Biochemical aspects of forecasting obstetric and perinatal complications in chronic pyelonephritis

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Abstract: Presented results of research on the biochemical indices in 60 pregnant women with chronic pyelonephritis in the acute stage and out of aggravation , which indicate the presence of pathological changes , most pronounced during exacerbation of the disease. Found that metabolic dysfunction contributes to the development of obstetric and perinatal complications. Shown that these biochemical parameters are of prognostic informative for predicting obstetric and perinatal complications in pregnant women with chronic pyelonephritis.
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1. Introduction

On today are developed and in practice a large number of methods for diagnosis of pyelonephritis in pregnant women, different information content, complexity, availability and cost. To determine renal function is widely used definition of the content creatinine in serum of blood [1].

In Chronic Illness Kidney concentration in serum creatinine concentration at only 30-50% of the theoretical level, which corresponds to the measured values of glomerular filtration rate (GFR), as from 16 to 66% of creatinine removed by out glomerular mechanisms.

Under what – or acute changes in renal function serum creatinine did not accurately reflect the real picture until it reaches a certain stabilization condition that most often occurs only after 2 to 3 days after initiation of disease [2].

Most accurate indicator reflecting renal function GFR is calculated by the clearance of endogenous filtration markers (creatinine) and the formulas based on serum levels of endogenous markers (creatinine, cystatin C). The most accurate endogenous marker of GFR is cystatin C.

Cystatin C, is now recognized worldwide medical community as the most accurate endogenous marker of glomerular filtration rate (GFR), in its diagnostic performance significantly superior to creatinine, an early marker of preeclampsia [2, 3, 4].

According to numerous studies, normal serum levels of cystatin C due to a constant rate of its synthesis, a constant rate of excretion from the body, which is mainly determined by renal function. In the pathology, its level in the blood rises. The heavier renal pathology, the worse the cystatin C is filtered in the kidney and the higher blood levels. A single measurement of cystatin C in the blood allows us to calculate the values of GFR. Cystatin C can be used for early diagnosis of renal disorders in pregnancy.

Cystatin C – a reliable, useful and promising marker of GFR in pregnant women. Cystatin C is almost completely filtered by the glomerulus, and so it is the most reliable indicator of safety functions in glomerular filtration. Cystatin C is not an acute phase protein, respectively, does not vary its level in various inflammatory reactions [3, 4].

The main diagnostic criterion of chronic renal disease is the glomerular filtration rate (GFR) – the best marker of renal function. [5] It is generally accepted that the determination of Glomerular Filtration Rate is necessary for the diagnosis and monitoring of renal function disorders [6].

In present time sufficient detail studied the biological effects of average weight molecules (MSM). Neurotoxic activity, inhibition of the biosynthesis of protein, inhibition activity of some enzymes induce a state of immunosuppressant secondary alter erythropoiesis, phagocytosis, microcirculation. There is evidence that MSM can cross the placental barrier, exerting a direct toxic effect on the fetus, causing multiple organ violations of different nature. Education endotoxins recorded in chronic inflammatory processes in the kidney. Diagnostic value of MSM large inflammations of various kinds, in toxicosis of different origin.

Storage MSM is a marker of accumulation endointoxication and exacerbates the disease process,

acquiring the role of secondary toxins, affecting the livelihoods of all organs and systems [7].

2. Material and Methods

Biochemical studies were performed by ELISA using diagnostic kits EJA (Germany). Statistical processing of the results of research carried out with the help of the program «Statgraph», the significance of differences was assessed by Student test.

3. Results

To determine the values of biochemical parameters in the evaluation of renal function in pregnant women with chronic pyelonephritis and their role in predicting obstetric and perinatal complications of this disease in our comparative analysis of biochemical parameters were determined and calculated their prognostic information content in the development of pathological conditions in 60 women with chronic pyelonephritis. With this basic group (n=30) were patients with chronic pyelonephritis without exacerbation, the comparison group (n=30) – patients with chronic pyelonephritis in the acute stage and a control group (n=30) – patients with uncomplicated pregnancy.

To all studied groups of patients were defined blood levels following biochemical parameters: cystatin C, creatinine, glomerular filtration rate value, uric acid, average molecular weight. In chronic pyelonephritis without exacerbation found that the level of cystatin C in the blood was in the I trimester was – 46,2±3,0 ng/ml, a significant increase it to 26% (53,3±5,4 ng/ml) in the II, 65% (64,4 ± 4,0 ng/ml) in the III trimester of gestation (at p<0.05), while the level of cystatin C had increased by 24%.

In uncomplicated pregnancy levels of cystatin C was within 44.4 - 52.0 ng / ml, while no significant difference on the data registered first trimester (Table 1).

Table 1 - Contents of cystatin C in the blood in the course of pregnancy in chronic pyelonephritis

Pregnancy	Cystatin C (ng/ml)		
	1trimester (n=30)	II trimester (n=30)	III trimester (n=30)
Without exacerbation	46,2±3,0	53,3±5,4	64,4±4,0*/**
Complicated pyelonephritis	53,5±1,9/**	67,3±2,3*/**	88,4±5,5*/**
Uncomplicated pregnancy	44,7±2,2	49,6±3,0	52,0±2,1*
* - Reliable data on the 1 trimester pregnancy at p <0.05 ** - Reliable data on the uncomplicated pregnancy at p <0.05			

Table 1 shows that during pregnancy, chronic pyelonephritis, complicated exacerbation compared with data uncomplicated pregnancy protein level increased by 20% (53,5±1,9 ng/ml) I, 36% (67,3±2,3 ng/ml) in II trimester and 70% (88,4 ± 5,5 ng/ml) in the III trimester.

Elevated cystatin C is an unfavorable sign, indicates a violation of the filtration function of the kidney, which is consistent with the literature [8, 9, 10]. Corroborating the established correlation between the content and the value of cystatin C and GFR (r=0,94).

In order to determine the prognostic significance of the revealed law, we have analyzed the incidence of obstetric and perinatal complications, depending on the content of cystatin C in the blood. The data obtained are presented in Table 2.

Table 2 - Prognostic determining the informational content of cystatin C in blood by Fischer

Content cystatin C, ng/ml	Number of observations		
	In all	Perinatal complications	Without complications
<50,0	30	5	25
>50,0	30	26	4
Total	60	31	29

As follows from the content data with less cystatin C 50,0 p1=5/30=0.16; when the content of cystatin C over 50,0 p2=26/30=0.87, the difference dp=0,87-0,16=0,71.

Find the error of the difference and determine the weighted share:

P(0,16x30x30 0.87)/(30 +30)=0.51

q=1-0,51=0,49;

Sdp=√0,51x0,49 h(1/5+1/26)=√0,059=0,244

Student's criteria=0.71/0,244=2.9, which exceeds the critical point t st=2,7

for K=60-2=58, 0.1% significance level.

The zero hypothesis is refuted by a high level of significance 0,01<p>0,001.

Therefore, with high probability we can predict the development of obstetric and perinatal complications in pregnant women with pyelonephritis. Prediction accuracy was 87%, specificity 71%.

Prognostic informative development of perinatal complications confirmed high correlation between cystatin C and fetal hypoxia (r=0,77), hypoxic - ischemic CNS newborn (r=0.81), IUGR (r=0,88), the development of preeclampsia (r=0,92).

In the control mechanisms of renal function can not, however, exclude the role of creatinine – a product of the metabolism of creatine phosphate excreted by filtration in the renal glomerula and not undergoing re absorption.

Creatinine in the blood in chronic pyelonephritis without exacerbation, significant differences were found in the III trimester of pregnancy (100,2±6,6 mmol/l) with respect to the I trimester – 75,5±6,2mmol/l, an increase of 32% significant differences in relation to indicators of uncomplicated pregnancy is not revealed.

In chronic pyelonephritis in the acute stage creatinine increased by 39% in the II trimester – 122,5±4,3 mmol/l and 72% in the III trimester – 151,6±7,4 mmol/l with respect to the values in the I trimester pregnancy – 88,0±6,1 mmol/l (Table 3).

In uncomplicated pregnancy serum creatinine trimester I was in the range – 66.4 - 99.7 mmol/l, while significantly increasing in the course of pregnancy, which is apparently associated with an increase in muscle mass.

Table 3 - The content of creatinine in the blood dynamics pregnancy in chronic pyelonephritis

	Creatinine (mkmol/l)		
Pregnancy	I trimester (n=30)	II trimester(n=30)	III trimester(n=30)
Without exacerbation	75,5±6,2	80,8±5,9	100,2±6,6*
Complicated pyelonephritis	88,0±6,1/**	122,5±4,3*/**	151,6±7,4*/**
Uncomplicated pregnancy	66,4±4,0	84,2±5,5*	99,7±3,3*
* - Reliable data on the 1 trimester pregnancy at p <0.05 ** - Reliable data on the uncomplicated pregnancy at p <0.05			

In a comparative perspective in pregnancy complicated by acute exacerbation of chronic pyelonephritis in relation to these uncomplicated pregnancy rate increased by 32% in the I trimester, 45% in II and 52% in the III trimester of pregnancy. Without exacerbation creatinine was lower than in the acute stage by 35% in the II and III trimester of pregnancy.

Growth of blood creatinine with chronic pyelonephritis usually occurs when reducing glomerular filtration rate of 20-30 % of the normal level. The foregoing is confirmed by glomerular filtration quantity determined in our studies (Table 4).

In chronic pyelonephritis without exacerbating found a decrease in glomerular filtration rate values in the III trimester - 70,5±4,0 ml/min. compared with the data I trimester (86,8±5,4 ml/min) – 19%. At the same time there were significant differences in performance with uncomplicated pregnancy.

A similar orientation is found in the course of pregnancy in chronic pyelonephritis in the acute stage. In this case , the value of glomerular filtration rate in the I trimester of pregnancy was – 83,5±2,2 ml/min , which is higher than 16% of the values II – 71,7±1,8 ml/min and 32% better than III trimester of pregnancy – 59,8±2,5 ml/min. In a comparative perspective in relation to these uncomplicated pregnancy value of glomerular filtration rate decreased by 30% in I and III trimester, 21% in the II trimester of pregnancy. Increase in glomerular filtration rate in early pregnancy is associated with high production of human chorionic gonadotropin, a subsequent decline in glomerular filtration due to a decrease of the hormone titer and with the increase of 17 hydro corticoids placental origin [1, 8].

Table 4 - The value of glomerular filtration rate in dynamics pregnancy in chronic pyelonephritis

	Glomerular filtration (ml/min)		
Pregnancy	I trimester (n=30)	II trimester (n=30)	III trimester(n=30)
Without exacerbation	86,8±5,4/**	76,2±3,4/**	70,5±4,0*/**
Complicated pyelonephritis	83,5±2,2/**	71,7±1,8*/**	59,8±2,5*/**
Uncomplicated pregnancy	119,2±3,5	90,0±4,7*	84,8±5,6*
* - Reliable data on the 1 trimester pregnancy at p <0.05 ** - Reliable data on the uncomplicated pregnancy at p <0.05			

In uncomplicated pregnancy there was a decrease of its value by 25% in the II trimester – 90,0±4,7 ml/min and 29% in the III trimester – 84,8±5,6 ml/min, about the data I trimester – 119,2±3,5 ml/min. In the III trimester of pregnancy, significant differences with respect to indicators II trimester of pregnancy was not revealed.

Concentration of uric acid in pregnancy not folded also increased and was within 150 – 350 mmol/L (Table 5). Without exacerbation of chronic pyelonephritis observed growth pattern identical levels of uric acid in the second trimester to 46 % - 243,0±22,0 mmol/l, in the III trimester – 396,7±21,0 mmol/l , which is 2,4 times higher ($p<0.05$). In a comparative perspective in relation to the data in the acute stage, significant differences were found only in the III trimester of pregnancy.

When pregnancy complicated pyelonephritis in the acute stage , the concentration was – 183,5 – 439,0 mmol/l, with hyper uricemia found in the III trimester of pregnancy. Figure rose to 22% in the I trimester – 183,5±10,6 mmol/l, 27% in the II trimester – 279,5±21,2 mmol/l, and 25% in the III trimester – 439,0±20,2 mmol/l on the data uncomplicated pregnancy. It is known that the level of uric acid has a close correlation with lipid metabolism and function of the endocrine system , which values during pregnancy increase several times [1, 8].

Therefore we analyzed by indicators uric acid and newborn mass while installed correlation between the level of uric acid and fetal hypotrophy (r=0,90).

Table 5 - Concentration of uric acid in the blood in dynamics pregnancy in chronic pyelonephritis

Pregnancy	Uric acid (mk mol / l)		
	I trimester(n=30)	II trimester (n=30)	III trimester(n=30)
Without exacerbation	166,7±10,5	243,0±22,0*	396,7±21,0*/**
Complicated pyelonephritis	183,5±10,6/**	279,5±21,2*/**	439,0±20,2*/**
Uncomplicated pregnancy	150,0±13,0	220,0±19,2*	350,0±25,4*
* - Reliable data on the 1 trimester pregnancy at p <0.05 ** - Reliable data on the uncomplicated pregnancy at p <0.05			

To confirm prognostic informative prediction fetal hypotrophy based on the data of uric acid in the III trimester transgressions we conducted analysis (within two Sigma) who showed that with fetal hypotrophy 86,6 % of uric acid was over, and in 13.3% - absence of malnutrition (Table 6).

Table 6 - informative prognostic determination of uric acid in the blood by Fischer

Contents of Uric acid	Number of observations		
	In all	Fetus of hypotrophia	Absence of hypotrophia
<400 mmol/l	21	2	19
>400 mmol/l	9	7	2
Total	30	9	21

As follows from the data in the uric acid content of less than 400,0 p1=2/21=0,095; when uric acid content of more than 400.0

p2=7/9=0,777 , difference dp=0,777-0,095=0,682.

Find the error of the difference and determine the weighted share:

P(0,095x21x9 0,777)/30=0,29

q=1-0,29=0,71; Sdp=√0,29x0,71x(1/2 1/7)=0,300

Student's criteria=0,682/0,300=2,3, which exceeds the critical point t st=2,1 for K=30-2=28, and 0,1% level of significance.

The zero hypothesis is refuted by a high level of significance 0,01<p>0,001.

Therefore, with high probability we can predict the development of fetal malnutrition in pregnant women with pyelonephritis. Prediction accuracy was 78%, specificity 68%.

Our studies for the determination of erythropoietin (EPO) in the blood showed that its level of pyelonephritis in the acute stage was significantly different from that uncomplicated pregnancy (Table 7).

Table 7 - The content of erythropoietin in the blood during pregnancy in dynamics chronic pyelonephritis

Pregnancy	Erythropoietin (ng/ml)		
	1 trimester (n=30)	II trimester (n=30)	III trimester (n=30)
Without exacerbation	33,3±1,5	42,6±2,0*#	54,8±3,0*#
Complicated pyelonephritis	47,3±1,1#	58,8±1,8*#	77,2±2,6*#
Uncomplicated pregnancy	29,5±1,7	35,8±2,0*	45,5±2,4*
* - Reliable data on the 1 trimester pregnancy at p <0.05 ** - Reliable data on the uncomplicated pregnancy at p <0.05			

From the table shows the contents without exacerbation erythropoietin trimester I was – 33,3±1,5 ng/ml, which was significantly increased by 22% in the II trimester – 42,6±2,0 ng/ml and 64% in III trimester (54,8±3,0 ng/ml) pregnancy (p<0,05). When pregnancy, peaking complicated pyelonephritis, revealed a similar focus – a significant increase of 24% (58,8±1,8) in II trimestere and 63% (77,2±2,6) in III trimestere pregnancy on the indicators I trimester (47,3±1,1) and 31% - on the data II trimester pregnancy. As I trimester with uncomplicated pregnancy content erythropoietin was – 29,5±1,7 ng/ml, in II – 35,8±2,0 ng/ml, the figure was significantly increased by 21% in III trimester pregnancy – 45,5±2,4 ng/ml, which is 54% more compared to the data I trimester and 27% with respect to data II trimester (at p<0,05), which is consistent with a number of authors [11, 12, 13].

In a comparative aspect of the content of erythropoietin in pregnancy with chronic pyelonephritis was significantly increased by 20% in III trimester pregnancy. During exacerbation of chronic pyelonephritis EPO level increased by 60% in I trimester, 64% in II, 69,7% in III trimester pregnancy (at p<0,05). Accumulation of erythropoietin in pregnancy due to the dynamics of power erythropoies [11, 12, 13, 14, 15].

With given the presence of correlations between the content of EPO and frequent occurrence of obstetric and perinatal pathology, based on the data to modify the content of EPO in chronic pyelonephritis without exacerbation and in the acute stage, we have calculated the prognostic factor of development of obstetric and perinatal complications, depending on the level of EPO in chronic pyelonephritis.

Analysis of the incidence of obstetric and perinatal pathology depending on the level of erythropoietin is presented in Table 8.

Table 8 - Prognostic informative determination of erythropoietin in the blood of pregnant by Fischer

Erythropoietin ng/ml	Number of observations		
	In all	Availability and obstetric perintal pathology	Absence obstetric perintal pathology
< 34,0	30	6	24
> 34,0	30	27	3
Total	60	33	27

As follows from the data presented at a level less than erythropoietin 34,0 p1=6/30=0,2; erythropoietin content at a 34,0 p2=27/30=0,9, a difference dp=0,9-0,2=0,7

Find the error of the difference and determine the weighted share:

P(0,2x30x30 0,9)/(30+30)=0,55

q=1-0,55=0,45;

Sdp=√0,55x0,45x(1/6 1/27)=√0,050=0,223

Student's criteria=0,7/3,1=0,223, which exceeds the critical point t st=2,5 for K=60-2=58, and 0,5% level of significance.

Zero hypothesis is refuted by a high level of significance 0,01<p>0,001.

Therefore, with high probability we can predict the development of obstetric and perinatal pathology.

Prediction accuracy of 90%, specificity of 70%.

Prognostic informative development of obstetric and perinatal pathology confirmed the high level of correlation between erythropoietin and threatened miscarriage pregnancy (r=0,90), the development of pre-eclampsia (r=0,85), threatened preterm labor (r=0,62).

A detailed study of clinical and laboratory changes revealed the presence of infectious factors contributing to the possibility of endogenous intoxication in pregnancy, complicated pyelonephritis.

On the possibility of increasing the level of endogenous intoxication evidence we have obtained data on the change in the concentration of erythropoietin characteristic of hypoxic condition . This circumstance for our assumption plays a key role, as established that irregularities in oxygen regime in the tissues initiates the formation of middle molecules [7].

Checking our assumption showed (Table 9) that in chronic pyelonephritis revealed increased concentration of MSM in II trimester 26%-0,240±0,02 USD in III trimester 52%-0,290±0,025 USD in comparison with the indicators I trimester pregnancy – 0,190±0,015 USD There were significant differences uncomplicated pregnancy and pyelonephritis in the acute stage in the II and III trimester pregnancy.

Table 9 - the average mass concentration of molecules in the blood in the dynamics of pregnancy pyelonephritis

	Average molecule mass (euro)		
Pregnancy	I trimester (n=30)	II trimester(n=30)	III trimester(n=30)
Without exacerbation	0,190±0,015	0,240±0,02*/**	0,290±0,025*/**
Complicated pyelonephritis	0,212±0,02/**	0,271±0,03*/**	0,352±0,03*/**
Uncomplicated pregnancy	0,172,0±0,01	0,200±0,02*	0,250±0,01*
* - Reliable data on the 1 trimester pregnancy at p <0.05 ** - Reliable data on the uncomplicated pregnancy at p <0.05			

In complicated pregnancy MSM level was within 0,212 – 0,352 USD and significantly higher than in all given uncomplicated pregnancy trimeste - 23%, 35%, 41%, respectively (p<0.05).

The correlation relationship between the content of erythropoietin and IMS (r=0,88), between uric acid and MSM (r=0,78).

An uncomplicated pregnancy was a significant increase in MSM by 16% in the II trimester – 0,200±0,02 USD and 45% in III trimester pregnancy – 0,250±0,01 euro regarding data I trimester – 0,172,0±0,01euro.

4. Discussions

The results of these studies indicate the presence of pathological changes found in chronic pyelonephritis, both outside and in the acute stage, the identified changes are most pronounced in the acute stage.

It was found that the metabolic dysfunction contributes to the development of obstetric and perinatal complications. Indicators of biochemical studies to determine the concentration cystatina C, creatinine, uric acid, the magnitude of glomerular filtration erythropoietin molecules have moderate predictive informative for predicting obstetric and perinatal complications in chronic pyelonephritis in pregnant women.

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References

1. Kamyshnikov, R.S., 2000. Handbook of clinical and biochemical laboratory diagnosis. Belarus, pp: 495.
2. Grubb, A., J. Bjork, V. Lindstrom et al., 2005. A cystatin C - based formula without anthropometric variables estimates glomerular filtration rate better than creatinine clearance using the Cockroft - Gault formula. Scand J Clin Lab Invest, 65(2): 153-62.
3. Roos, J.F., J. Doust, SE. Tett et al., 2007. Diagnostic accuracy of cystatin C compared to serum creatinine for the estimation of renal dysfunction in adults and children - a meta - analysis. Clin. Biochem., 40(5-6): 383-91.
4. Herget-Rosenthal, S., A. Bokenkamp, W. Hofmann, et al., 2007. How to estimate GFR - serum creatinine, serum cystatin C or equations? Clin. Biochem., 40(3-4); 153-61.
5. Turk, V., V. Stoka, D. Turk, 2008. Cystatins: biochemical and structural properties, and medical relevance. Front Biosci., 13, 5406-5420.
6. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evolution, classification. Am J Kidney Dis. 2002; 39: 1-286.
7. Aksenov, V.M., A.V. Starkov, 1998. Diagnostic value of determining the level of the average molecular weight substances in the plasma of infants undergoing intrauterine hypoxia. Perm. med. magazine, T. 15, 1: 25-28.
8. Cushing, A.A., 2007. Guidance on laboratory methods of diagnosis. Media, pp: 800.
9. Kulakov, V.I., B.L. Gurtovoiy, A.I. Emelyanova, 2005. Scientific and practical results of the diagnosis and treatment of pregnant women,

pyelonephritis (30 years experience). Obstetrics and Gynecology, 6: 3-8.
10. Shehtman, M.M., 2000. Obstetric nephrology. Moscow, pp: 255.
11. Zak, K.P., A.K. Butenko, A.N. Anuchin, 2002. Biological and therapeutic properties of erythropoietin. Physician business, 8: 113-120.
12. Rumyantsev, A.G., E.F. Morschakova, A.D. Pavlov, 2002. Erythropoietin: biological properties, the regulation of erythropoiesis age, clinical application. Geotar Med, Moscow, pp: 395.
13. Dzhamanaeva, K.B., 2001. Clinical and pathogenetic aspects of anemia in pregnant women: Author diss .... Doctor . med. Sciences, pp: 102.
14. Ailamzyan, E.K., M.A. Tarasov, A.A. Zaitsev, A. Samarin, 2003. The role of erythropoietin in the pathogenesis and treatment of iron deficiency anemia during pregnancy and the postpartum period. Zh. midwives. and wives. disease., VII (4): 17-22.
15. Carretti, N., M.R. Paticchio, G.A. Eremita, 1997. Intervenous iron therapy for severe pregnancy anemia with high erythropoietin levels. Obstet Gynecol (NY), 90(4): 650- 653.

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