

Microbial landscape and antibiotic resistance of the main causative agents of asymptomatic bacteriuria of pregnant women for the period 2013 - 2016

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Abstract: a retrospective analysis of the microbial landscape and antibiotic resistance of the main pathogens of asymptomatic bacteriuria of pregnant women for the period 2013-2016 was carried out. It has been shown that *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcus agalactiae* are the main causative agents of latent bacteriuria in pregnant women. In addition, during the analyzed period, there is a gradual increase in the resistance of *E. coli* and *Streptococcus agalactiae* to all groups of antibiotics, *Staphylococcus aureus* - to cephalosporins and fluoroquinolones.

Keywords: microbial landscape, asymptomatic bacteriuria, pregnant women, antibiotics, resistance.

Relevance: Urinary tract infection during pregnancy remains one of the most important problems in obstetrics, urology and perinatology. This is due to changes in the clinical signs of urinary tract infections during pregnancy, approaches to diagnosis and treatment, as well as a high risk of urological, obstetric and neonatal complications [1, 2, 3, 4].

Asymptomatic bacteriuria occupies a special place in the structure of urinary tract infections. As a preclinical form of a number of diseases of the urinary system, asymptomatic bacteriuria is characterized by a persistent recurrent course with a low percentage of self-healing, a high risk of complications from the mother, fetus and newborn, and a high probability of manifestation in a symptomatic form of urinary tract infection. According to literature data,

asymptomatic bacteriuria occurs in 6% of pregnant women (from 2 to 13% depending on socio-economic conditions) [5, 6, 7, 8].

The standard case definition of a urinary tract infection (as recommended by the CDC) is based on clinical evidence (fever over 37.5°C, urge to urinate, urinary frequency, dysuria, suprapubic tenderness) and bacteriological data - detection in urine culture > 10⁵CFU/ml (colonies in ml) no more than two types of microorganisms. The most reliable method for diagnosing nosocomial urinary tract infections, along with clinical data, remains microbiological studies. In this case, clinically significant bacteriuria should be distinguished from insignificant. If the concentration of the microorganism in the urine is more than 10⁵CFU/ml, the results should be considered clinically significant.

In this regard, an important task is, first of all, timely diagnosis and rational etiotropic therapy of asymptomatic bacteriuria in pregnant women as the main measure for the prevention of ascending urinary tract infection and the development of a number of complications from the mother, fetus and newborn [9, 10, 11, 12, 13].

According to the Protocol of diagnostics and treatment "Maintaining physiological pregnancy" (approved by the minutes of the meeting of the Expert Commission on the development of health care of the Republic of Kazakhstan No. 18 dated September 19, 2013), when registering, all pregnant women are prescribed a urine test for bacteriuria. Treatment of bacteriuria reduces this risk. Thus, it is recommended that pregnant women be screened for bacteriuria using a urine culture at least once in early pregnancy, and, if positive results are obtained, treat it.

Thus, the successful resolution of many problems associated with asymptomatic bacteriuria during pregnancy presents a real opportunity to improve the quality of medical care for pregnant women and reduce the number of complications from the mother, fetus and newborn [14, 15].

Purpose of the study – analysis of the microbial landscape of asymptomatic bacteriuria pathogens in pregnant women and the dynamics of resistance of the main pathogens to antibacterial drugs.

Materials and methods: a bacteriological study of biomaterial (urine) of pregnant women was carried out: in 2013 - 4572 samples, 2014 - 10857 samples, 2015 - 11451 samples, 2016 - 10490 samples. All examined women were registered for pregnancy with gynecologists of Nur-Sultan primary health care organizations, had no history of urinary system diseases. The study was carried out by the classical bacteriological method. The release of an infectious agent at a concentration of 10⁵ CFU/ml or more was taken as true bacteriuria. The identification and

determination of the sensitivity of the isolated strains of microorganisms to antibacterial drugs was carried out in accordance with the current regulatory legal acts.

Results and discussion: analysis of the data of bacteriological studies of urine for 2013 showed that latent bacteriuria was detected in 16.9% of 4572 pregnant women examined by the bacteriological method. In 2014, out of 10857 urine samples of pregnant women, microbial flora was isolated in 12.2%; in 2015 - latent bacteriuria was revealed in 12.3% of the surveyed, and in 2016 this indicator was 13.0%.

As can be seen from Table 1, the leading etiological agent in latent bacteriuria of pregnant women in 2013 was *E. coli*, which was isolated in almost 71% of cases, the second most important is *Staphylococcus aureus* (7.8%).

Table 1. Microbial landscape of microorganisms isolated from urine of pregnant women for the period 2013-2016.

№	Type of microorganism	%			
		2013	2014	2015	2016
1	<i>Escherichia coli</i>	70.9	68.2	63.1	63.3
2	<i>Klebsiella pneumoniae</i>	3	2.7	2.8	3.0
3	<i>Enterobacter aerogenes</i>	2.7	2.6	1.8	1.7
4	<i>Proteus mirabilis</i>	1.5	1.3	1.4	1.6
5	<i>Proteus vulgaris</i>	0.8	0.8	0.6	0.7
6	<i>Acinetobacter spp.</i>	0.3	0.1	0.2	0.2
7	<i>Pseudomonas aeruginosa</i>	0.5	0.5	0.4	0.4
8	<i>Staphylococcus epidermidis</i>	2	6.7	4.4	3.3
9	<i>Staphylococcus saprophyticus</i>	1.1	4.4	0.4	0.3
10	<i>Staphylococcus haemolyticus</i>	4.7	0	4.5	5.5
11	<i>Staphylococcus aureus</i>	7.8	8.7	7.4	7.0
12	<i>Enterococcus faecalis</i>	3.9	3.7	7.8	9.3
13	<i>Streptococcus agalactiae</i>	0.8	0.3	5.2	3.7

A similar situation was obtained when analyzing the data of bacteriological examination of urine for 2014 - 2016 (table 1).

Analysis of the microbial landscape of the main etiopathogens of latent bacteriuria showed that the main pathogens are Gram-negative bacilli, which belong to the *Enterobacteriaceae* family (from 79.2% in 2013 to 70.5% in 2016) and to the *Pseudomonadaceae* family (0.5% and 0.4 % respectively). Gram-positive cocci are represented

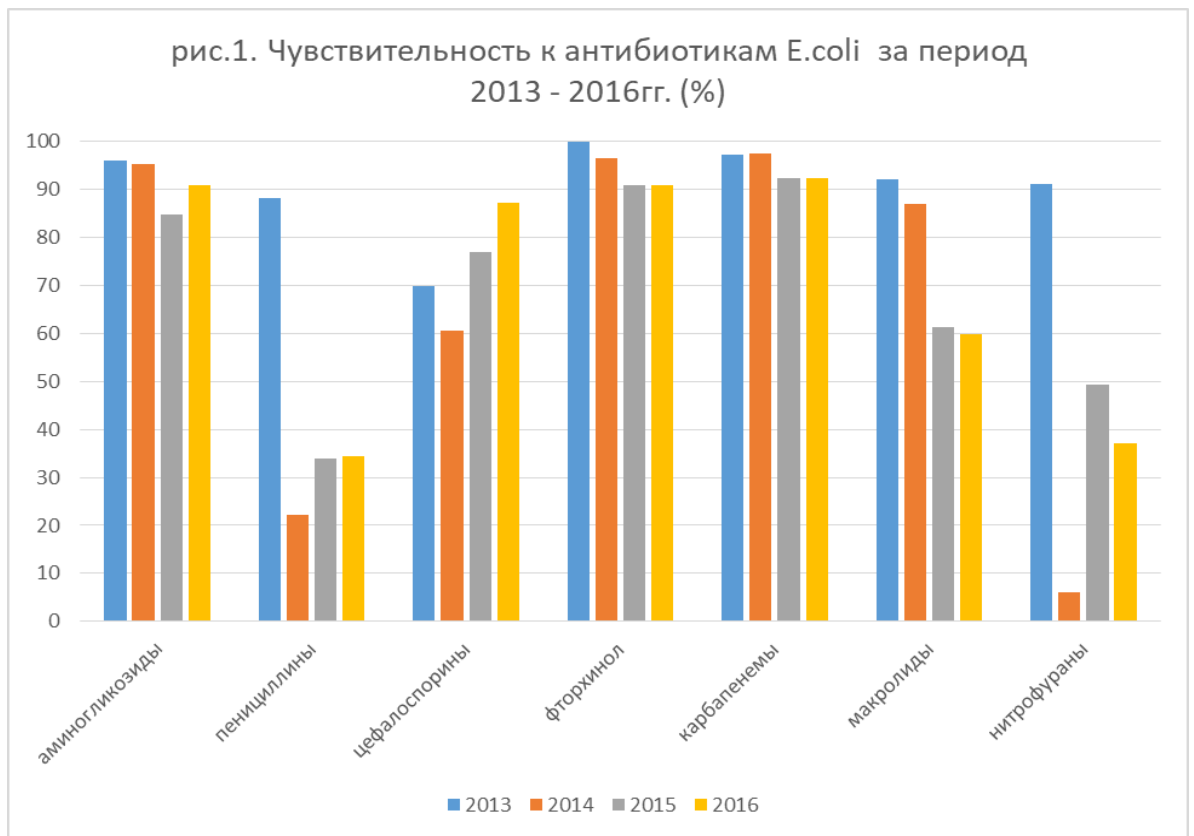
by three families - *Staphylococcaceae* (15.6 - 16.0%), *Streptococcaceae* (from 0.8% in 2013 to 3.7% in 2016) and *Enterococcaceae* (3.9% in 2013, 9 in 2016, 3%). Despite the leading role of *Escherichia coli* in the pathology of the urinary tract of pregnant women, there is a significant decrease in its etiological significance: if in 2013 *E. coli* was isolated in almost 71% of cases, then by 2016 its seeding rate was 63.3%. The sowing rate of *Enterobacter aerogenes* also decreases from 2.7% in 2013 to 1.7% in 2016. The rest of the *Enterobacteriaceae* family were sown with a stable frequency throughout the analyzed period.

Among staphylococci, the main causative agents of asymptomatic bacteriuria in pregnant women are *Staphylococcus aureus* and *Staphylococcus haemolyticus*. At the same time, the etiological significance of *Staphylococcus aureus* decreases from 7.8% in 2013 to 7.0% in 2016, against the background of an increase in the role of hemolytic staphylococcus (from 4.7% in 2013 to 5.5% in 2016) and epidermal staphylococcus (from 2.0% to 3.3%).

According to the literature, group B streptococcal infection is detected in 10-30% of pregnant women without the prior onset of symptoms. While streptococcal infection is not a threat to the mother, it can pose a serious threat to the child's health. One of the most dangerous gram-positive cocci belonging to group B streptococci is *Streptococcus agalactiae*, which can live on the mucous membrane of the digestive system, in the rectum and in the vagina. Thus, our studies have shown a 4.6-fold increase in the role of *Streptococcus agalactiae* in asymptomatic bacteriuria of pregnant women (0.8% in 2013, 3.7% in 2016) [8, 10, 11, 15].

When analyzing the sensitivity of the isolated members of the *Enterobacteriaceae* family to antibiotics, it was revealed that in 2013 98.8% of the isolated strains showed sensitivity to fluoroquinolones (ciprofloxacin). In the period 2014 - 2016, most of the isolated strains of enterobacteriaceae are sensitive to carbapenems (to imipenem - 96.7% and meropenem - 97.4% of the isolated strains).

The main etiological role in urinary tract infections is played by opportunistic microorganisms. These are *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus*, *Klebsiella*, *Serratia*, as well as staphylococci, streptococci, enterococci, *Candida* fungi and their associations. There are differences in the etiological structure of urinary tract infections depending on the gender of the patient. In women, there is a predominance of *E. coli* (up to 85%), in men, *Proteus* and *Pseudomonas aeruginosa* are more often excreted. Due to the fact that the purpose of our study is to examine the sensitivity to antibiotics of the main causative agents of latent bacteriuria in pregnant women, it was of interest to carry out a comparative analysis of the sensitivity by years of the isolated strains of *Escherichia coli* (fig. 1).



As can be seen from fig. 1, the sensitivity of *E. coli* to all groups of antibiotics gradually decreases over the entire analyzed period. There is a 2.5-fold decrease in the sensitivity of *E. coli* to penicillins and nitrofurans. At the same time, the sensitivity of the isolated *E. coli* strains to cephalosporins increases (1.3 times).

Staphylococcus in urine during pregnancy is a potential source of urinary tract infection. To this predispose hormones of pregnancy, causing changes in the urinary tract. As pregnancy progresses, the weight of the uterus puts pressure on the bladder, preventing it from emptying completely and increasing the risk of bacteria entering the bladder. Timely treatment is necessary to avoid complications that can lead to kidney infections. In this regard, we carried out a comparative analysis of the sensitivity of *Staphylococcus aureus* to antibacterial drugs (fig. 2).

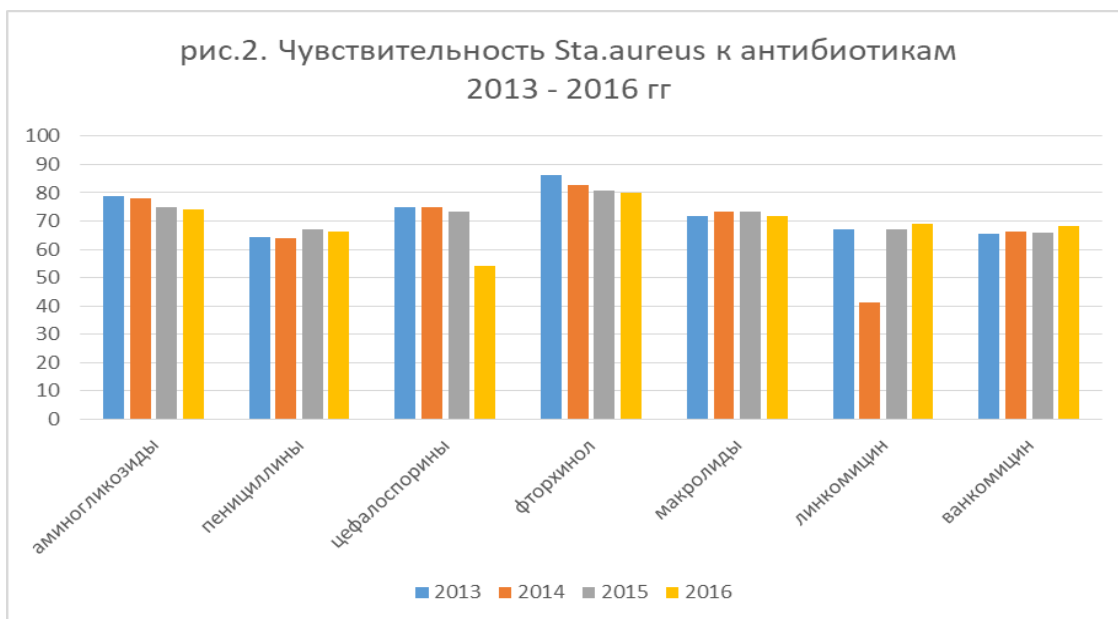
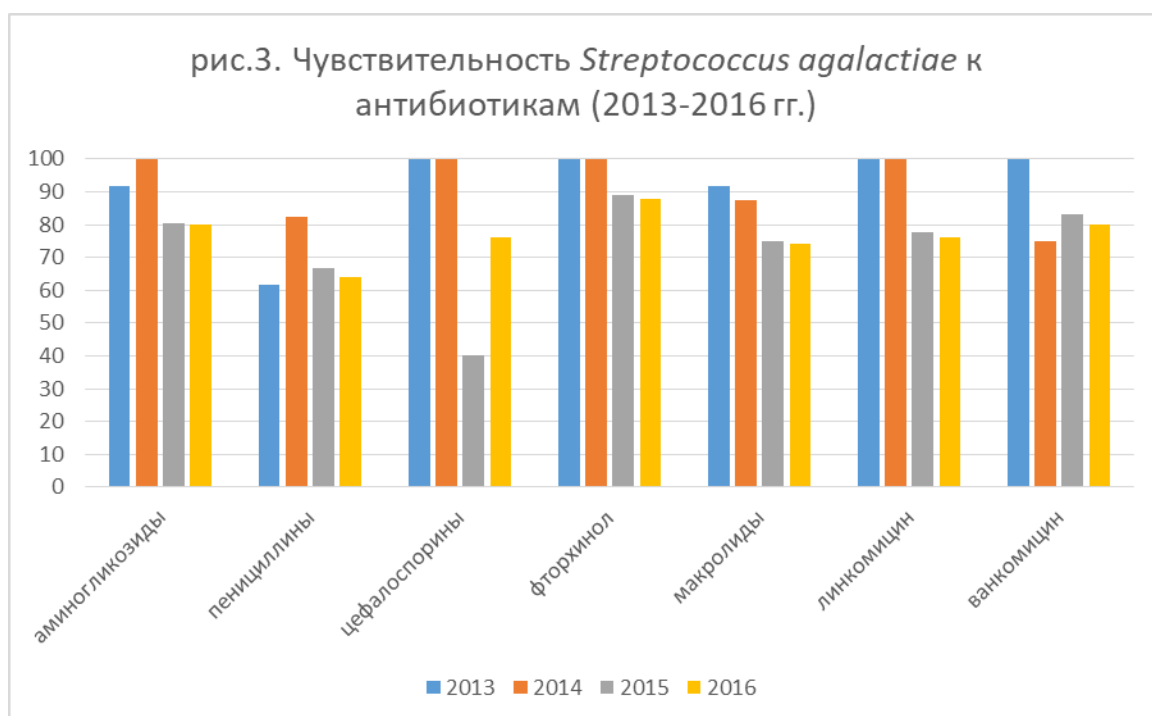


Figure 2 shows that the sensitivity of *Staphylococcus aureus* to cephalosporins for the period 2013 - 2016 decreases 1.4 times, and to fluoroquinolones - 1.1 times. At the same time, there is a slight increase in the sensitivity of this pathogen to lincomycin and vancomycin.

Group B streptococci are among the main causative agents of sepsis and meningitis in newborns. In adults, infections with group B streptococci are associated mainly with pregnancy and childbirth.



Infection with *Streptococcus agalactiae* can lead to the development of an ascending urogenital infection in the postpartum period in women, which is fraught with the development of sepsis. When analyzing the microbial landscape of urine in bacteriuria of pregnant women, a 4.6-fold increase in the etiological role of *Streptococcus agalactiae* in asymptomatic bacteriuria of pregnant women was obtained (2013 - 0.8%, 2016 - 3.7%). At the same time, the sensitivity of *Streptococcus agalactiae* to the main antibacterial drugs is gradually decreasing (fig. 3). So, in 2013 - 2014 there was 100% sensitivity to cephalosporins, and by 2016 it had decreased by 25%. A similar situation is observed with respect to lincomycin (2013 - 2014 - 100%, 2016 - 76%).

Based on the studies carried out, the following **conclusions** can be drawn:

1. The frequency of detection of latent bacteriuria of pregnant women during the analyzed period decreased by 3%.
2. The main causative agent of latent bacteriuria in pregnant women is *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus agalactiae*, and the etiological significance of *Streptococcus agalactiae* increased 4.6 times during the analyzed period.
3. An analysis of the sensitivity of the isolated members of the *Enterobacteriaceae* family to antibiotics showed that the vast majority of strains are sensitive to fluoroquinolones and carbapenems.
4. Gram-positive cocci showed sensitivity to fluoroquinolones and aminoglycosides.
5. Over the entire analyzed period, there is a gradual increase in the resistance of *E. coli* and *Streptococcus agalactiae* to all groups of antibiotics, *Staphylococcus aureus* - to cephalosporins and fluoroquinolones.

Thus, the main causative agents of asymptomatic bacteriuria in pregnant women are representatives of the Enterobacteriaceae family, in particular *E. coli*, which are sensitive to fluoroquinolones and carbapenems. From gram-positive cocci, staphylococci, including *Staphylococcus aureus*, and streptococci (Enterobacteriaceae *Streptococcus agalactiae*) were most often sown. Gram-positive cocci are sensitive to ciprofloxacin and penicillin. Further research is needed to assess the optimal duration of treatment for asymptomatic bacteriuria during pregnancy, taking into account the sensitivity of the isolated pathogen to antibiotics. In addition, taking into account the increased resistance of the main etiopathogens to antibacterial drugs, it is necessary to take cardinal measures to control the prescription and use of antibiotics, as well as to prohibit the over-the-counter sale of antibacterial drugs.

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