutions specialized in infectious diseases. In comparison with the 1<sup>st</sup> group, their pregnancy was relatively moderate. The pregnancy ended with the miscarriage in 1 patient (10%), with the stillbirth - in 2 patients (20%); and the pregnancy of 1 patient (10%) ended with instillation abortion related to open thorax of the fetus in the III trimester. There was no congenital defect in postnatal period. Thus, the immunity

formed against the rubella impacted positively on perinatal fetal development and the pregnancy proceeded without any complication in 4 pregnant women (40%).

155 pregnant women, observed by us, had genital organs diseases. Myoma was detected in 30 of them (19%). There was subserosal myoma in 15 (50%), interstitial myoma in 10 (33%) and submucosal myoma in 5 patients (17%). The localization of the myoma of pregnant women was as follows: it was located in the cervix in 17 (57%), in the uterus in 11 (37%) and between the leaves of broad ligament of uterus in 2 patients (6%).

The bleeding occurred in 3 patients (10%) among pregnant women in the I trimester. The bleeding was suspended in conservative way in 1 patient, and conservative myomectomy was implemented in laparoscopic way in 2 patients.

The pregnancy was maintained in all 3 patients. There was the miscarriage in 2 patients on the last weeks of the I trimester.

Massive bleeding occurred in other 2 patients (7%) in the II trimester was suspended by means of surgical operation. However, the pregnancy of both of them ended with the miscarriage. The III trimester proceeded without any complication. There was early rupture of the membranes in 5 (19%) of 26 pregnant women (87%), the pregnancy of which ended with a birth. Massive bleeding occurred in 4 pregnant women during a childbirth and the uterus was removed as it was impossible to suspend this bleeding. 4 newborns (15%) were born with the defects.

Thus, the pregnancy proceeded with severe complications in 23 patients (77%) among pregnant women with uterine fibroid.

Conservative myomectomy was implemented in 14 patients (64%) among these pregnant women at different time after postnatal period. And 8 pregnant women were treated using pharmacotherapy. They repeatedly became pregnant 1-5 years after the treatment and was registered in our clinic.

There was the miscarriage only in 1 patient (4.5%) among 22 pregnant women in the II trimester and oligohydramnios in another one in the III trimester. There was early rupture of the membranes in

1 (5%) of 20 pregnant women who had been able to complete their pregnancy, however there was no defect among the newborns.

Thus, uterine myoma is a risk factor for the pregnancy. However, after it was treated, the pregnancy complications among pregnant women decreased from 77% to 13.5% (i.e., by 63.5%).

Arcuate uterus was detected in 19 patients (12%) among pregnant women. Their pregnancy also was unsuccessful. Thus, there was embryonic miscarriage in 3 patients (16%) among pregnant women, fetal miscarriage in 5 patients (26%), stillbirth in 6 patients (32%) and backward fetus in the same amount of the patients.

Thus, the pregnancy proceeded with severe complications in 14 (74%) of 19 pregnant women and the pregnancy was completed only in 26% of pregnant women.

We performed surgical operation in 13 patients among these pregnant women and provide normal configuration of the uterus. 9 patients applied to our clinic with repeated pregnancy 1-3 years after surgical operation. There were no severe complications during the pregnancy. There was early rupture of the membranes only in one of pregnant women in intranatal period and the pregnancy of another one ended with premature birth. Thus, the pregnancy ended with 22% slight complication after surgical operation performed in connection with arcuate uterus.

28 patients (18%) who had been under our supervision were infected with the chlamydiosis. Of course, chlamydiosis is an infection of genital organ and is able to grow in this environment. On the one hand, increase of its titre strengthens the intoxication, on the other hand, blunts the immunity. Both of the factors prevent embryonic and fetal development, so they impact on the course of the pregnancy. There was miscarriage in 3 patients (11%) among pregnant women and stillbirth in 7 patients (25%). 8 (44%) of 18 newborns were lightweight. Also, there was congenital defect in 2 of them (11%). Thus, the pregnancy in 71% of pregnant women infected with genitourinary chlamydiosis was complicated.

Based on our recommendations, they applied to the infectious disease doctor after postnatal period and was treated at the hospital, as well outpatiently. 11 patients repeatedly became pregnant 3-7

years after the treatment. The chlamydia titre decreased sharply in 8 (73%) of 11 patients and significantly in 3 patients (27%).

The pregnancy was disrupted with the miscarriage in the last 3 patients (27%). There was the stillbirth in 1 patient (9%). Remaining 7 patients completed their pregnancy with a childbirth. Intranatal period was also complicated. There was early rupture of the membranes in one (25%) patient among pregnant women and the pregnancy of 3 (75%) patients ended with premature birth.

Thus, the analysis of the results of our clinic observations shows that the values of complicated course of the pregnancy after the treatment of genital chlamydiosis remain high (64%). However, in comparison with the 1<sup>st</sup> group, the complications occurred in the 2<sup>nd</sup> group were not so severe.

35 patients (23%) who had been under our supervision were infected with the herpes simplex. Valacyclovir was prescribed to them twice a day during 5 days.

Despite the treatment of herpes simplex, the values of the complications during the pregnancy were high.

There was embryonic miscarriage in 2 patients (6%) in the I trimester. The fetus was retarded in 5 patients (14%) in the II trimester. Despite the treatment provided, the pregnancy ended with the stillbirth in 3 of them (60%). There was the miscarriage in 2 patients (6%). Also, the pregnancy was disrupted because of unviable monstrous fetus (the head separated from the body, retarded brain, absence of the left hand) in 3 patients.

Also, there was stillbirth in 2 more patients (6%) in the III trimester. The pregnancy of 20 patients (59%) ended with a childbirth. There was oligohydramnios in 3 (15%) of 20 pregnant women, premature birth in 2 patients (10%) and early rupture of the membranes in 3 patients (15%). There was hypoxia in 3 newborns (13%), hydrocephalus in 2 newborns (10%) detected in postnatal period.

Thus, the pregnancy was complicated in 24 (69%) of 35 pregnant women infected with the type 2 herpes simplex.

16 women applied to the clinic with repeated pregnancy 1-4 years after reasonable treatment of the type 2 herpes simplex. They

continued to use valacyclovir based on the recommendation of the infectious disease doctor. Despite that the I trimester of pregnant women proceeded without any complication, there was miscarriage in 1 patient (6%) in the II trimester and stillbirth in 1 patient (6%) in the III trimester. Remaining 14 patients (87.5%) completed their pregnancy with a childbirth.

There was early rupture of the membranes in 2 of pregnant women (14%) in intranatal period and the pregnancy of 1 of them (7%) ended with premature birth.

There was the hydrocephalus only in 2 (14%) of 14 newborns. Thus, prenatal fetal development was abnormal in 44% of 16 pregnant women.

20 patients (13%) among pregnant women, who took part in the research, were infected with the mycoplasma. There was miscarriage in 3 pregnant women (15%) in the I trimester, stillbirth in 2 patients (10%) in the II trimester and monstrous fetus in 3 patients (15%) in the III trimester. One of them had retarded orbit, another one - retarded thorax. And the head of last one was separated from the body. The pregnancy ended with premature birth in 2 (14%) of 12 pregnant women (60%) who completed their pregnancy with a childbirth. Also, the pregnancy ended with early rupture of the membranes in 1 of them (7%). 4 newborns (33%) were born with congenital birth defect.

Thus, the pregnancy proceeded with different complications in 15 patients (75%) among pregnant women, infected with the mycoplasma.

7 women repeatedly became pregnant 1-2 years after corresponding treatment. When registering them, in comparison with the previous period, the mycoplasma titre decreased significantly.

There was embryonic miscarriage in 1 patient (14%) among pregnant women in the I trimester, and fetal miscarriage in another 1 patient (14%) in the II trimester. The pregnancy ended with a childbirth in 5 patients (71%). And 1 newborn (29%) was born with the hydrocephalus.

Thus, prenatal development was abnormal in 3 patients (43%) among pregnant women who had treated at specialized medical

institutions before the pregnancy. However, in comparison with the 1<sup>st</sup> group, the complications decreased by 7%, the formation of dead and monstrous fetus was prevented.

20 (13%) of 155 pregnant women who took part in the research were infected with gonorrhoea. Pregnant women were examined based on received protocol and the pregnancy management plan was drawn up together with the infectious disease doctor. There was the miscarriage in 3 patients (15%) in the II trimester. Also, there was early rupture of the membranes in 3 patients (15%). Thus, the pregnancy was complicated in 12 (60%) of 20 pregnant women.

After the treatment, 9 patients repeatedly became pregnant. There was no severe complication detected in perinatal period. However, the pregnancy of 2 patients (22%) ended with premature birth. One of the newborns was lightweight.

Thus, the pregnancy was complicated in 3 patients (33%) among pregnant women who had become pregnant after the treatment.

106 patients among pregnant women who took part in the research were addicted to different bad habits. 43 of them (41%) used alcohol. Depending on the use of alcohol, pregnant women were divided into 3 groups.

13 patients from the 1<sup>st</sup> group used alcohol before the pregnancy.

18 patients from the 2<sup>nd</sup> group had used to drink alcoholic beverages before, but reduced its use during the pregnancy.

12 patients from the 3<sup>rd</sup> group had used to drink alcoholic beverages before the pregnancy, and continued its use in the same manner during the pregnancy.

There was the miscarriage in 1 (8%) of 13 pregnant women from the 1<sup>st</sup> group by the end of the I trimester. The pregnancy of another one woman was disrupted because of the retardation of frontal bone of the fetus.

The pregnancy ended with premature birth in 2 patients (15%) in intranatal period. There also was early rupture of the membranes in 1 patient (8%).

1 newborn (9%) among 11 newborns was born with the defect, and 10 newborns (91%) - without any defect. Thus, the pregnancy was complicated in 6 patients (46%) who had used to drink alcoholic beverages and gave it up after becoming pregnant; also, the pregnancy proceeded without any complication in 7 patients (54%).

There was the miscarriage in 2 (11%) of 18 pregnant women from the 2<sup>nd</sup> group in the I trimester and the stillbirth in 3 patients (17%) in the II trimester. The pregnancy ended with instillation abortion because of the retardation of frontal bone in 1 patient (5.5%) in the II trimester and of the left orbit in another 1 patient in the III trimester. Thus, the pregnancy was disrupted in 7 patients (39%) among pregnant women from the 2<sup>nd</sup> group because of complicated prenatal period.

The pregnancy ended with premature birth in 3 patients (17%) in intranatal period. There also was early rupture of the membranes in 2 patients (11%). 3 newborns were born with congenital defect.

The analysis of obtained results shows that the pregnancy was complicated in 15 patients (83%) among pregnant women from the 2<sup>nd</sup> group.

The pregnancy complication cases were much more in pregnant women from the 3<sup>rd</sup> group. There was the miscarriage in 3 patients of 12 pregnant women in the I trimester. There was the stillbirth in 2 patients (16%) in the II trimester. Instillation abortion was performed in 1 patient (8%) because the head of the fetus was separated from its body. Another instillation abortion was implemented in the III trimester. 2 newborns (17%) were born with congenital defect in postnatal period.

Thus, the pregnancy in 75% of pregnant women regularly using alcoholic beverages proceeded with severe complications. The pregnancy in 58% of them was disrupted.

Based on our recommendations, 20 (46.5%) of 43 patients was treated under the supervision of narcologist and psychologist after postnatal period. 11 of them (55%) gave up the alcohol use and repeatedly became pregnant 2-4 years after the treatment. The course

of their pregnancy was as follows. The I trimester proceeded well. However, the miscarriage occurred in 1 of them (9%) in the II trimester. There was cleft lip only in 1 (10%) of 10 newborns. Thus, the pregnancy proceeded without any complication in 9 (82%) of 11 patients who repeatedly became pregnant after giving up the alcohol use.

In order to clarify the pathogenesis of the complications occurred in fetal development impacted by the alcohol, we conducted an experiment with 50 female white rats. We created the alcohol infection model in these rats and studied functional status of the ovary.

Experimental rats were divided into 4 groups.

The 1<sup>st</sup> group was the control group and was kept in intact state (5 rats);

15 white rats were left in intact state for the mating in the 2<sup>nd</sup> group.

Before 15 white rats were left for the mating in the 3<sup>rd</sup> group, they had been given 2 ml of pure alcohol 3 times per day during 15 days. And they continued to drink alcohol after they were left for the mating.

15 experimental rats, included in the 4<sup>th</sup> group, were tested in the manner same with the 3<sup>rd</sup> group, but after the mating was over, 125 mg/kg tiisetam once a day was applied to their abdominal cavity till the end of the gestation.

Experimental rats got pregnant after the mating were selected and decapitated in the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> weeks after the fetus formation in accordance with Helsinki declaration of European Committee on Bioethics on the manner of handling with experimental animals, and the level of ovary hormones in the blood, as well energy resources (M.Creatine phosphocinase and density of ATP) in the homogenate made of the pituitary gland were determined. The results of the experiment showed that starting from the 2<sup>nd</sup> week of the gestation, the energy balance in the pituitary gland started to tend towards the decrease. However, the changes in the energy balance went down in the 4<sup>th</sup> week of the gestation. Based on these experiments, we can say that energy materials in the pituitary gland start to decrease during

the gestation. However, this was in certain physiological frame and the stabilization was achieved by the last weeks of the gestation.

But the decrease in the energy materials in the homogenate made of the pituitary gland of the rats included in the 3<sup>rd</sup> group became more intensive. In comparison with the results obtained in the 2<sup>nd</sup> week of the mating of experimental rats included in the 2<sup>nd</sup> group, density of M.CPC decreased by 30.5% and density of ATP - by 17.5. At the same time, sharp increase in the density of cortisol and estradiol in the blood occurring as a result of the impact of the alcohol, results not only in the pituitary gland, but also ovary disfunction. The longer the pregnancy period, the more aggravated pathological process. The level of the prolactin was 103%, density of cortisol 78%, density of progesterone 124%, density of estradiol 42%, luteinizing hormone 122% higher than standard value in the 4<sup>th</sup> week of the mating. Density of FSH decreased by 16%.

And the density of mCPC energy resource markers in the pituitary gland was 23% lower. In comparison with the 3<sup>rd</sup> group, density of cortisol in the blood decreased by 13.5%, density of progesterone - by 6%, density of estradiol by 9%, luteinizing hormone - by 32%, density of FSH increased by 17% in white rats included in the 4<sup>th</sup> group in the 2<sup>nd</sup> week of the mating. There were positive changes in the 2<sup>nd</sup> week of the gestation under the effect of tiostatam not only in the ovary, but also in the pituitary gland. Despite that the density of mCPC in the pituitary gland tissue was kept stable, the density of ATP decreased by 8%. It had not reached the standard value yet.

The difference detected between the 3<sup>rd</sup> and 4<sup>th</sup> group became more intensive in the 4<sup>th</sup> week of the mating. Density of prolactin in the blood decreased by 34%, density of cortisol - by 24%, density of progesterone - by 31%, density of estradiol - by 19.5%, luteinizing hormone - by 39%; and the density of FSH increased by 3%, however, in comparison with the 3<sup>rd</sup> week of the 4<sup>th</sup> group it was kept stable.

There was positive dynamic also in the energy balance of the pituitary gland. Thus, the density of mCPC increased by 20%, and density of ATP - by 18%.

Thus, summarizing the experiments implemented by us, we can say that the alcohol use before and during the pregnancy results in severe malformations in accumulation of the energy resources and functioning of the pituitary gland. The result obtained by us allow to say that the complications occurred in the course of the pregnancy of pregnant women addicted to the alcohol were caused by the pituitary gland and ovary dysfunction. This is also proved by positive results obtained in the course of the pregnancy of the women who used Tiosetam during the pregnancy.

54 patients (51%) among the women, controlled by us, smoked. In order to correctly build the research in terms of the methods, the women were divided into 4 groups depending on if they smoked or not.

The 1<sup>st</sup> group included 20 patients (37%) who regularly smoked.

The 2<sup>nd</sup> group included 15 patients (28%) who used to regularly smoke before the pregnancy.

The 3<sup>rd</sup> group included 19 patients (35%) who smoked not often.

As a result of implemented observations, it was detected that the pregnancy was complicated in 60% of the women who regularly smoked. Thus, starting from the I trimester (including the last one), the pregnancy of 11 patients (55%) among pregnant women was disrupted as a result of instillation abortion implemented because of miscarriage, stillbirth, detection of monstrous fetus.

And congenital developmental defect was detected in 25% of 5 newborns in postnatal period.

The pregnancy was complicated in pregnant women included in the 2<sup>nd</sup> group. Different complications were detected in 73% of them (11 patients).

The pregnancy was disrupted in connection with different complications in 6 patients (40%) among pregnant women in prenatal period, including miscarriage (1 patient), stillbirth (4 patients) and detection of monstrous fetus (1 patient). Botallo's duct was open in 1 (9%) of 9 newborns, another one had esophageal atresia with multiple fistulas, 2 newborns had cleft lip. 1 newborn

had short stature. Thus, 33% of the newborns was born with the defect.

In comparison with pregnant women included in the 1<sup>st</sup> group, the pregnancy disruption of pregnant women from the 2<sup>nd</sup> group decreased by 7%.

And the pregnancy was disrupted in 4 pregnant women as a result of the complications, occurred in pregnant women from the 3<sup>rd</sup> group in prenatal period. 1 pregnant woman had miscarriage, 2 women had the stillbirth and the pregnancy ended with instillation abortion in 1 pregnant woman because of monstrous fetus. Also 4 newborns were born with the defect (open Botallo's duct, head circumference, weight and height lower than standard) in postnatal period.

Thus, 9 (47%) of pregnant women included in the 3<sup>rd</sup> group had different complications.

There was the miscarriage in 1 patient (8%) among pregnant women included in the 4<sup>th</sup> group and the pregnancy of 92% of them was completed. Also, there was insignificant congenital defect only in 1 newborn (8%). It is hereof clear that the pregnancy of 17% of the women who used to regularly smoke and became pregnant 3 years after giving it up was complicated. The results obtained prove that the nicotine is also included in a high risk group preventing prenatal fetal development.

Summarizing the research implemented by us, we can say that the pregnancy was disrupted in 64 (16.2%) of 396 women with extragenital disease. Taking into consideration that extragenital diseases is a high risk for the pregnancy and the abilities of the obstetrician- gynaecologist to help her during the pregnancy are limited, we provided them with the direction to corresponding specialized physicians in order to treat their disease after postnatal period. After the treatment the pregnancy was disrupted in 13% of 153 pregnant women, who had applied to us with repeated pregnancy. As we can see hereof, after main disease had been treated, the completion of the pregnancy of the women decreased by 3.3%. The results obtained prove the importance of the presence of therapists, cardiologists, endocrinologists, urologists and their

joint activities with the obstetrician- gynaecologist in the pregnancy management.

## SUMMARY

1. Extragenital diseases is main factor disrupting normal course of the pregnancy. The pregnancy was disrupted in 16% of pregnant women as a result of miscarriage in 6% of 396 pregnant women, stillbirth in the same number of pregnant women and development of monstrous fetus in 4%. Implemented preventive measures reduced the cases of monstrous fetus formation by 3% and decreased the number of disrupted pregnancies to 13%. The pregnancy was completed in 100% of pregnant women with arterial hypertension and heart defect disease. However, there were no significant result obtained in pregnant women with hepatitis of non-viral origin and diabetes [7,17,27].
2. Not depending on the term of arterial hypertension, the defects occurred in intrauterine fetal development resulted in the miscarriage in 5% of pregnant women, the stillbirth in the same number of pregnant women, untimely separation of the placenta in 20% and congenital defect in 12% of them. Dydrogesterone, folic acid and riboflamin prescribing reduces the miscarriage percentage to zero and decreases untimely separation of the placenta by 12% [10,14,28].
3. Bland diet is to be prescribed in the I and II trimesters to pregnant women with chronic constipation; and duphalac are to be used in the III trimester. The term of evacuation of eaten food in pregnant women treated on this scheme shorten by 6.5% in the 1<sup>st</sup> week, by 15% in the 2<sup>nd</sup> week and 25.5% in the 3<sup>rd</sup> week.
4. When residual nitrogen level in the blood in pregnant women with the kidney pathology in the I trimester is  $46\pm 3,3$  mg/dl, urea level is  $87,07\pm 4,8$  mg/dl, density of CPC is  $2,82\pm 0,23$  mg/dl or more, the probability of occurring the miscarriage increases [5,18].
5. The newborns were born with the defects in 45% of pregnant women with the hepatitis of non-viral origin, 16% of pregnant women with the heart defect, 15% of pregnant women with gastrointestinal system diseases, 11% of pregnant women with arterial hypertension. Preventive measures implemented reduce the number of defective children born from the women with

extragenital diseases (except for the hepatitis of non-viral origin) to zero [26].

6. The defects in fetal development in pregnant women with the hepatitis of non-viral origin depend on the virus type [22]. The pregnancy is not completed in 12,5% of pregnant women infected with A virus, 21% of pregnant women infected with B virus, 43,5% of pregnant women infected with C virus, 30% of pregnant women infected with A and B virus and 35% of pregnant women infected with B and C virus [39]. As a result of preventive measures implemented, the pregnancy is not completed with a childbirth in 100% of pregnant women infected with A virus, 28,5% of pregnant women infected with B virus, 18% of pregnant women infected with C virus, 30% of pregnant women infected with BC virus.
7. Genitourinary diseases and general infection are the risk factors for the pregnancy. The pregnancy is very complicated in 29% of pregnant women. There is the miscarriage in 10%, the stillbirth in 13% and instillation abortion because of monstrous fetus in 6% of pregnant women. Preventive measures implemented in accordance with each infection positively impact on the course of the pregnancy in pregnant women infected with chlamydia, toxoplasmosis, cytomegalovirus, herpes simplex and decrease the amount of miscarriage, stillbirth and monstrous fetus formation cases. However, they do not create positive changes in pregnant women infected with the rubella [3,31].
8. They significantly decrease the complication able to be occurred in pregnant women infected with toxoplasmosis, cytomegalovirus, mycoplasma, gonococcus in intranatal period, as well provide uncomplicated pregnancy in pregnant women infected with the rubella. However, they do not impact on pregnant women infected with chlamydia and herpes simplex infections.
9. Cytomegalovirus and herpes simplex are the factors, which increase the risk of stillbirth, miscarriage and monstrous fetus formation. The complications, occurring in intranatal and postnatal period, including early rupture of the membranes, rectal atresia and birth of lightweight newborn are the characteristic of

high cytomegalovirus and herpes simplex titre. Decrease of the cytomegalovirus titre in the blood did not impact on the miscarriage, however it decreased miscarriage risk by 3%, monstrous fetus formation risk - by 100%, early rupture of the membranes risk - by 5%, premature birth - by 8%, rectal atresia - by 100%.

10. The rubella infection is higher risk factor for intranatal period. There was premature birth in 20% of pregnant women with high rubella titre in the blood, early rupture of the membranes - in 7% and congenital defects in 5% of the newborns. Despite that the number miscarriage and stillbirth risks in pregnant women with decreased rubella titre are at the level same with those with high rubella titre, intranatal and postnatal periods proceed without any complication.
11. Great negative impact of the alcohol use on perinatal fetal development is related to the dysfunction caused by this factor in the pituitary gland. The alcohol use during and before the pregnancy creates conditions for complicated course of the pregnancy by severe malfunction of the accumulation of the energy resources (ATP and mCPC) in the pituitary gland and ovary dysfunction. Tiosetam application prevents this process on some extent, but do not regulate it completely [11,12,15,38].
12. All 3 periods of the pregnancy in smoker pregnant women proceed with the complications ranging from the miscarriage to different fetal defects. The pregnancy is disrupted in 35% of pregnant women. The severity of the defects is in correlation with the frequency of smoking. Monstrous fetus development is characteristic of pregnant women tended towards the drug addiction. This problem causes the disruption of the pregnancy in 78% of pregnant women.

## PRACTICAL RECOMMENDATION

1. In pregnant women with the hypertension, the course of pregnancy is to be controlled by gynaecologist, as well cardiologist, nephrologist, endocrinologist and ophthalmologist. If there are stillbirth, habits or miscarriage in the anamnesis of pregnant woman, it is necessary to determine the amount of the progesterone in her blood taken in the morning. If the progesterone level is low, dydrogesterone is to obligatorily be prescribed for pregnant woman.
2. Gallstone disease is not a contraindication for the pregnancy. However, in order to provide normal fetal development, reasonable treatment is to be performed before the pregnancy; and 2 tablets of heptural are to be given to pregnant women during the day in order to prevent exacerbation of the disease. When gallstone and biliary tract diseases are exacerbated, it is possible to perform laparoscopic surgical operation in the I and II trimesters.
3. The women with heart defect and arterial hypertension are to be examined by a cardiologist before the pregnancy and to be treated correspondingly. The women are to become pregnant in compensatory period of the disease; and the course of the pregnancy is to be under the control of an obstetrician-gynaecologist, as well cardiologist and ophthalmologist during this period. The delivery is to be performed using the caesarean section.
4. The plasmapheresis is to be performed in the first weeks of the I, II and III trimesters for the patients with significantly increased blood creatinine level. Performing the plasmapheresis creates real conditions for successful completion of the pregnancy.
5. The life of the fetus of pregnant women with bronchial asthma is in more danger in the I trimester, so starting from the first days of the pregnancy, the pregnancy management based on the treatment protocol drawn up by the obstetrician- gynaecologist together with allergist and psychologist will ensure that the pregnancy is not disrupted in the II-III trimesters. Therefore, bronchial asthma is

not the contraindication for the pregnancy if the pregnancy management is performed under joint control of psychologist, allergist and obstetrician- gynaecologist.

6. The anti-depressant use is a contraindication for pregnant women with the alcoholic psychosis starting from the first days of the pregnancy to the end of it, because the anti-depressants increase the risk of the pregnancy disruption.
7. It is necessary to perform surgical operation and eliminate the defects in the uterus before the pregnancy in pregnant women with arcuate uterus and fibromyoma. As a result of reparative surgical operation, the miscarriage and stillbirth are completely (100%) prevented. And as a result of the fibromatosis removal, a number of the complications able to be occurred in intranatal period, including massive bleeding and uterine atony, are prevented.
8. The women with gonorrhoea are to apply Cephalosporin and Azithromycin before the pregnancy and become pregnant after the gonococcus titre lowers to the standard. Also, gonococcus titre in the blood is to be measured every trimester. If the gonorrhoea titre is at standard level or near it, it is able to reduce complicated pregnancy risk by 11%.

## List of published articles.

1. Actual problems of treatment of genitourinary diseases candidiasis. Aliyev A.R., Garayeva K.G., Aliyeva Z.S., Hamidova A.A. Health, 2006, №1, P. 173-175.
2. Female infertility and its main problems. Garayeva K.G., Mammadova G.S., Huseynova G.K. //Health, 2006 №3, P. 173-175.
3. Modern approach to the treatment of bacterial vaginosis. Aliyev A.R., Garayeva K.G., Aliyeva Z.S., Rasulova Sh.A. //Health, 2006, №5, P. 89-90.
4. The effectiveness of Viburcol haematopoietic suppository in labor pain relief. Aliyev A.R., Garayeva K.G., Ramazanova Ch.K., Hamidova A.V. //Health, 2006, №10, P. 170-171.
5. Pyelonephritis and pregnancy. Idrisova Kh.S., Garayeva K.G., Ramazanova G.K. //Health. 2007, №2. P. 190-194.
6. The most important problems of chlamydia infection and ways of their realization. Idrisova Kh.S., Garayeva K.G., Huseynova G.K. //Health. 2007, №4, P. 187-190.
7. The course of the pregnancy in the patients with the liver cirrhosis. Aliyeva F.K., Karomova L.R., Akhundova N.N., Garayeva K.G., Aghayeva G.Sh. //Health, 2007, №4, P. 183-185.
8. Echographic signs of early diagnosis in the threats of miscarriage and non-developing pregnancy. Badalova G.M., Garayeva K.G., Mammadova A.G. // Health, 2008, №6, P. 183-187.
9. Genetic screening. Mammadova A., Garayeva K.G., Badalova G., Ramazanova G. //Health, 2008, №9, P.160-162.
10. Placental insufficiency. Garayeva K.G., Huseynova G.K. // Health, 2009, №3, P. 173-177.
11. Defects in fetal development conceived from the men with alcoholism disease. K.G. Garayeva //Family health in the XXI century. Papers of the XVI international Scientific Conference 27 April – 4 may 2012 Budapest, Hungary. Part I, P.35.

12. Change dynamic of the sex hormones in the blood plasma in the dynamic of the development of alcohol intoxication model. Garayeva K.G., Hajiyeva G.Yh. //Health, 2012, №4, P. 155-158.
13. Some aspects of the effect of CA antagonists on reproductive function. Ganiyev M., Kazimova A.Y., Garayeva K.G. //Health, 2013, №5, P. 17-21.
14. Impact of long-term calcium antagonists use on the level of luteinizing hormone and estradiol in the blood. Kazimova A.U., Garaeva K.G. //Kazan medical journal. 2014, №3, P. 389-391.
15. On the question of edema of liver tissue at the alcoholic hepatitis. Garayeva K.G. //European Science and Technology. Materials of the IX International research and practice conference. V.I. December 24<sup>th</sup> – 25<sup>th</sup>, 2014. Munich. Germany 2014, P.433-436.
16. Modern views on the functioning of reproductive system of the women. Mehdiyeva D.A., Garayeva K.G. //Actual matters of modern gynaecology and perinatology 2015, № 2, P. 24-30.
17. Congenital heart defects. Garayeva K.G. //Azerbaijan cardiology journal 2015, №2, p. 31-37.
18. Congenital developmental defects and their risk factors. Garayeva K.G., Rasulova Sh.A. //Actual matters of modern gynaecology and perinatology. 2016, №1, P. 16-20.
19. Pathological changes in the body of the women caused by the alcoholism. Garayeva K.G. //Azerbaijan medical journal, 2016, № 3, P. 151-158.
20. Uterine myoma and its etiological factors. Garayeva S.G. Garayeva K.G. //Azerbaijan oncology journal, 2016, №2, P. 85-88.
21. Congenital defects and new aspects of their prevention. Garayeva K.G. //Azerbaijan medical journal, 2017, №3, p. 133-138.
22. The role of the diseases of viral etiology in fetal development with defects. Garayeva K.G. //Actual matters of modern gynaecology and perinatology. 2017, № 1, p. 9-14.
23. Congenital skull defects and their etiological factors. Garaeva K.G. // Modern technologies: Actual matters, achievements and

- innovations. Collection of the articles written by the winners of the V International Scientific and Practical Conference took place in Penza city on February 27, 2017. Penza 2017, p. 173-177.
24. The dynamic of the neuroendocrine system in postnatal fetal development subjected to the stress in perinatal period. Mehdiyeva D.A., Ismayilov Y.B., Garayeva K.G., Ismayilova A.T., Garayeva S.G., Guliyev N.O. //Bulletin of Azerbaijan National Academy of Sciences (biological and medical sciences). 2017, №2, p. 55-59.
  25. Impact of the stress on the mechanism of the hypothalamic neuroendocrine system in pregnant rats and their offspring in postnatal period. Mehdiyeva D.A., Ismayilov Y.B., Garayeva K.G., Garayeva S.G., Guluyeva S.V., Ismayilova A.T., Guliyev N.O. //Bulletin of surgery of Kazakhstan. 2018, №1, P. 5-12.
  26. Perinatal fetal development in pregnant women with the heart defects. Garayeva K.G., Hajiyeva F.R. //Reproductive health Eastern Europe 2018, №3, P. 202-208.
  27. The course of the pregnancy in the women with chronic pulmonary diseases. Garayeva K.G., Hajiyeva F.R. //Reproductive health Eastern Europe 2018, №3, P. 336-342.
  28. Impact of arterial hypertension on intrauterine fetal development. Garayeva K.G. //Bulletin of Russian Military Medical Academy. 2018, №2, P. 81-85.
  29. Modern approach to the pregnancy management in the patients with a uterus scar after the myomectomy. Ismayilova A.F., Garayeva K.G., Aliyeva T.Sh. //Actual matters of modern gynaecology and perinatology 2018, №3, p. 24-26.
  30. Pregnancy, accompanying with the diseases of the gastrointestinal system. Garayeva K.G. //Bulletin of surgery in Kazakhstan 2018, № 3, p.5-10.
  31. Impact of genitourinary chlamydia on perinatal fetal development. Garayeva K.G., Hajieva S.I., Safaraliyeva L.Kh. //The V Russian interdisciplinary scientific and practical conference with international participation. Mat. Conferences. October 30, November 02, 2018. Sochi 2018, P. 50-51.

32. The role of agonist gonadotropin releasing hormone in the treatment of uterine myomas. Garayeva S.G., Garayeva K.G., Musayeva M.Kh. //Actual matters of modern gynaecology and perinatology 2018, №1, p. 46-50.
33. Relation between uterus fibroids, dyslipidaemia and sex hormones hypersecretion. Gurbanova J.F., Amirova A.F., Garayeva K.G., Aliyeva T.Sh., Gahramanova N.V., Abdullayeva A.A. //Actual matters of modern gynaecology and perinatology. 2018, №2, p. 27-32.
34. Investigation of uterus preserving operations with fibroids and the ways to improve its ontocome. Garayeva K.G., Ismayilova A.F., Aliyeva T.Sh., Gahramanova N.V., Abdullayeva A.A. //The XXII World obstetrics and gynaecology congress. Brazil RIO 2018. October 14-19.
35. Congenital defects of nervous system. Garayeva K.G. //National oncology journal (Scientific and practical journal). 2018, №2, p.15-20.
36. Features of pregnancy in patients with uterus scar after myomectomy. Ismayilova A.F., Gurbanova J.F., Garayeva K.G. //Materials of the XXVI European Perinatal Medicine Congress Saint Petersburg 2018.
37. The result of food ration pregnancy in pregnant women with diabetes. Konul Garayeva Galib. //The I Black Sea international multidisciplinary researches congress. Medical sciences Editor Dr. Fatih bal. www.Karadeniz kongresi. org/.Giresum March 15-17, 2019, P. 996-998.
38. Regulation of the pregnancy in the women with the hepatitis of alcoholic origin. Garayeva G.K. //6<sup>th</sup> international Conference on Innovations and Development Patterns in Technical and natural Sciences 20<sup>th</sup> March 2019. Vienna 2019, p.41-45.
39. Pregnancy results for women infected with hepatitis A virus. Konul Garayeva Galib. //Scientific Research of the scocountries: Synergy and integration Materials of the international Conference September 28. 2019. Beijing China 2019.
40. Clinical and anamnestic results of examination of pregnant women suffering from the thyroid diseases. Garayeva K.G.

//Bulletin of Russian Military Medical Academy. 2019, №4, P. 42-46.

41. Dynamic of the liver tests in pregnant women with the hepatitis of non-infectious genesis during the prescribing ademetonine. Garayeva K.G. //Kazan Medical Journal 2020, №2, P. 296-303.
42. The role of endocrine and metabolic factors in the etiology and pathogenesis of the myomas. Garayeva K.G., Hajiyeva F.R., Garayeva S.G., Abdullayeva A.A., Gahramanova N.V., Gachabayov E.Y. //Actual matters of modern gynaecology and perinatology 2020, №1, p. 47-49.
43. The Effect of Metrofibroma on the Prenatal Development of the Fetus. Garayeva K.G., Garayeva S.G., Shahmaliyeva U., Hasanova A., Abdullayeva A. //Journal Research in Medical and Dental Science November 2020. Volume 8. Issue 7, Page No 215-218.

The dissertation defence of will be conducted on 24.06.22 at 14<sup>00</sup> at the meeting of the ane time BED 2.11 Dissertation Council organized under the Azerbaijan State Advanced Training Institute for Doctors named after A Aliyev.

Adress: AZ 1012, Muzaffar Hasanov 35. Baku, Azerbaijan.

The dissertation is available in the library of the Azerbaijan State Advanced Training Institute for Doctors named after A Aliyev.

Electron version of the dissertation and abstract are posted on the official website: [http:// www.adhti.edu.az](http://www.adhti.edu.az).

The abstract was to relevant  
adresses on date 17 05 \_\_\_\_\_ 2022.

Paper format: 60x841/16.  
The volume: 76100.  
Edition: 100.