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Likhikh D.G.<sup>1</sup>,  
Lazareva G.A.<sup>2</sup>**EFFICACY AND SAFETY OF PHARMACOLOGICAL TREATMENT  
OF THE WITH CLINICALLY APPARENT BACTERIURIA AND  
ASYMPTOMATIC BACTERIURIA IN THE PREGNANT WOMEN**<sup>1</sup>GlaxoSmithKline, 17 bldg. 3 Krylatskaya St, Moscow, 121614, Russia<sup>2</sup>Kursk State Medical University, 3 K. Marksa St., Kursk, 305040, Russia, e-mail: *lichich@yandex.ru***Abstract.**

The article explores the problem of urinary tract infection in pregnant women. It presents the statistical analysis of the frequency of different forms of urinary tract infection during pregnancy. Our data is compared to the statistics given by other national and international researchers. This research makes an attempt to compare two different treatment methods: using cefixime in dose 400mg 1 per day for 7 days and amoxicillin/clavulanate in dose 625mg 3 per day for 7 days. During the research conducted from September 2009 until June 2012 at State Healthcare Institution "Regional perinatal centre", 984 patients in I, II and III pregnancy trimesters were studied. In order to find out a potential influence of urinary tract microflora character for the intrauterine development, as well, as presence of infectious inflammatory diseases in neonates, a clinical observation of neonatal period for all the children born from the studied mothers was conducted. A special attention was directed to appearance of different clinical infection forms. We find out that the pregnant women with the asymptomatic bacteriuria should be administered the antibiotics treatment in order to prevent clinically apparent urinary tract infections, to stop uropathogen flora growth and to limit their affect on fetus development. Microbiological urine testing for the patients in the course of the urinary tract infection may be employed as an informative test for evaluating the antibiotics treatment efficacy. Given a positive effect Amoxicilline/Clavulanate and Cefixime treatment may be recommended to the pregnant women with clinically apparent UTI and with asymptomatic bacteriuria

**Keywords:** urinary tract infections, asymptomatic bacteriuria in the pregnant women, clinically apparent bacteriuria, acute cystitis, pielonephritis, antibacterial therapy, Amoxicillin/Clavulanate, Cefixime.

**Introduction.**

Urinary tract infections (UTI) are one of the most common ailments that require significant expenditures. These infections most often occur

during pregnancy; according to a number of researchers [1-7], their morbidity rate in the demographic ranges from 8 to 17 percent. Unfortunately, precise data on morbidity rate of various UTI during pregnancy and their impact on the patients' quality of life in Russia may not be acquired. Although, such information is of crucial importance for carrying out an efficient treatment.

There may be distinguished three major nosological entities of the UTI in the pregnant women: asymptomatic bacteriuria, acute cystitis and pielonephritis. The asymptomatic bacteriuria should be given a special attention in the system of infections, as it is attributed a constant relapse of its course with a low percentage of self-recovery, a high risk of complications development in mother, unborn child and neonate with a high probability of the infection symptomatic form onset in the urinary tract [8-14]. Presence of clinically apparent UTI form or of the asymptomatic bacteriuria in the mother subjects her to a significantly higher risk of premature delivery, preeclampsia, hypertension, hypohemia and postdelivery endometritis; while on the side of the unborn child, not rarely it turns out into complications, such as: arrested intrauterine development, fetal prematurity and congenital abnormalities development resulting in a higher risk of perinatal mortality [15, 16, 17].

Despite the fact that currently, researches on infection process in the urinary tract of mother organism influencing pathologic behaviour in the fetoplacental system are intensely conducted, yet the diagnostic and treatment algorithms, approaches to treatment and strategies of following the pregnant women in ambulatory and in-patient conditions have not been developed ultimately [9, 17]. Absence of a single established approach for bacteriological urine testing often leads to longer terms of diagnosing the asymptomatic bacteriuria and unsuitable treatment processes [18, 19, 20].

Success in resolving many problems related to the urinary tract infections (UTI) and the bacteriuria in the pregnant women depends directly upon

conducting a rational etiotropic therapy, which represents one of integral parts in actual preventive treatment of potential complications provoked by such infections. At gestational UTI, choice of antibiotics in the most cases is made empirically based on local data of uropathogenes' sensitivity. Currently, for therapeutical purposes, Amoxicillin/Clavulanate is acknowledged as the most prospective in category of penicillins. It is regarded as a medicine with a vast spectrum of effect, pertaining a bactericidal impact on gram-positive and gram-negative pathogens. This antibiotic is widely applied in urinary tract infection processes treatment during pregnancy, and is practically safe in relation to its effect on fetus [19, 21-24]. An alternative for the UTI treatment are cephalosporins, which surpass the penicillins in antimicrobial effect due to their resistivity against plasmid betalactamase. The cephalosporins are tolerated well, while allergic reactions that are typical for betalactame antibiotics occur less often, and have a much lighter course as compared to the penicillins. Like other antibiotics of the penicillin class, the cephalosporins are considered to be relatively safe for pregnant women and neonates. Until currently, however, there arise discussions regarding these or that UTI and bacteriuria treatment methods applied during pregnancy; an optimal and acceptable treatment regimen of these diseases in the pregnant women have not been determined finally [25, 26, 27].

Medicobiological and social significance of the problem regarding the urinary tract infections during pregnancy and necessity of treatment efficacy improvement have served as the grounds for conducting this research and studying pharmacological safety and efficiency of treating such diseases in the pregnant women.

**Purpose of the research**

Evaluation of morbidity rate and risk factors for the asymptomatic bacteriuria development in the pregnant women and elaborating antibacterial therapy approaches.

**Data and methods**

During the research conducted from September 2009 until June 2012 at State Healthcare Institution "Regional perinatal centre", 984 patients in I, II and III pregnancy trimesters were studied. At the first research stage, 984 pregnant women were subjected to clinical and laboratory screening study for urogenital infections, which included physical examination, clinical urine analysis and bacteriological urine testing (determining sensitivity to the antibiotics as well). All the patients were arranged into three groups according to duration of gestation (see Table 1).

Table 1

**Description of the pregnant women subjected to screening study (n=984)**

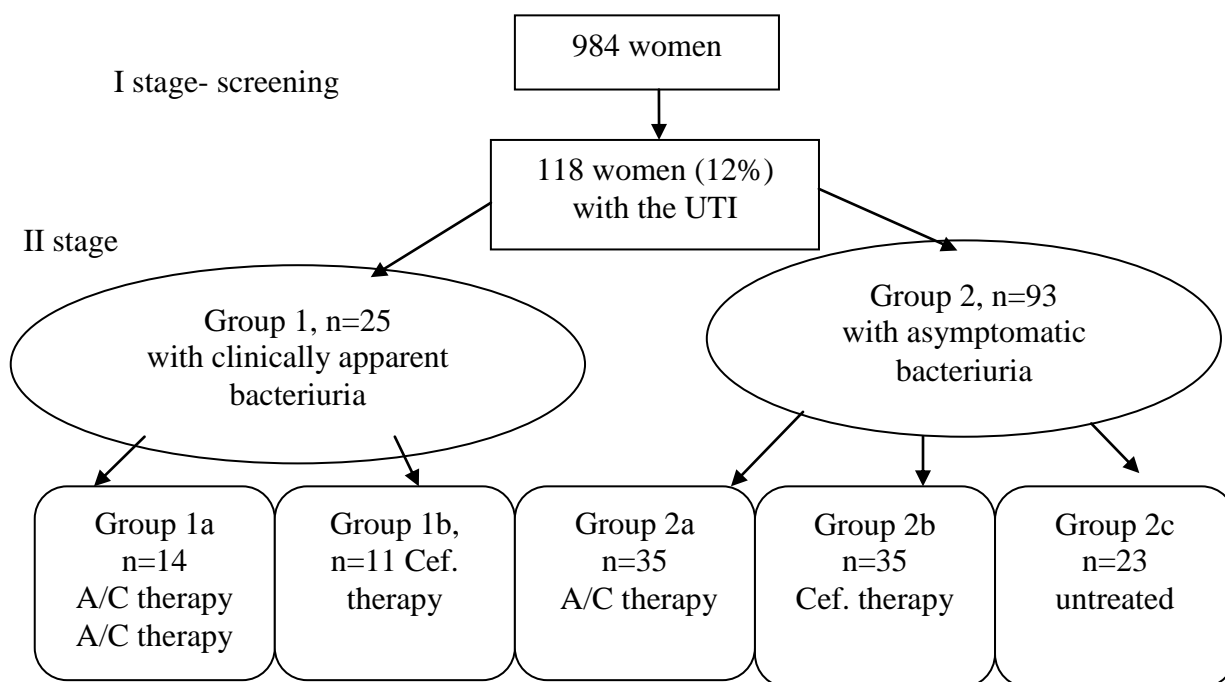
Group description	I Group (n=369)	II Group (n=320)	III Group (n=295)
Age, years	29.5±3.6	27.8±2.8	28.6±3.1
Women with the UTI signs (%)	31 (8.4%)	38 (11.9%)	49 (16.6%)
Healthy women (%)	338 (91.6%)	282 (88.1%)	246 (83.4%)

I Group (369 persons – 37.5%) – are the women in 5-14 weeks of gestation period, II Group (320 persons – 32.5%) – women in 15-28 weeks of the period, III Group (295 persons – 30%) – women in 29-40 weeks of the period.

The age of the patients studied ranges from 18 to 47 years and averagely constituted: 29.5±3.6 years – for the pregnant women in I Group; 27.8±2.3 – in II Group; 28.6±3.1 – in III Group. The prevailing women age was between 25-29 years (38.8%).

The second research stage suggested a further study of 118 (12%) of the pregnant patients, who proved positive at the first stage in the bacteriological urine test taken twice at no less than 24-hour interval. A comparative efficacy and safety analysis of the urinary tract infections treatment performed with two different methods was conducted on these patients. The patients were divided into two groups: the first group (group 1) included 25 women with clinical UTI signs, the second group (group 2) included 93 patients without clinically apparent UTI. Subsequently, for a comparative study of various treatment regimens efficacy, the patients, who agreed to receive antibiotics therapy were randomised using random numbers method in two subgroups: subgroup A took Amoxicillin/Clavulanate in 625 mg dosage three times in 24 hours, their therapy lasted 7 days, subgroup B took Cefixime in 400 mg dosage once in 24 hours with the therapy lasting 7 days as well. The first group (25 women) included: 1a subgroup – 14 patients; 1b subgroup – 11 patients. The second group (93 pregnant women) included: 2a subgroup – 35 patients; 2b subgroup – 35 patients. Out of 93 patients without clinically apparent UTI, 23 rejected the antibiotics therapy, explaining that they had not any complaints and troubles regarding this case. They constituted a separate 2c group (Fig. 1).

Examining all the patients, an anamnestic data analysis was carried out together with clinical, laboratory and microbiological in particular; ultrasound and statistical research methods were applied as well.



**Figure 1.** The Research procedure

Urine culture study in aspect of asymptomatic bacteriuria screening was carried out for all patients of obstetric clinical hospital. Screening along with the urine culture study aspect was also performed for ambulant patients of the clinical hospital, as well, as if bacteria were detected in the urine hypostasis, or the patients complained of dysuric manifestations and drawing pain in lumbus region.

Before collecting the urine for culturing, the women received a detailed instruction on the urine collecting rules, following which conditioned reliability of microbiological test results and, ultimately, the treatment efficiency.

The microbiological test and culturing of the medicine was performed in microbiological laboratory of the City hospital №6 in Kursk, Russia.

Clinical efficacy of the treatment was evaluated on the basis of the pregnant women general state improvement with related data acquired using an interactive questionnaire of the University of Wisconsin Interstitial Cystitis Scale, 1998, which was modified by staff scientists of the Physical and Chemical Medicine Research Institute ("NII FKHM").

Table 2

**The evaluation of pharmacotherapy efficacy in points**

	Symptoms	0 points	1 point
1.	Intoxication symptoms: ailment, general muscular weakness	No	Present
2.	Complaints about pain: described as short-term, long-term, continuous; described as sharp, dull, colic-like; focalization: above pubic, perineal, in genitalia, with radiation to hip, in groin region, vulval lips, perineum; influence of body position on pain appearance, urination, physical load, medicine treatment	No	Present
3.	Dysuria: amount per 24 hours, urination intervals, incontinence type, urinary urgency; presence of difficulties: initial retention, in 2 acts, sense of urinary bladder emptied incompletely	No	Present
4.	Pain manifestation focalization during urination in urethra, above pubic, behind pubic, in perineum, in genitalia region; pain sense occurrence at the beginning and at the end of urination	No	Present
5.	Urine quality alteration: colour, transparency – not altered, turbid, opalescent	No	Present
6.	Pain and enlargement in peripheral nodes	No	Present
7.	Body temperature rise above 37 C°	No	Present
8.	Pain in lumbus region	No	Present
9.	Hyperhidrosis	No	Present
10.	Headache	No	Present

Incidence of after-antibiotic-treatment side effects was evaluated with a questionnaire, which included a list of symptoms (Table 3).

Table 3

**Incidence evaluation  
of after-pharmacotherapy side effects**

Symptoms	Sign present	Sign absent
Headache, dizziness	+	-
Itching, rash (allergic reactions)	+	-
Loss of appetite	+	-
Pain in epigastrium	+	-
Nausea, vomiting	+	-
Bowel disorders (flux, opstipation)	+	-
Depression	+	-

Laboratory efficacy was evaluated on the basis of microorganisms titer decrease acquired form results of culturing in 3-5 days and in 28 days after the antimicrobial treatment was finished.

Statistical data processing was conducted using standard packages of Microsoft Excel 2007 and Statistica 10 software applications. Variants of qualitative and quantitative analyses were employed during the research.

**THE RESEARCH RESULTS AND DISCUSSION**

The UTI morbidity rate relative to gestation duration of the women is given in Figure 2. In I group, a positive culturing result was found in 32 women (8.7% of cases), in II group – in 38 women (11.9%), in III group – in 48 women (16.6%).

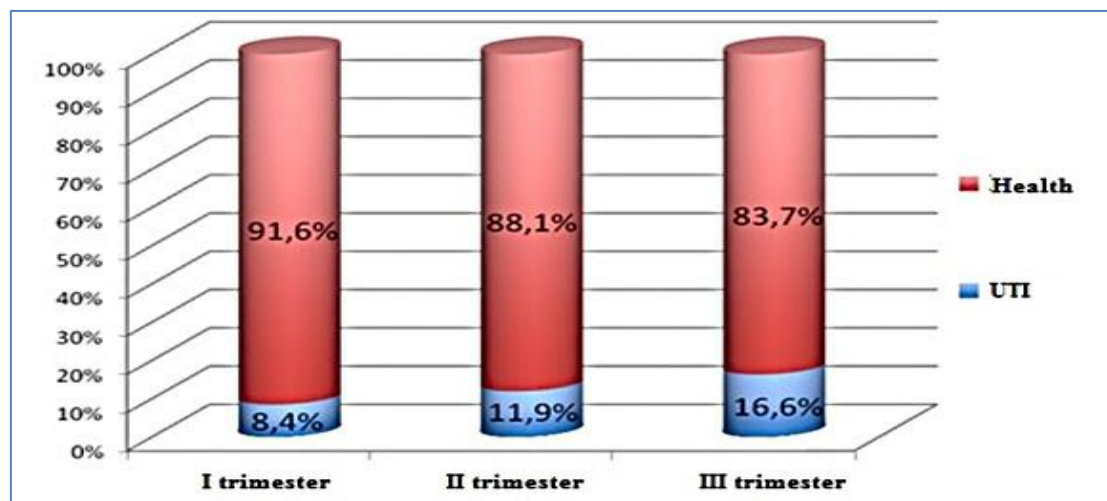


Figure 2. The UTI morbidity rate/gestation duration in the women

The asymptomatic bacteriuria was diagnosed in case bacteria were detected in two urine samples collected consequently at 24-72 hour intervals in titer  $>10^5$  CFU/ml. According to the results of screening study performed on 984 women, the asymptomatic bacteriuria was found in 93 pregnant women (9.4%). The data acquired indicate a sufficiently high morbidity rate of the asymptomatic bacteriuria among the pregnant. Given this, almost every tenth woman at a mature term has an undiagnosed asymptomatic bacteriuria.

Upon gestation term progression, a higher morbidity rate of the asymptomatic bacteriuria cases was observed ( $p < 0.05$ ), as compared to the total

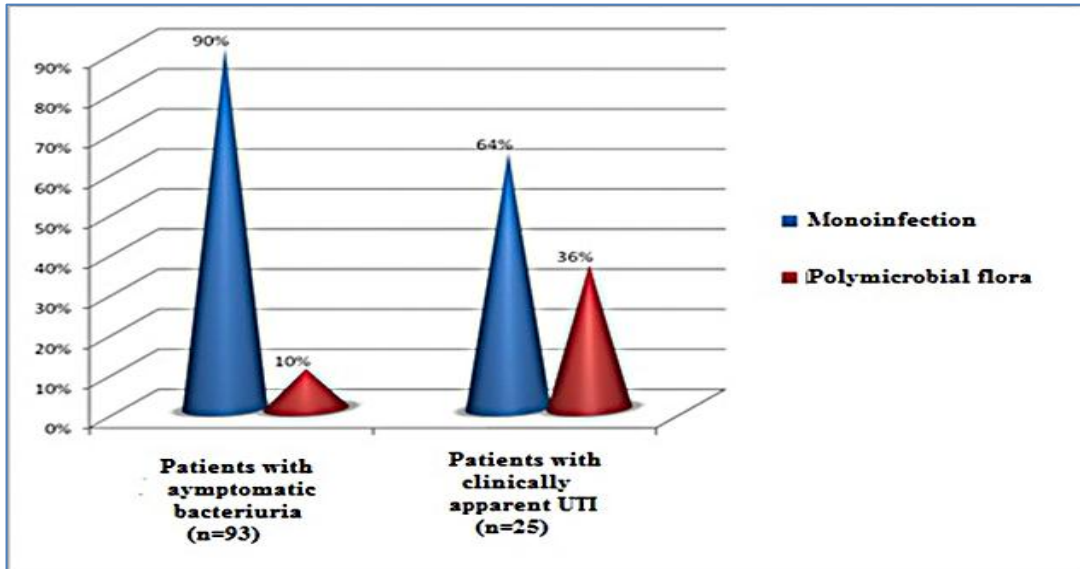
Clinically apparent urinary tract infection (according to anamnesis, general examination, tool and laboratory research data) was found in 25 women (2.5%). Acute cystitis was observed in 18 women (1.8%) and acute pielonephritis – in 7 women (0.7%). In two cases, the acute pielonephritis was combined with urinary stone disease. An etiological structure of asymptomatic bacteriuria germ was found in the

number of the UTI detected. Thus, in group 1 the asymptomatic bacteriuria was found in 68.8% of cases (22 women), in group 2 – 78.9% (30 women), in group 3 – 85.4% (41 women).

Authors consider as appropriate a tendency toward the UTI morbidity rate increase upon gestation progression. Factors that contribute to their development, such as the urinary tracts dilatation, the forward and upward urinary bladder disposition resulting from womb enlargement, increased renal blood flow, glomelural filtration and incomplete bladder emptying increase and aggravate upon the gestation progression.

pregnant women upon conducted microbiological study. Monoinfection proved to be prevailing in the following: one germ was cultured in 84 patients (90.3%), 2 and more – in 9 patients (9.7%). While in the patients with clinically apparent bacteriuria, a mixed infection was found in 36% of cases (9 women) and the monoinfection – in 64% of the cases (16 women) (see Figure 3).



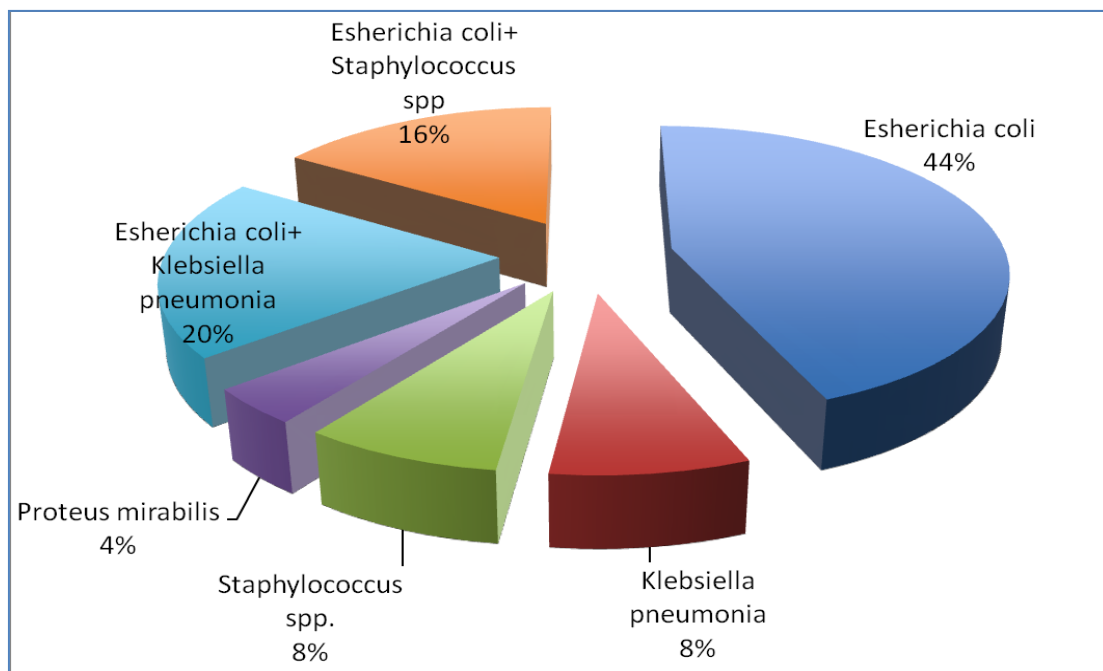


**Figure 3.** The structure of germs in the pregnant women with the asymptomatic and clinically apparent bacteriuria

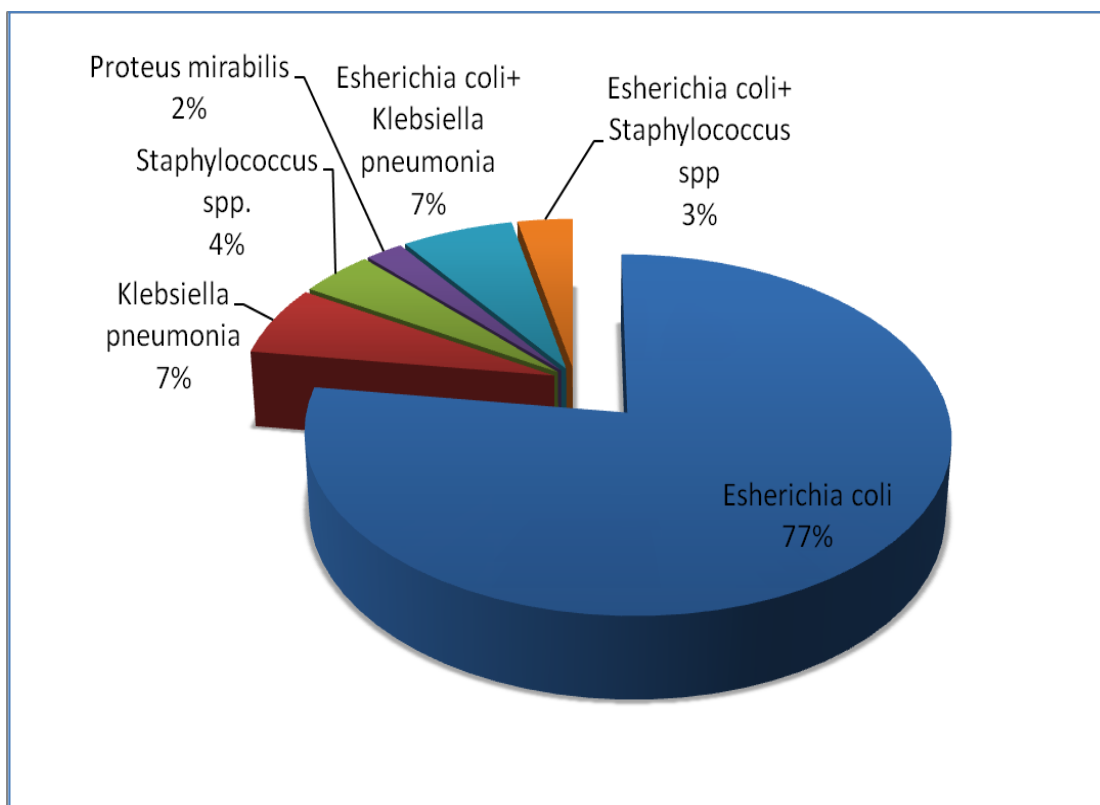
According to the data acquired from culturing, group of pregnant women with clinically apparent bacteriuria was revealed to have the following: esherichia coli was found in 11 women (44,0%), klebsiella pneumonia – in 2 women (8,0%), a staphylococcus spp. – in 2 women (8,0%), proteus mirabilis – in 1 woman (4%); a combination of two germs: esherichia coli+klebsiella pneumonia was detected in 5 women (20%) and esherichia coli+staphylococcus spp – in 4 women (16%).

According to the data acquired from urine

culturing, in group of the pregnant women with the asymptomatic bacteriuria the following was revealed: esherichia coli was found in 72 women (77,4%), klebsiella pneumonia – in 6 women (6,4%), a staphylococcus spp. – in 4 women (4,3%), proteus mirabilis – in 2 women (2,2%); a combination of two infectious agents: esherichia coli+klebsiella pneumonia was found in 6 women (6,5%), esherichia coli+staphylococcus spp – in 3 women (3,2%) (Fig. 5).



**Figure 4.** Culturing results in patients with the clinically apparent bacteriuria (n=25)



**Figure 5.** Culturing results in patients with the asymptomatic bacteriuria (n=93)

Clinical efficacy and safety of antibiotics treatment was evaluated using enquirers that listed clinical symptoms and side effects of the disease: 1 group included 25 pregnant women with clinically apparent bacteriuria and 2 group included 93 women with asymptomatic bacteriuria. Description of the two groups is given in Table 4.

Table 4

**Description of patients with the UTI (n=118)**

Group description	1 group – clinically apparent UTI	2 group – asymptomatic bacteriuria
Women/ %	25/ 21.2%	93/ 78.8%
Age, years	29.2±3.0	28.6±3.2
Enquirer points	8.5±0.8*	0

Note: \* p<0.05 – proven differences between the two groups

Repeated clinical and laboratory study was performed after 3-5 days and 28 days after the therapy was finished. Subsequently, the patients in I and II groups were subjected to examination each 28 days and until delivery.

In order to analyse clinical manifestations of the urinary tract infections in the pregnant women during the research, anamnesis and disease analysis was performed, examinations were conducted, as well, as

routine clinical and laboratory tests were carried out, such as clinical blood test, biochemical blood test, clinical urine analysis; urine culture and ultrasound scanning were executed for all the patients.

Clinical examination of the pregnant women with clinically apparent bacteriuria revealed their most frequent complaints: ailment, general weakness and often urination in 100% of cases, gripes and discomfort at urination, subfebrile body temperature in 72% of cases.

Analysis of pregnancy progress in the patients with the urinary tract infection revealed a high incidence of complications: 93 women (78.8%) had differently manifested swells; mild preeclampsia was observed in 47 women (39.8%); while severe gestosis was not found in the examined group. According to the data of the ultrasound scanning, the pregnant women with clinically apparent urinary tract infection revealed a proven disturbance incidence increase as compared to control group of practically healthy women. Thus, 12 patients (48.0%) were diagnosed with hydroamniosis, 6 (24.0%) – with hypamnion, 5 (20.0%) – with presence of foreign matters in amniotic fluid, 3 (12.0%) – with fetal growth retardation and chronic fetal hypoxia, 5 (20.0%) – with alteration in placenta maturity degree and thickness (p<0.05). At the same time, in the pregnant women with the asymptomatic

bacteriuria the following was observed: hydroamniosis found in 43 (46.2%) women, hypamnion found in 26 (28.0%), presence of foreign matter in amniotic fluid found in 11 (11.8%), fetal growth retardation found in 6 (6.5%), alteration in placenta maturity degree and thickness found in 10 (10.8%), which also reliably proved to be higher as compared to the group of practically healthy women ( $p < 0.05$ ).

During the research, a comparative study of medicine application efficacy, such as Amoxicilline/Clavulanate and Cefixime was conducted.

After receiving an informed consent from the pregnant patients, those with clinically apparent bacteriuria in 1a subgroup were administered 625 mg of Amoxicilline/Clavulanate three times in 24 hours, for 7 days duration; in 1b subgroup – 400 mg of Cefixime daily, 7 days duration as well. In 2a subgroup, the pregnant patients with asymptomatic bacteriuria were administered 625 mg of Amoxicilline/Clavulanate three times in 24 hours for 7 days; in 2b subgroup – 400 mg of Cefixime daily for 7 days, and 2c subgroup was a control group, which was not treated with the antibiotics.

According to the data of control laboratory testing (performed 3-5 days after the antibiotics treatment was commenced), the efficacy of Amoxicilline/Clavulanate and Cefixime treatment for the pregnant patients group with clinical manifestation of the bacteriuria comprised 100%.

Although, in single cases, 28 days after the therapy was over, microflora growth was observed after Amoxicilline/Clavulanate treatment in 7% of cases. In 3-5 days after taking Amoxicilline/Clavulanate, germ elimination was revealed in 100% of cases; in II group after Cefixime treatment, the germ elimination was revealed in 97% of cases, as urine culture results showed. In 28 days, microflora growth was found in urine culture of two pregnant women (5.7% of cases) treated with Cefixime and in one pregnant woman (2.8%) treated with Amoxicilline/Clavulanate. This may be related to that many bacteria species are able to live parasitically inside cells, showing affinity for various host cells, which is a facultative parasitism. For instance, *Escherichia coli* may parasitize in epithelium cells and in macrophagocytes, creating intracellular bacterial communities (IBC). Present fimbriae and microorganisms' enzymatic activity provides their penetration into cell or into intracellular space. Thus, a renewed bacteria growth may be related to difference between metabolic activity and growth speed of separate bacteria cells, as many antibiotics do not have effect on resting cells, as well, as because of a limited penetration of antimicrobial substances through biofilms. On the other hand, bacterial infection recurrence is conditioned by a particular microorganism's biological properties and host protection defects.

Table 5

**The symptoms dynamics 28 days after the pregnant patients with clinically apparent bacteriuria were treated with the antibiotics**

Symptoms/ women (%)	subgroup 1a before treatment	subgroup 1a after Amox./Clav. treatment	subgroup 1b before treatment	subgroup 1b after Cefixime treatment
General weakness	14 (100%)	2 (14.3±3.2%)↓*	11 (100%)	0 (0%)↓*
Complaints for pain: above pubic, in genitalia and perineum	14 (100%)	0 (0%)↓*	11 (100%)	1 (9.1±1.7%)↓*
Dysuria:	14 (100%)	0 (0%)↓*	8 (72.7±11.6%)	0 (0%)
Urine quality alteration: colour, transparency	11 (78.6±11.4%)	0 (0%)↓*	5 (45.5±7.4%)	0 (0%)
Pain manifestations at urination	10 (71.4±10.8%)	0 (0%)↓*	8 (72.7±11.6%)	0 (0%)↓*
Pain and enlargement of peripheral nodes	6 (42.8±9.1%)	0 (0%)↓*	5 (45.5±7.4%)	0 (0%)↓*
Body temperature rise above 37C°	10 (71.4±10.8%)	0 (0%)↓*	8 (72.7±11.6%)	0 (0%)↓*
Pain in lumbus region	7 (50.0±9.4%)	0 (0%)↓*	7 (63.6±10.4%)	0 (0%)↓*
Hyperhidrosis	9 (64.3±10.2%)	1 (7.1±1.5%)↓*	9 (81.8±12.7%)	1 (9.1±1.7%)↓*
Headache	9 (64.3±10.2%)	0 (0%)↓*	9 (81.8±12.7%)	0 (0%)↓*

Note: \*  $p < 0,05$  – are the proven differences from the indicator before the treatment, alteration of the indicator relative to initial value

In 2c subgroup (n=23), the pregnant patients with asymptomatic bacteriuria, who were not treated with antimicrobial medicine; 11 (47.8%) women were observed to adjoin clinical UTI in 2-13 weeks (6.1±0.8 on average), which was accompanied by germ titer increase. As for clinical symptoms, a more often urination (43.5%) with discomfort and itching or pain at the urination (39.1%) was observed. In 12 pregnant women (52.2%), the germ titer was found to increase: in 7 women (30.4%) with 100000 to 1 million CFU, and in 5 (21.7%) women with 100000 to 500000 CFU without adjoined clinical UTI.

Symptoms related to infective inflammatory process in the pregnant women with clinical presentations of the bacteriuria showed a positive tendency for decrease after 3 days of antimicrobial medicine treatment.

So, in more than 80% of cases treated with the antimicrobial medicine, 1a and 1b subgroup patients were observed to have a rapid elimination of general weakness and hyperhydrosis, while painfulness and nodes' enlargement was observed to decrease in 50% of the patients.

After 28 days of antimicrobial medicine treatment, the patients in both subgroups witnessed a significant improvement of their general state, in particular, none of the pregnant women complained for dysuric disorders or nodes enlargement and none was found to have a body temperature rise.

Although, no proven differences in the studied medicine efficacy were found,  $p > 0.05$  (see Table 6).

Table 6

**The comparative description of Amoxicilline/Clavulanate and Cefixime efficacy for treating clinically apparent bacteriuria in the pregnant patients.**

Description groups	subgroup 1a n=14	subgroup 1b n=11
Women/ %	14/ 56%	11/ 44%
Age, years	29.1±2.8	28.8±3.0
Enquirer points before treatment	8.65±0.62	8.37±0.76
Enquirer points 28 days after treatment	0.78±0.05↓*	0.65±0.08↓*

Note: \*  $p < 0,05$  – are the proven differences from the indicator before the treatment, ↑↓ – alteration of the indicator relative to initial value.

In the pregnant women group with clinical presentations of the UTI, 7 patients showed indicators improvement 28 days after the antibiotics therapy, according to ultrasound scanning results. Thus, disturbance incidence in this group decreased from 88.0% to 60.0%.

After the patients with the asymptomatic UTI were treated, percentage of those with disorders decreased from 72.9% to 56.7%. In the group of pregnant women with asymptomatic UTI, who were not subjected to the treatment, pathological signs incidence was observed to increase from 69.6% to 78.3% after 30 days, which was revealed by the ultrasound scanning.

Table 7

**The morbidity rate of the UTI signs in the pregnant women revealed by the ultrasound scanning**

Ultrasound scanned symptoms/ groups	Clinically manifested bacteriuria (treated patients) n=25		Asymptomatic bacteriuria, (treated patients) n=70		Asymptomatic bacteriuria (untreated patients) n=23	
	Before antibio treat.	After antibio treat.	Before antibio treat.	After antibio treat.	1st ultrasound scan	2nd ultrasound scan
Hydroamniosis	12	9	31	24	12	14
Hypannion	6	5	20	13	6	5
Foreign matters in amniotic fluid	5	4	7	4	4	5
Fetal growth retardation	3	2	4	4	2	2
Alteration of placenta thickness and maturity degree	5	4	6	4	4	6

As seen in Table 7, the disorders incidence for the both groups, which were subjected to the antibiotics treatment, showed a tendency toward decline, while in the control study group without the medicine treatment, incidence rose after 28 days.

An important fact is that none of the pregnant women witnessed side effects for the antibiotic

treatment, which were related to the medicine taking, demanding the medicine administration cancellation.

In order to find out a potential influence of urinary tract microflora character for the intrauterine development, as well, as presence of infectious inflammatory diseases in neonates, a clinical observation of neonatal period for all the children born from the studied mothers was conducted. A



special attention was directed to appearance of different clinical infection forms. A pathological loss of initial body weight and umbilical wound state,

which is not a typical infection manifestation, were also considered.

Table 8

**The complications upon delivery**

Delivery outcome and neonate state	Group 1a n=14	Group 1b n=11	Group 2a n=35	Group 2b n=35	Group 2c n=23
Small-for-gestational-age fetus	0	0	1 (2.9±0.8%)	1 (2.9±0.8%)	3 (13.0±2.6%)*
Neonate condition less than 7 on Apgar scale	2 (14.3±2.8%)	1 (9.1±2.1%)	4 (11.4±2.3%)	3 (8.6±2.0%)	3 (13.0±2.6%)
Premature delivery	1 (7.1±1.9%)	1 (9.0±2.1%)	1 (2.9±0.8%)	1 (2.9±0.8%)	4 (17.4±2.9%)*
Preterm amniorrhea	1 (7.1±1.9%)	0	1 (2.9±0.8%)	2 (5.7±0.9%)	3 (13.0±2.6%)
Inherent vesicopustulosis	0	0	0	1 (2.9±0.8%)	2 (8.7±2.0%)
Conjunctivitis	0	0	1 (2.9±0.8%)	0	1 (4.3±0.9%)
Umbilical wound delayed healing	0	0	0	0	2 (8.7±2.0%)*
Pneumonia	0	0	0	0	0
Sepsis, meningitis, neonate deaths	0	0	0	0	0

Note: \*  $p < 0,05$  – are the proven differences from prior-to-treatment indicators

Small-for-gestational-age fetus was evaluated on the basis of weight and height indicators, that is, if a neonate's body weight to height ratio was below 60. In is worth noting, that the small-for-gestational-age fetus was proven to be higher ( $p < 0.05$ ) in untreated 2c group, as compared to the other groups.

Upon delivery, all the children's state was evaluated according to the Apgar scale with point range 1-10 at 1st and at 5th minutes of their lives. The state of the most neonates was evaluated at 8-9 points. Number of the children born with less than 7 points ranged from 8.6% to 14.3%, although, proven differences in the studied groups were not found. Among clinical infection manifestations found in the children were: inherent vesicopustulosis found in three cases, umbilical wound delayed healing, as well, as conjunctivitis found in two cases. No cases of pneumonia, sepsis, meningitis and neonate deaths were registered in the studied groups.

Among the studied groups of pregnant women, proven differences in these infectious complications were detected in cases with a delayed healing of the umbilical wound (8.7%) and premature delivery (17.4%).

The data acquired provides a high degree of proven ground to relate microorganisms' persistency in lower urinary tracts to the neonates born with small-for-gestational-age fetus signs, morphofunctional dismataturity, umbilical wound

delayed healing and tendency to premature delivery in cases with bacteriuria.

**Discussion of results**

In conclusion, a high therapeutic efficacy of Amoxicilline/Clavulanate and Cefixime, and a high tolerance to the medicine in the pregnant women, as well, as absence of their effect on fetus state provide grounds for recommending a 7-day treatment programme of Amoxicilline/Clavulanate in 625 mg dosage, three times in 24 hours, as an efficient method of the urinary tract infection treatment during II and III trimesters of pregnancy. Along with a low possibility of side effects and complications, and in case of the patients' intolerance for Amoxicilline/Clavulanate, a 7-day treatment with 400 mg Cefixime once a day, orally, may be recommended as an alternative for treating the urinary tract infections in the pregnant women during II and III trimesters.

In the research conducted, upon comparison of Amoxicilline/Clavulanate and Cefixime application for treating the pregnant women with a clinically apparent and asymptomatic bacteriuria, both medicines were found to be highly efficient, and the recovery rate was 93% and 97% correspondingly, which agrees well with the results of the researches conducted earlier. It should be noted that the acquired treatment tolerance data definitely proved these two medicines to be comparable in side effects incidence. Having calculated cost/efficiency indicators, the

following was revealed: for Amoxiclav it was 525 rubles, and 859 rubles for Suprax, which indicates that the first medicine is more cost-effective.

In total, therefore, combination of a high therapeutic efficacy, good tolerance and safety of Amoxicilline/Clavulanate and Cefixime brings us to conclusion that they may be reasonably applied for clinically apparent and asymptomatic bacteriuria treatment during the three pregnancy trimesters.

We believe that the results of the conducted research we have achieved our goal. Data from our study coincide with those in the foreign press, and will complement the data published in Russian sources.

### Conclusion

1. According to results of screening study performed on 984 pregnant women, the urinary tract infection morbidity rate was 12% (118 women); bacteriuria morbidity rate was found to increase along with gestation progression from 8.4% (31 women) in 5-14 pregnancy weeks and 11.9% (38 women) in 15-28 weeks to 16.6% (48 women) in 29-40 weeks.

2. The clinically apparent urinary tract infection (according to anamnesis, general examination, tool and laboratory research data) was found in 25 women (2.5%). Acute cystitis was observed in 18 women (1.8%) and acute pielonephritis in 7 women (0.7%). The asymptomatic bacteriuria was detected in 93 pregnant women (9.4%).

3. The monoinfection prevailed in pregnant women with the asymptomatic bacteriuria: 90.3% of cases (84 women); 2 and more uropathogenes were revealed in 9.7% of cases (9 women). While in the patients with clinically apparent bacteriuria, the monoinfection was found in 64% of cases (16 women) and the mixed infection was found in 36% of cases. The uropathogenes' structure of the urinary tract infections in the pregnant women comprises the following microorganisms: *Escherichia coli* – 79.1%, *Klebsiella pneumoniae* – 8.3 %, *Proteus mirabilis* – 6.7%, *Staphylococcus spp.* – 5.9%.

4. The antibacterial therapy provides a sustained and apparent clinical-and-laboratory tested effect. The group of patients, who were subjected to antibacterial therapy revealed a statistically significant decrease of the urinary tract infection symptoms, a lower rate of positive culturing in 93-97% of cases ( $p < 0.05$ ) and absence of significant side effects from the antibiotics treatment ( $p > 0.05$ ). In case, the antibiotic treatment was not conducted at the asymptomatic bacteriuria, clinical urinary tract infections were observed to adjoin in 47.8% of cases,

while the germ titer increased; an isolated germ titer increase in the urine was observed in 52.2% of cases.

5. The results of performed clinical and laboratory study did not reveal proven differences in efficacy and safety of the two antimicrobial medicines (Amoxicilline/Clavulanate and Cefixime), ( $p > 0.05$ ). Thus, the antimicrobial medicines may be recommended to the pregnant women with the urinary tract infections and with the asymptomatic bacteriuria for the scope of germ elimination.

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**Likhikh Dmitry Gennadievich** – Medical Scientific Liaison.

**Lazareva Galina Anatolievna** – Doctor of Medical Sciences, Professor Department of obstetrician and gynecology.