

## Ways of Prognosis and Reduction of Obstetric and Perinatal Complications at Pregnancy Chronic Pyelonephritis

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### ABSTRACT

The paper deals with the results of the researches focused on reduction of obstetric and perinatal complications at pregnancy chronic pyelonephritis. For prognosis and preventions of obstetric and perinatal complications it is recommended to highlight a high-risk group of progression of these complications at chronic pyelonephritis and creation of the algorithms for prognosis of this pathology. According to the algorithm of female examination, the first stage of examination requires surveying using the prognostic clinical and anamnestic table of risk factors on progression of obstetric and perinatal complications. At the second stage the laboratory blood analysis of the high-risk patients is conducted, at that the results of the biochemical research are considered integrally. At the third stage the identified regularities are corrected. In order to define the effectiveness of pathogenetically substantiated pyelonephritis and improvement of renal function as well as assessment of pathogenetic significance and correlation between the qualitative parameters of blood chemistry values (erythrocyte, Hb, Ht, ESR, EPO, C cystatin, creatinine, uric acid etc.) with clinical manifestations complicating chronic pyelonephritis we explored the possibility of the r-HuEPO application.

**Keywords:** Chronic pyelonephritis, Pregnancy, Erythropoetin, Prognosis, Diagnosis, Treatment.

### INTRODUCTION

The problem of prenatal care among the females having extragenital pathology is very acute. In the structure of extragenital pathology the leading position is occupied by renal diseases, which is one of the most frequent problems among the pregnant, and over the last years there is a tendency towards the increase in frequency of this pregnancy pathology<sup>1, 2</sup>. Pyelonephritis among pregnant is detected in 48% of the cases, while among the puerperants – in 35%. Urinary tract infections in past medical history can be observed among 39.6–92.5% of the surveyed females<sup>3, 4</sup>.

The rationale of studying etiopathogenetic and diagnostic aspects of chronic pyelonephritis is defined not only by its prevalence but also by its clinical significance, particularly, by the tendency towards the increase in purulent-destructive form of the disease and progression of complications<sup>2,5,6,7</sup>.

Presence of focus of infection in renal system even at the asymptomatic disease course leads to progression of intrauterine infection, to the threatened miscarriage, anomalies of placentation and premature separation of placenta, hypertension, immature delivery, hydramnion, placental insufficiency, fetal distress and birth of children with low body weight<sup>8, 9</sup>.

The most frequent complication at pyelonephritis is anemia caused by the disbalance between cellular and humoral components of immune system, increase in toxic exchange products and circulating immune complexes in the body, intensity of which is defined by the severity of anemia and activity of inflammatory process in the renal system<sup>10, 11, 12</sup>. Anemia accompanied by decrease in the amount of erythrocytes leads to the decrease in the oxygen delivery to the renal tissues, to stimulation of epithelial-mesenchymal ductule cells transformation and release of anti-inflammatory molecules and fibrosis mediators, i.e. to activation of the main mechanism of the renal pathology progression – interstitial fibrosis and damage of the intact renal units<sup>13, 14, 15, 6</sup>.

40% of pregnant with chronic pyelonephritis have progressing gestational toxicosis and renal blood flow malperfusion. According to L.V. Poiseyeva (2005) at chronic pyelonephritis one can observe renal haemodynamic compromise: decrease in the volume of renal blood flow and increase in the renal vascular resistance<sup>17</sup>.

In this regard in-depth analysis of clinical laboratory features of maternal and fetal malfunctions at pregnancy pyelonephritis may contribute to improvement of the early diagnosis and prognosis of gestational process abnormality as well as to the reduction of cases of obstetric and perinatal pathology which is important for obstetrics.

### **Objective of the Research**

Development of the criteria for prognosis of obstetric and perinatal complications at chronic pyelonephritis and improvement of the measures aimed at correction of the identified irregularities.

### **Methods of the Research**

General, biochemical (tests on erythropoetin, Ñ cystatin, creatinine, uric acid, average weight molecules, glomerular filtration), biophysical (ultrasonic diagnosis, prenatal fetal monitoring), and statistical.

## **RESULTS AND DISCUSSION**

### **Retrospective Study Analysis**

Prognosis of any pathology requires integral

approach which allows considering maximum number of risk-factors contributing to emergence of some or another pathology.

Considering the possibility of early progression of obstetric and perinatal complications and their high frequency among pregnant suffering from chronic pyelonephritis, we took an attempt to create mathematical model of prognosis of obstetric and perinatal complications progression at this disease. In this regard on the basis of assessment of clinical and anamnestic data among 300 females suffering from chronic pyelonephritis and conduction of correlation analysis in the groups without exacerbation (main group) and with exacerbation of chronic pyelonephritis (experimental group) we selected 23 most significant risk-factors of obstetric and perinatal complications progression at chronic pyelonephritis (table 1). The described complex of manifestations being the most significant for prognosis of obstetric and perinatal complications progression at chronic pyelonephritis was unified in the table of prognosis of obstetric and perinatal pathology at chronic pyelonephritis, constructed with the application of the sequential Wald analysis (18). In the course of the prognosis procedures we calculated the corresponding prognosis coefficient (PC) having numerical value with positive (+) or negative (-) sign.

Sign “+” is attributed to the prognostic coefficients of manifestations evidencing the possibility of implementing the prognosis, i.e. progression of obstetric and perinatal progressions at chronic pyelonephritis, while sign “-” – to the manifestations providing the possibility of the prognosis failure. For settlement of the prognosis the algebraic addition of the prognosis coefficients is implemented; the numerical threshold for making certain conclusion (with 95% possibility) is equal to +13. If the sum of the PC is more than or equal to +13 points, than unfavorable prognosis is concluded (i.e. 95% possibility of obstetric and perinatal complications progression among pregnant suffering from chronic pyelonephritis). Negative sum of PC equal to -13 and more evidences irrelevance of the prognostic pathology with 95% probability. Cases the sum of PC is equal to +9 – +12 points – show 75% probability of the prognosis, while when the

PC sum is below +8 points – uncertain prognosis is concluded (table 2)<sup>18</sup>.

As a result of the posthoc analysis of gestation course and outcome of pregnancy among the females suffering from chronic pyelonephritis, we found high frequency of obstetric and perinatal complications at this pathology recrudescence which is a reason of high degree of perinatal losses in past medical history and perinatal pathology. Subsequently, for prognosis and prevention of obstetric and perinatal complications we recommend highlighting a high risk group of these complications progression at chronic pyelonephritis and creation of the algorithms for this pathology prognosis. Thus, all the measures aimed at reducing the frequency of obstetric and perinatal complications progression at chronic pyelonephritis should be connected with the timely diagnosis, prognosis and treatment of this pathology.

#### **Prospective Study**

We assessed functional state of the renal system of pregnant in the researched groups on the basis of the results of clinical and biochemical analyses of blood, common urine analysis, Zimnitsky's test, Nechiporenko's test, urine culturing, vaginal flora with identification of bacteria species composition and calculation of microbial number, definition of sensitivity to antibiotics, as well as according to the results of ultrasound investigation of renal system.

Clinical analysis of blood showed that Hb level at noncomplicated pregnancy varied from 107 to 115 GM/DL, erythrocytes varied from  $3.5$  to  $3.7 \times 10^{12}$  GM/DL, hematocrit – 29.4–31.5 %. At the stage of recrudescence values of Hb were averagely equal to 86–93 GM/DL, hematocrit (Ht) – 24.9–27.2 %, erythrocytes –  $3.0$ – $3.2 \times 10^{12}$  GM/DL. In the absence of recrudescence the level of Hb varied from 102 to 106 GM/DL, erythrocytes  $3.3$ – $3.4 \times 10^{12}$  GM/DL, Ht – 28–29%. 70% of female patients suffering from recrudescence of chronic pyelonephritis often had increased amount of leucocytes (21 out of 30), and in average it was equal to  $12.3 \times 10^9$  GM/DL, which twofold exceeded the corresponding value in the group of noncomplicated pregnancy; 73% of the patients had the number of stab neutrophils increased

(22 out of 30), in average it was equal to  $(7.8 \pm 0.5)\%$  and by 2.2 times it was higher compared to the same parameters of noncomplicated pregnancy. ESR of pregnant suffering from recrudescence of chronic pyelonephritis in average was equal to  $45.0 \pm 4.3$  mm/h, and 66.7% of the patients had it increased (20 out of 30).

Based on the conducted research we suggested the algorithm of examination (figure 1) of the general cohort of the female patients for prognosis of obstetric and perinatal complications at chronic pyelonephritis of pregnant. This algorithm provides division of the patients into the groups with the risk of obstetric and perinatal complications progression at chronic pyelonephritis and without it at each examination. Depending on adherence to some or another group the further examination is conducted step by step. Taking into account the data obtained from clinical and laboratory researches detected negative influence of chronic diseases of urinary system on gestation course, particularly, negative influence is defined by the character of chronic pyelonephritis, its chronicity and severity (frequent recrudescences). Diseases of urinary system are potential risk-factors of obstetric and perinatal complications progression, as they provoke renal haemodynamic compromise, changes in canalicular-glomerulose apparatus, thus becoming the cause of severe organic lesion of urinary system, gestational toxicosis, Multiple Organ Dysfunction Syndrome, hypoxia and small-for-gestational-age fetus<sup>17, 18</sup>.

According to the algorithm of the female examination developed by us, at the first stage one should conduct survey in accordance with the prognostic clinical-anamnestic table of risk-factors of obstetric and perinatal complications progression. At detection of the sum of points above “+13” the female patient belongs to the high-risk group of obstetric and perinatal complications progression, while at the sum of the points equal to “-13” and less the female patient belongs to the low-risk group.

At the second stage laboratory examination of the patients' blood in the high-risk groups is carried out, at this the results of biochemical research are considered integrally.

**Table 1: Clinical-Anamnesic Table of Prognosis of Obstetric and Perinatal Pathology at Chronic Pyelonephritis**

<b>Risk-Factors of Obstetric and Perinatal Complications Progression</b>	<b>PC+</b>	<b>Manifestations Indicating Absence of Obstetric and Perinatal Complications</b>	<b>PC-</b>
1	2	3	4
The chronicity of pyelonephritis is more than 5 years	6	The chronicity of pyelonephritis is less than 5 years	2
Chronic pyelonephritis with recrudescences during pregnancy	4	Chronic pyelonephritis without recrudescences during pregnancy	2
Moderate anemia	2	Absence of moderate anemia	2
Severe anemia	4	Absence of severe anemia	0
Arterial hypertension	6	Absence of arterial hypertension	2
Upper respiratory tract disease	2	Absence of upper respiratory tract disease	2
Hepatic and bile duct diseases	2	Absence of hepatic and bile duct diseases	2
Gastrointestinal tract diseases	2	Absence of gastrointestinal tract diseases	2
Diseases of the endocrine system	4	Absence of diseases of the endocrine system	2
Menstrual disorder	2	Absence of menstrual disorder	1
Presence of inflammatory processes of uterus and abnexitis	4	Absence of inflammatory processes of uterus and abnexitis	2
Sexually-transmitted infections	4	Absence of sexually-transmitted infections	2
Spontaneous miscarriages	2	Absence of spontaneous miscarriages	1
Infertility in past medical history	4	Absence of infertility in past medical history	1
Preeclampsia in past medical history	6	Absence of preeclampsia in past medical history	2
Birth of children with the symptoms of hypotrophy or asphyxia	3	Birth of children with normal body-weight ratio, without asphyxia in past medical history	0
Perinatal losses in past medical history	7	Absence of perinatal losses in past medical history	0
ARVI across pregnancy	2	Absence of ARVI across pregnancy	1
Threatened miscarriage	2	Absence of threatened miscarriage	1
Threatened immature delivery	2	Absence of threatened immature delivery	1
Chronic DIC syndrome	6	Absence of chronic DIC syndrome	0
Placental insufficiency	5	Absence of placental insufficiency	0

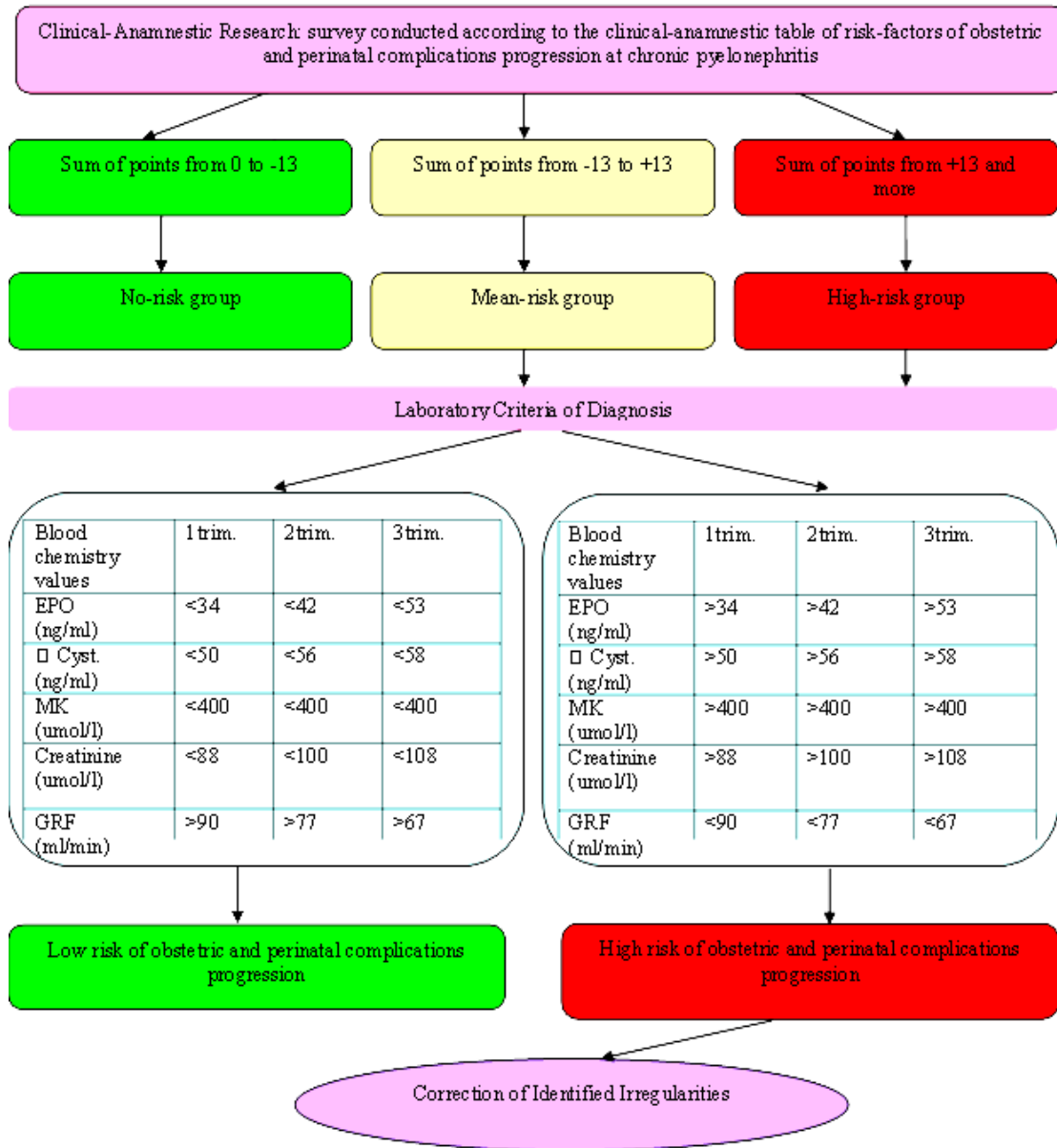
At the third stage the indicated irregularities are being corrected.

obstetric and perinatal complications at chronic pyelonephritis.

That's why prevention of recrudescences of chronic pyelonephritis, improvement of renal hemodynamics and optimization of female's metabolic processes are an important link in the chain of treatment and prevention measures of

**Improvement of Measures Aimed at Correction of Obstetric and Perinatal Complications of Pregnant Suffering from Chronic Pyelonephritis**

Complex of remedial measures for the female patients suffering from chronic pyelonephritis



**Fig. 1: Algorithm of diagnosis and prognosis of obstetric and perinatal complications at chronic pyelonephritis**

in the phase of recrudescence had an impact on all the stages of genesis, was composed of several stages and included the following:

1. impact on the main extragenital pathology – chronic pyelonephritis
2. impact on obstetric pathology
3. correction of the identified irregularities.

Besides, we considered the severity and chronicity of the disease as well as the results of functional state of renal system. Selection of treatment requires effective and save method for pyelonephritis therapy both for mother and fetus.

Traditional treatment of chronic pyelonephritis in the phase of recrudescence

**Table 2: Scheme of the Prognosis Results Assessment (sequential Wald – Genkin analysis)**

Increase in the Risk of Obstetric and Perinatal Complications Progression at Chronic Pyelonephritis						
Sum of Prognostic Coefficients						
-13	-9	-7	0	7	9	13
95% probability of the prognosis failure	75% probability of the prognosis failure	Absence of the tendency towards prognostication	uncertain prognosis	tendency towards prognosis	75% probability of progression	95% probability of progression

**Table 3: Analysis of gestational course and outcome of pregnancy among females suffering from chronic pyelonephritis treated (main group) and not treated (comparison group) with r-HuEPO as a part of traditional treatment**

Group Complications of gestational course	Main Group (n=30)		Comparison Group (n=30)		$\chi^2$
	abs. number	M±m, %	abs. number	M±m, %	
Threatened miscarriage	6	20.0±2.2m	10	33.3±2.6m	$\chi^2=5.3$
Threatened immature delivery	3	10.0±1.6	5	16.7±2.1	$\chi^2=2.7$
Light preeclampsia	2	6.7±1.4	8	26.7±2.4mm	$\chi^2=15.0$
Severe preeclampsia	-	-	2	6.7±1.4	-
Eclampsia	-	-	1	3.3	-
Mean anemia	2	6.7±1.4	9	30.0±2.5mm	$\chi^2=18.1$
ARVI	2	6.7±1.4	5	16.7±2.1m	$\chi^2=6.0$
Chronic DIC Syndrome	-	-	2	6.7±1.4	-
Placental Insufficiency	2	6.7±1.4	6	20.0±2.2mm	$\chi^2=8.8$
Labor, incl.: at term	29	96.7±0.9	26	86.7±1.8	$\chi^2=1.1$
Immature Delivery	1	3.3	4	13.3±1.9mm	$\chi^2=7.5$
Poor Uterine Contraction Strength	2	6.7±1.4	3	10.0±1.6	$\chi^2=1.1$
Untimely Discharge of Amniotic Fluid	5	16.7±2.1	6	20.0±2.2	$\chi^2=0.5$
Atonic Hemorrhage	-	-	2	6.7±1.4	-
Premature Detachment of Normally Situated Placenta	-	-	1	3.3	-

m – p<0,05mm – p<0,001

included antibacterial therapy. The choice of tactics for antibacterial therapy of the female patients suffering from recrudescence of chronic pyelonephritis is caused by study of sensibility of the cultures of facultative anaerobic bacteria extracted from the urine to antibacterial chemicals.

According to the obtained data, the most effective towards the extracted cultures of the bacteria were cephalosporins of the 1<sup>st</sup> and 3<sup>rd</sup> generation (71.4–100%). All the patients suffering from recrudescence of chronic pyelonephritis underwent conservative therapy: cefazoline 1 gr i.m. 3 times a day or cefuroxime 1g 2 times a day; metronidazole 100.0 ml i.v. 3 times a day during 5–7 days, disintoxication, infusion, and desensitizing therapy.

In order to define effectiveness of pathogenically substantiated therapy of chronic pyelonephritis and improvement of renal function as well as assessment of pathogenetic significance and interconnection of quantitative parameters of blood chemistry values (erythrocytes, Hb, Ht, ESR, EPO,  $\bar{N}$  cystatin, creatinine, uric acid etc.) with clinical manifestations complicating chronic pyelonephritis, we studied the probability of using r-HuEPO.

EPO is a glycoprotein generated in kidney that is being mitosis enhancing factor and differentiation hormone contributes to formation of erythrocytes from progenitors of erythropoiesis.

We used r-HuEPO together with the traditional treatment for prevention of obstetric and perinatal complications at chronic pyelonephritis in the phase of recrudescence, because this medication affects erythropoiesis, improves hemodynamics and renal functioning<sup>21, 22</sup>.

We observed 30 pregnant (main group) with chronic pyelonephritis in the phase of recrudescence, who were treated with r-HuEPO in conjunction with pathogenetic therapy (traditional therapy) and 30 pregnant (comparative group) only provided with traditional therapy.

Alongside with traditional prevention course r-HuEPO was prescribed in the amount of 20 AU per 1 kg, injected subdermally 3 times a week with the monitoring of AP, hematologic values (Hb, Ht, erythrocytes) and blood chemistry values (EPO,  $\bar{N}$  cystatin, uric acid, creatinine, GFR,  $\bar{N}$ ) from the 2<sup>nd</sup> trimester of pregnancy to achievement of the best level of hemoglobin (110-120 GM/DL) and

**Table 4 : Analysis of perinatal complications among females suffering from chronic pyelonephritis, treated (main group) and not treated (comparison group) with r-HuEPO as a part of traditional treatment**

Group Perinatal Complications	Main Group (n=30)		Comparison Group (n=30)		$\chi^2$
	abs. number	M $\pm$ m, %	abs. number	M $\pm$ m, %	
asphyxia:	3	10.0 $\pm$ 1.6	6	20.0 $\pm$ 2.2?	$\chi^2=5.0$
light	2	6.7 $\pm$ 1.4	4	13.3 $\pm$ 1.9	$\chi^2=3.3$
severe	1	3.3	2	6.7 $\pm$ 1.4	$\chi^2=1.7$
cerebrovascular disease:	3	10.0 $\pm$ 1.6	6	20.0 $\pm$ 2.2	$\chi^2=5.0$
1 phase	2	6.7 $\pm$ 1.4	3	10.0 $\pm$ 1.6	$\chi^2=1.1$
2 phase	1	3.3	3	10.0 $\pm$ 1.6?	$\chi^2=4.5$
respiratory distress syndrom:					
1 type	-	-	5	16.7 $\pm$ 2.1	-
intrauterine infection	1	3.3	4	13.3 $\pm$ 1.9**	$\chi^2=7.5$
small-for-gestational-age fetus	1	3.3	6	20.0 $\pm$ 2.2**	$\chi^2=14.2$

\* - p<0.05

\*\* - p <0.001

hematoñrit (30-35%); EPO in the 2<sup>nd</sup> trimester – 29–42 ng/ml, in the 3<sup>rd</sup> trimester – 38–53 ng/ml; Ñ cystatin in the 2<sup>nd</sup> and 3<sup>rd</sup> trimester – 46–58 ng/ml; uric acid in the 2<sup>nd</sup> trimester – 162–277 umol/l and in the 3<sup>rd</sup> trimester – 400 umol/l.

During the r-HuEPO application the hemoglobin values were significantly improved. Dynamics of hematological values was manifested beginning with 2-3 injections of the medication. Initial level of hemoglobin of pregnant was equal to 86–93 GM/DL, after the treatment – 111–116GM/DL, hematoñrit – 24.9–27.2%, after the treatment – 30–32%, erythrocytes –  $3.0\text{--}3.2 \times 10^{12}$ GM/DL, after the treatment –  $3.4\text{--}3.64 \times 10^{12}$ GM/DL, reliable decrease in erythropoetin after the treatment was observed: in the 2<sup>nd</sup> trimester – by 37%, while in the 3<sup>rd</sup> trimester – by 34%. Additional prescription of iron supplements in usual dosage is necessary as a part of the treatment for saturation of body with iron and in combination with B vitamins (Â1, Â6, Â12 and folic acid).

Selection of the gestational age and frequency of the r-HuEPO application is defined by the degree of manifestation of clinical symptoms and the level of endogenic EPO. Effectiveness of the therapy depends on the adequacy of the individual treatment scheme. Normal level of effectiveness of the conducted therapy – growth in hematoñrit from by 0.5 to by 1% per 1 week before the best level of hemoglobin (110–120 GM/DL) and hematoñrit (30–35%) is achieved.

Effectiveness of r-HuEPO application may be explained by increase in the level of EPO in blood, which contributes to improvement of the renal functioning. It is proved by the results of biochemical and functional research methods served the objective criteria of the medication effectiveness.

In the framework of this paper we assessed clinical effect of r-HuEPO in accordance with the following criteria: peculiarities of gestation course and outcome of pregnancy, state of newborn infants and frequency of perinatal pathology. In this regard we analyzed the gestational course, labor and frequency of perinatal complications in the groups of patients who were and were not treated with the medication.

As one may conclude from table 30, the group of pregnant treated with r-HuEPO as a part of traditional therapy (main group) is characterized by more favorable gestational course, i.e. had fewer pregnancy complications in comparison with the group only treated traditionally. So, in the main group in comparison with the group only treated traditionally, the frequency of ARVI was reliably less ( $p < 0.001$ ), the manifestations of threatened miscarriage were more rarely ( $p < 0.001$ ), anemia was almost not observed in the comparison group, placental insufficiency was by 3 times less ( $p < 0.001$ ). Light preeclampsia was by 4 rarer in the group not treated with r-HuEPO.

At comparison of analysis of gestational course and outcome of pregnancy in the compared groups we found that frequency of delivery at term and average time of pregnancy are reliably higher in the group of the investigated females treated with r-HuEPO ( $p < 0.001$ ), while frequency of immature deliveries is by 3 times less. Complications of labor are by 1.4 times rarer among those treated with r-HuEPO. Untimely discharge of amniotic fluid, poor uterine contraction strength, premature detachment of normally situated placenta in the investigated group treated with r-HuEPO in combination with traditional treatment were not observed (table 3).

More favorable gestational course at application of r-HuEPO also influenced the state of the newborn infants, at that average mass of those from the mothers of the main group was equal to  $3420.0 \pm 85.0$  gr against  $2970.0 \pm 77.0$  gr in the comparative group not treated with r-HuEPO ( $p < 0.001$ ).

Application of r-HuEPO alongside with the traditional therapy contributed to decrease in the frequency of perinatal complications almost by 3 times ( $p < 0.001$ ). At this, the frequency of fetal asphyxia decreased by 2 times ( $p < 0.001$ ), frequency of small-for-gestational-age fetus decreased by 5 times ( $p < 0.001$ ), frequency of cerebrovascular disease decreased by 2 times ( $p < 0.001$ ), respiratory distress syndrom decreased by 3 times ( $p < 0.001$ ), in comparison with the group treated with a traditional method (table 4).



Thus, the obtained data allow supposing that r-HuEPO is an effective mean for prevention of obstetric and perinatal complications at chronic pyelonephritis. Application of r-HuEPO allowed significantly improving the values of peripheral blood (Hb, erythrocytes, hematocrit), normalizing the level of erythropoetin, decreasing the frequency of obstetric and perinatal complications. At this, in the group of females treated with r-HuEPO the frequency of recrudescence of chronic pyelonephritis decreased almost by 2.5 times, threatened miscarriages – by 1.7 times, frequency of immature delivery – by 4

times. Positive effect of r-HuEPO also influenced the state of the newborn infants, at this mass and height values as well as state estimation according to Apgar scale were reliably higher, while frequency of perinatal complications was reliably higher in the female group treated with r-HuEPO ( $p < 0.05$ ,  $\delta < 0.001$ ).

We have found that it is efficient and reasonable to prescribe r-HuEPO, with the purpose of prevention of obstetric and perinatal complications progression among the patients suffering from

**Table 5: Erythropoetin in blood (ng/ml) at chronic pyelonephritis before and after the traditional treatment**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	58.8±1.8	77.2±2.6
After traditional treatment	50.3±2.5*	60.0±3.0**
% to the values before treatment	85%	77%

**Table 6: C cystatin in blood (ng/ml) at chronic pyelonephritis before and after traditional treatment**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	67.3± 2.3	88.4±5.5
After traditional treatment	59.4±1.9*	70.0±4.0**
% to the values before treatment	88%	79%

**Table 7: Creatinine in blood (umol/l) at chronic pyelonephritis before and after traditional treatment**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	122.5±4.3	151.6±7.4
After traditional treatment	100.3±6.0*	128.5±5.5*
% to the values before treatment	81%	84%

**Table 8: Value of glomerular filtration in blood (mL/min) at chronic pyelonephritis before and after traditional treatment**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	71.7±1.8	59.8±2.5
After traditional treatment	78.8±2.0*	71.1±3.6*
% to the values before treatment	111%	119%

chronic pyelonephritis, beginning with the 3<sup>rd</sup> trimester of pregnancy.

At studying biochemical values at treatment of chronic pyelonephritis in the phase of recrudescence using traditional way, we noted the tendency towards decrease in the erythropoetin (table 5). In the 2<sup>nd</sup> trimester decrease of its level was equal to 85% (50.3±2.5 ng/ml) from the values before the treatment – 58.8±1.8 ng/ml and in the 3<sup>rd</sup> trimester we found the biggest decrease – by 23% (60.0±3.0 ng/ml).

After traditional treatment we noted the changes at the level of C cystatin in the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters of pregnancy (table 6). In the 2<sup>nd</sup> trimester the level of C cystatin decreased by 12% (59.4±1.9 ng/ml), while in the 3<sup>rd</sup> trimester – by 21% (70.0±4.0 ng/ml).

Values of creatinine and glomerular filtration also evidence improvement of filtrating renal function. So, creatinine reliably decreased by 19% (100.3±6.0 umol/l) and 16% (128.5±5.5 umol/l) in the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters of pregnancy respectively (table 7).

**Table 9: Concentration of uric acid in blood (umol/l) at chronic pyelonephritis before and after traditional treatment**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	279.5±21.2	439.0±20.2
After traditional treatment	250.5±15.0	390.0±12.4*
% to the values before treatment	90%	88%

**Table 10: Concentration of average weight molecules in blood (umol/l) at chronic pyelonephritis before and after traditional treatment**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	0.271±0.03	0.352±0.03
After traditional treatment	0.235±0.02	0.290±0.02*
% to the values before treatment	87%	82%

**Table 11: C cystatin in blood (ng/ml) at chronic pyelonephritis before and after traditional treatment + r-HuEPO**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	67.3±2.3	88.4±5.5
After traditional treatment + r-HuEPO	53.4±2.3*	58.0±3.6**
% to the values before treatment	79%	66%

**Table 12: Creatinine in blood (umol/l) at chronic pyelonephritis before and after traditional treatment + r-HuEPO**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	122.5±4.3	151.6±7.4
After traditional treatment + r-HuEPO	89.6±5.2*	98.5±6.0*
% to the values before treatment	73%	63%

At this, the value of glomerular filtration after treatment increased by 11% ( $78.8 \pm 2.0$  mL/min) in the 2<sup>nd</sup> trimester and to a greater extent in the 3<sup>rd</sup> trimester of pregnancy – by 19% ( $71.1 \pm 3.6$  mL/min) (table 8).

Growth in concentration of uric acid, observed before treatment, was not found after traditional treatment. In the 2<sup>nd</sup> trimester of pregnancy concentration of uric acid after traditional treatment was equal to  $250.5 \pm 15.0$   $\mu\text{mol/l}$  and there was a tendency towards decreasing, in the 3<sup>rd</sup> trimester reliable decrease by 12% ( $390.0 \pm 12.4$   $\mu\text{mol/l}$ ) was stated (table 9).

Traditional treatment led to reliable decrease in the value of endogenous intoxication in the 3<sup>rd</sup> trimester of pregnancy –  $0.290 \pm 0.02$   $\mu\text{mol/l}$ , in the 2<sup>nd</sup> trimester there is a tendency towards decreasing –  $0.235 \pm 0.02$   $\mu\text{mol/l}$  (table 10).

Thus, the conducted researches showed positive effect of the traditional treatment, therewith these changes are mostly seen by the end of the gestational period. Subsequently, the direction of the treatment measures towards pregnant at chronic pyelonephritis in the phase of recrudescence should include the medications not only normalizing at the end of pregnancy, but also beginning with the 2<sup>nd</sup> trimester of pregnancy, which will possibly exclude the complication of this phenomena from the fetus.

We stated that erythropoetin in the blood of pregnant in the 2<sup>nd</sup> trimester decreased and was equal to  $37.0 \pm 3.4$  ng/ml against the data before the treatment –  $58.8 \pm 1.8$  ng/ml. In the third trimester of pregnancy it decreased by 34%.

Introduction of r-HuEPO alongside with the traditional treatment contributed to the decrease in C cystatin beginning with the 2<sup>nd</sup> trimester of pregnancy (table 11). At this, decrease in the trimesters was

**Table 13: Value of glomerular filtration in blood (mL/min) at chronic pyelonephritis before and after traditional treatment + r-HuEPO**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	$71.7 \pm 1.8$	$59.8 \pm 2.5$
After traditional treatment + r-HuEPO	$86.5 \pm 3.1^*$	$82.0 \pm 3.3^*$
% to the values before treatment	21%	37%

**Table 14: Concentration of uric acid in blood ( $\mu\text{mol/l}$ ) at chronic pyelonephritis before and after traditional treatment + r-HuEPO**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	$279.5 \pm 21.2$	$439.0 \pm 20.2$
After traditional treatment + r-HuEPO	$215.0 \pm 11.0$	$365.0 \pm 10.8^*$
% to the values before treatment	77%	83%

**Table 15: Concentration of average weight molecules of blood (c.u.) at chronic pyelonephritis before and after traditional treatment + r-HuEPO**

Groups	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Before treatment	$0.271 \pm 0.03$	$0.352 \pm 0.03$
After traditional treatment + r-HuEPO	$0.208 \pm 0.02$	$0.262 \pm 0.02^*$
% to the values before treatment	76%	74%

equal to – 79% (53.4±2.3 ng/ml) in the 2<sup>nd</sup> trimester, and 66% (58.0±3.6 ng/ml) in the 3<sup>rd</sup> trimester respectively.

We found decrease in creatinine by 27% in the 2<sup>nd</sup> trimester – 89.6±5.2 umol/l and by 37% in the 3<sup>rd</sup> trimester of pregnancy – 98.5±6.0 umol/l (table 11).

At that, value of  $\dot{V}_{GFR}$  value of glomerular filtration after treatment with r-HuEPO reliably increased by 21% in the 2<sup>nd</sup> trimester – 86.5±3.1 mL/min and by 37% in the 3<sup>rd</sup> trimester of pregnancy – 82,0±3,3 mL/min (table 12).

Concentration of uric acid decreased in the 2<sup>nd</sup> trimester by 23% (215.0±11.0 umol/l) and by 17% in the 3<sup>rd</sup> trimester of pregnancy – 365.0±10.8 umol/l (table 13).

Concentration of average weight molecules in the 2<sup>nd</sup> trimester after treatment was equal to 0.208±0.02 c.u., which is by 24% less than the data before the treatment; in the 3<sup>rd</sup> trimester of pregnancy it was equal to 0.262±0.02 c.u., which is by 26% less of the data before treatment (table 14).

## CONCLUSION

Thus, the conducted researches showed positive effect of the complex treatment, therewith the changes are observed beginning with the 2<sup>nd</sup> trimester of pregnancy. Thus, the represented data shows that the treatment of chronic pyelonephritis manifestations is the most effective if the therapeutic intervention is carried out with consideration of pathogenesis of this disease.

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