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ORIGINAL ARTICLE

PREVALENCE OF POSTPARTUM ENDOMETRITIS AND ANTIMICROBIAL RESISTANCE OF RESPONSIBLE PATHOGENS IN UKRAINE: RESULTS A MULTICENTER STUDY (2015-2017)

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ABSTRACT

The aim: To obtain the prevalence of postpartum endometritis women and antimicrobial resistance of responsible pathogens in Ukraine.

Materials and methods: We performed a retrospective multicenter cohort study. The study population consisted of all women who had a vaginal delivery or cesarean section in 14 Regional Women's Hospitals of Ukraine.

Results: Total 2460 of 25,344 patients were found to have postpartum endometritis, for an overall infection rate of 9.7%. The postpartum endometritis rates were 7.6% after vaginal delivery and 16.4% after cesarean section. Incidence of postpartum endometritis after cesarean section is affected mainly by the mode of delivery (scheduled caesarean deliveries (done before labor starts) – 13.8% and unscheduled caesarean deliveries (done after labor starts) – 22.5%. The predominant pathogens were: *Escherichia coli* (32.7%), *Enterococcus faecalis* (13.0%), *Streptococcus* spp. (12.1%), *Klebsiella* spp. (10.4%) and *Enterobacter* spp. (10%). Among the antimicrobial agents tested, the ertapenem, piperacillin/tazobactam, and cefotaxim were the most consistently active in vitro against Enterobacteriaceae in both vaginal deliveries and after cesarean section infections. The overall proportion of extended spectrum beta-lactamase (ESBL) production among Enterobacteriaceae was 22.8% and of methicillin-resistance in *Staphylococcus aureus* (MRSA) 15.4%. **Conclusions:** Postpartum endometritis and antimicrobial resistance of responsible pathogens presents a significant burden to the hospital system. Postpartum infections surveillance is required in all women's hospitals. This knowledge is essential to develop targeted strategies to reduce the incidence of postpartum infections.

KEY WORDS: Postpartum endometritis; vaginal delivery; cesarean section; antimicrobial resistance; pathogens

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INTRODUCTION

Bacterial infections during labour and the puerperium are among the leading causes of maternal morbidity and mortality worldwide [1, 2]. Postpartum endometritis is the most common infectious complications following childbirth and occurs in women from 1% to 30% [3-9]. This infection is more common after cesarean section than with vaginal delivery [10]. This is of particular concern as the number of Cesarean deliveries annually continues to rise and accounted for approximately 30% of all deliveries [11, 12]. Postpartum endometritis is also the major cause of prolonged hospital stay and comprise a large burden to health care system [9].

The epidemiology of postpartum endometritis is not well understood and remains underestimated because surveillance systems are often limited to the acute care setting. Bacterial postpartum endometritis is a polymicrobial infection usually involving two or three different organisms. It is often a mixed aerobic and anaerobic flora [3].

The resistance of bacteria to antibiotics increases and creates a therapeutic problem for doctors in the treatment of patients with postpartum endometritis. Guidelines encourage consideration of local bacterial resistance when prescribing antibiotics for postpartum infection treatment and prophylaxis [2, 3, 13, 14]. However, studies of postpartum infections and antimicrobial resistance of responsible pathogens are scant.

To identify postpartum endometritis prevention targets and reduce thus disparities between countries, ongoing surveillance is necessary. However, the epidemiology of postpartum endometritis in Ukraine and associated treatment outcomes are not well studied. National network for the surveillance of antimicrobial resistance is not in Ukraine [15, 16].

Resources are severely limited in country, creating difficulties implementing surveillance and establishing effective measures for infection control and postpartum infection prevention. This knowledge is essential to develop targeted strategies to reduce the incidence of postpartum infections. However, efforts to improve infection control training and begin postpartum infection surveillance have been underway. Previous reports of postpartum infection in Ukraine were limited.

THE AIM

The aim of this study was to obtain the first national estimates of the current prevalence rate of postpartum endometritis and antimicrobial resistance of responsible pathogens in Ukraine.

MATERIAL AND METHODS

STUDY DESIGN AND SETTING

A retrospective cohort study was based on surveillance data for Postpartum Endometritis and included all women's admitted to the 14 regional (tertiary) women's hospitals of Ukraine between January 1st, 2015 and December 31st, 2017. These hospitals provide care to individuals living within its catchment area (total 4 147 586 women's) and regularly take referrals from other (primary and secondary) hospitals. We have included women's hospitals that are similar in terms of medical equipment, personnel, and laboratory facilities. The hospitals had 1450 beds. All participating hospitals were required to have at least one full-time infection-control professional, a clinical microbiology laboratory with the capacity to process cultures. The follow-up of each patient was continued until discharge.

DEFINITION AND DATA COLLECTION

In our study the CDC/NHSN (Centers for Disease Control and Prevention/National Healthcare Safety Network, Atlanta, Georgia, USA) definition of endometritis was used. Postpartum endometritis as a healthcare-associated infection unless the amniotic fluid is infected at the time of admission or the patient was admitted more than 2 days after rupture of the membrane. (Day 1 = rupture day). Cesarean deliveries were classified as elective, urgent, or emergent by use of standardized criteria by the operative team. A standard data collection form was created to extract demographic and clinical data, microbiology (isolated pathogens and their antibiograms) and outcome information from routine patient records

MICROBIOLOGICAL SAMPLING AND SUSCEPTIBILITY TESTING

Uterine secretion samples were taken from women which clinical endometritis. Microbial isolates were identified using standard microbiological techniques, including automated microbiology testing (Vitek-2; bioMe'rieux, Marcy l'Etoile, France), and antibiotic susceptibility testing was performed by using the disk diffusion method (Kirby – Bauer antibiotic testing) according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) [17]. Strains showing inhibition zone diameters in the intermediate range were considered resistant.

ETHICS

The Shupyk National Medical Academy of Postgraduate Education (Kyiv, Ukraine) ethics committee approved the waiver of informed consent to participate in this study due to its retrospective design. All patient data were anonymised prior to the analysis. Ethical considerations including privacy of personal data were considered during all steps of the research.

STATISTICAL ANALYSIS

The incidence of Endometritis was reported as the percentage of the total number of patients. The analysis of statistical data was performed using Excel (Microsoft Corp., Redmond, WA, USA). Results are expressed as median (range), mean standard deviation for continuous variables, and number and corresponding percentage for qualitative variables. The primary endpoint was the epidemiology of Endometritis, pathogens and their resistance to antibiotics. Comparisons were undertaken using Student's t-test and Pearson's chisquared test or Fisher's exact test for categorical variables as appropriate. 'Statistical significance was defined as P<0.05.

RESULTS

PATIENT CHARACTERISTICS AND PREVALENCE OF POSTPARTUM ENDOMETRITIS

The study population consisted of 25,344 women's who underwent 19,326 vaginal deliveries and 6,018 cesarean sections. Mean cohort age was 25.2 years (standard deviation (SD) 5.5 years), 9811 (38.7%) were primiparous. During the study period (January 2015 and December 2017), 2460 of 25,344 patients were found to have postpartum endometritis, for an overall infection rate of 9.7% [95% CI 9.5 - 9.9]. The postpartum endometritis rates were 7.6% [95% CI 7.4 - 7.8] after vaginal delivery and 16.4% [95% CI 15.9 - 16.9] after cesarean section. Incidence of postpartum endometritis after cesarean section is affected mainly by the mode of delivery (scheduled caesarean deliveries (done before labor starts) - 13.8% [95% CI 13.3 - 14.3] and unscheduled caesarean deliveries (done after labor starts) - 22.5% [95% CI 21.5 - 23.5]. Characteristics of a cohort of women's admitted to the regional women's hospitals of Ukraine for delivery or postpartum care are presented in Table I.

ANTIBIOTIC PROPHYLAXIS

Of 6018 cesarean delivery participants who underwent chart review, 5471 (90.9%) were prescribed combination ceftriaxone and metronidazole postpartum, though there

Characteristics	Total cohort (n=25344)	Postpartum endometritis (n=2460)	Prevalence of postpartum endometritis [95% Cl ^b]
Age (years, mean, SD ^a)	25.2	22.6	
Age category			
<18	438 (1,7%)	118 (4.8%)	3.8 – 5.8
18-24	10868 (42,9%)	1257 (51.1%)	50.6 – 51.6
25-34	9304 (36,7%)	644 (26.2%)	25.7 – 26.7
35-44	3102 (12,2%)	313 (12.7%)	12.1 – 13.3
> 45	1632 (6,4%)	128 (5.2%)	4.7 – 5.8
Delivery mode			
Vaginal deliveries	19326 (76,3%)	1473 (7.6%)	7.4 – 7.8
Cesarean section	6018 (23,7%)	987 (16.4%)	15.9 – 16.9
Scheduled caesarean deliveries (done before labor starts)	4211 (70,0%)	581 (13.8%)	13.3 – 14.3
Unscheduled caesarean deliveries (done after labor starts)	1807 (30,0%)	406 (22.5%)	21.5 – 23.5
Total	25344 (100%)	2460 (9.7%)	9.5 – 9.9

Table I. Characteristics of a cohort of women's admitted to the regional women's hospitals of Ukraine for delivery or postpartum care (2015-2017) (P<0.05).

 $^{\rm a}{\rm CD}-{\rm standard\ deviation}$

 ${}^{\rm b}{\rm CI}$ – confidence interval

Table II. Bacterial pathogens detected in cases of postpartum endometritis in Ukrainian hospitals (2015-2017) (P<0.05)

	All pathogors	Postpartum	Postpartum endometrits			
Types of microrganisms	All pathogens (n=4879)	Cesarean section no. (%) of isolates	Vaginal deliveries no. (%) of isolates			
Aerobes	4417 (90.5%)	1189 (97.8%)	3228 (88.1%)			
Gram-positive cocci	1458 (29.9%)	458 (37.7%)	1000 (27.3%)			
Enterococcus faecalis	634 (13.0%)	222 (18.3%)	412 (11.2%)			
Streptococcus spp.	588 (12.1%)	84 (6.9%)	504 (13.8%)			
Staphylococcus aureus	236 (4.8%)	152 (12.5%)	84 (2.3%)			
Gram-negative bacilli	2959 (60.6%)	731 (60.1%)	2228 (60.8%)			
Escherichia coli	1594 (32.7%)	410 (33.7%)	1184 (32.3%)			
Klebsiella spp.	506 (10.4%)	65 (5.3%)	441 (12.0%)			
Enterobacter spp.	486 (10.0%)	92 (7.6%)	394 (10.8%)			
Proteus mirabilis	188 (3.9%)	42 (3.5%)	146 (4.0%)			
Pseudomonas aeruginosa	162 (3.3%)	106 (8.7%)	56 (1.5%)			
Acinetibacter spp.	23 (0.5%)	16 (1.3%)	7 (0.2%)			
Anaerobes	340 (7.0%)	25 (2.1%)	315 (8.6%)			
Bacteroides spp.	224 (4.6%)	14 (1.2%)	210 (5.7%)			
Clostridium spp.	74 (1.5%)	8 (0.7%)	66 (1.8%)			
Other	42 (0.9%)	3 (0.2%)	39 (1.1%)			
Fungi	122 (2.5%)	2 (0.2%)	120 (3.3%)			
Candida albicans	95 (1.9%)	2 (0.2%)	93 (2.5%)			
Other	27 (0.6%)	0	27 (0.7%)			
Total	4879	1216	3663			

Table III. Antibiotic susceptibilities (% susceptible) of aerobic Gram- negative bacteria isolated from patients with endometritis after cesarean section
(CS) and vaginal deliveries (VD) in Ukrainian woumen's hospitals (2015-2017).

Antibiotic	Escherichia coli (n=1594)		Klebsiella spp. (n=506)		Enterobacter spp. (n=486)		Proteus mirabilis (n=188)		P.aeruginosa (n=162)	
	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS
AMP	87.1	72.4	28.7	2.6	41.2	13.1	NT	NT	NT	NT
SAM	NT	NT	68.7	0	38.1	23.1	NT	NT	NT	NT
AMX	65.2	45.8	NT	NT	NT	NT	71.4	50.1	NT	NT
AMC	78.1	32.3	85.2	14.2	39.8	17.3	84.3	75.5	NT	NT
TIC	69.9	48.2	NT	NT	92.7	64.1	86.5	77.8	81.9	60.1
TZP	97.3	86.1	100	92.3	96.5	64.2	100	100	72.8	46.4
COL	NT	NT	100	97.0	100	95.7	NT	NT	100	98.5
CXM	71.1	61.8	88.7	20.4	77.4	43.5	NT	NT	NT	NT
CRO	74.2	68.7	78.9	22.6	65.9	40.9	NT	NT	NT	NT
СТХ	99.1	90.2	100	98.8	96.2	61.2	100	97.3	NT	NT
CAZ	88.7	71.7	94.5	21.8	96	36.4	100	97.5	78.6	25.9
FEP	92.1	78.3	86.7	24.2	100	40.7	100	77.6	51.2	20.3
IPM	100	100	84.7	40.2	100	61.5	100	100	88.4	33.4
MEM	NT	NT	NT	NT	NT	NT	NT	NT	100	100
EPM	100	100	100	100	100	100	100	100	100	100
AMK	97.1	95.6	88.6	65.5	100	80.8	100	100	84.7	48.4
NET	100	100	72.1	50.0	88.1	76.7	NT	NT	77.6	71.4
GEN	98.5	88.7	99.2	84.6	92.1	83.9	100	98.8	70.2	53.1
ATM	NT	NT	NT	NT	NT	NT	NT	NT	56.8	29.1
CIP	87.2	52.4	98.1	42.7	100	53.5	75	100	71.2	38.8
LVX	100	67.3	88.3	76.7	100	67	NT	NT	NT	NT
MFX	54.2	45.8	46.3	25.2	87.4	35.7	NT	NT	NT	NT
NOR	66.7	51.3	77.8	61.8	72.6	62.9	NT	NT	NT	NT
FOS	100	98.7	92.6	88.2	100	94.9	NT	NT	78.1	64.2
SXT	43.2	18.4	45.9	35.8	44.2	30.5	NT	NT	100	97.2
CFP	NT	NT	NT	NT	NT	NT	NT	NT	33.8	26.8

Notes:

AMP, ampicillin; SAM, ampicillin/sulbactam; AMX, amoxicillin; AMC, amoxicillin/clavulanic acid;

TIC, ticarcillin; TZP, piperacillin/tazobactam; COL, colistin; CXM, cefuroxime; CTX, cefotaxime;

CRO, ceftriaxone; CAZ, ceftazidime; FEP, cefepime; IPM, imipenem; MEM, meropenem;

EPM, ertapenem; AMK, amikacin; NET, netilmicin; GEN, gentamicin; ATM, aztreonam;

CIP, ciprofloxacin; LVX, levofloxacin; MFX, moxifloxacin; NOR, norfloxacin; FOS, fosfomycin;

CFP, cefoperazone, SXT, trimethroprim/sulfamethoxazole.

was little documentation of antibiotic receipt. Ceftriaxone and metronidazole was also prescribed for 1912/2460 (77.7%) participants meeting criteria for postpartum infections. Another 249/2460 (10.1%) had no antibiotic prescription, and 299/2460 (12.2%) were prescribed alternative antibiotic regimens. Overall, 5821/6018 (96.7%) women delivering by cesarean had a chart-documented prescription for β -lactam perisurgical antibiotic prophylaxis, including 2183/2460 (88.7%) of participants with postpartum infection. There were four in-hospitals maternal deaths, neither of which were due to infection.

MICROORGANISMS CAUSING OF POSTPARTUM ENDOMETRITIS

A total of 4879 different bacterial strains were isolated from 2460 women's with postpartum endometritis. In the present study, 5.7% samples did not show any microbial growth. Since these samples were taken from woumens showing clinical signs of endometritis, they cannot be bacteria-free. It is possible that the media/conditions used in the study were not favourable for the growth of micro-organisms present in these samples.

Aerobic gram-negative bacilli make up 60.6% and 29.9% gram-positive cocci from of all genital isolates.

VDCSVDCSVDCSPEN71.223.988.966.792.179.1AMP10084.261.350.088.971.6SAM10010010010084.773.9AMX92.482.110010084.773.9AMCNTNTNTNT72.566.7OXA92.177.2100100NTNTCRO63.458.666.458.6NTNTEPM10091.710091.7NTNTTEC10075.3NTNT100100AMK10097.110010088.755.2GEN10088.710010444.918.5NET84.577.410010088.755.2GEN10088.979.960.162.150.1LIN77.569.8NTNTNTNTAZM88.966.491.683.356.733.3VAN10010088.577.1100100100LIVXNTNT10010077.848.1CILNTNT10010077.848.1LIVXNTNT88.967.481.166.1CILNTNT88.967.481.166.1CILNTNT88.9 </th <th>Antibiotic</th> <th colspan="2">Staphylococcus aureus (n=236)</th> <th></th> <th>occus spp. 588)</th> <th colspan="2">Enterococcus faecalis (n=634)</th>	Antibiotic	Staphylococcus aureus (n=236)			occus spp. 588)	Enterococcus faecalis (n=634)	
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LIN77.569.8NTNTNTNTAZM88.966.491.683.356.733.3VAN10010088.577.1100100CIPNTNT10010077.848.1PEF10088.980.640.2NTNTMFX86.385.696.788.967.833.3LVXNTNT98.295.381.168.1CHLNTNT88.974.4NTNTFOS10010010010010099.6SXTNTNT95.175.2NTNT	GEN	100	88.7	100	14.4	71.0	37.1
AZM88.966.491.683.356.733.3VAN10010088.577.1100100CIPNTNT10010077.848.1PEF10088.980.640.2NTNTMFX86.385.696.788.967.833.3LVXNTNT98.295.381.168.1CHLNTNT88.974.4NTNTFOS10010010010099.6SXTNTNT95.175.2NTNT	CLI	79.9	88.9	79.9	60.1	62.1	50.1
VAN10010088.577.1100100CIPNTNT10010077.848.1PEF10088.980.640.2NTNTMFX86.385.696.788.967.833.3LVXNTNT98.295.381.168.1CHLNTNT88.974.4NTNTFOS10010010010099.6SXTNTNT95.175.2NTNT	LIN	77.5	69.8	NT	NT	NT	NT
CIPNTNT10010077.848.1PEF10088.980.640.2NTNTMFX86.385.696.788.967.833.3LVXNTNT98.295.381.168.1CHLNTNT88.974.4NTNTFOS10010010010099.6SXTNTNT95.175.2NTNT	AZM	88.9	66.4	91.6	83.3	56.7	33.3
PEF10088.980.640.2NTNTMFX86.385.696.788.967.833.3LVXNTNT98.295.381.168.1CHLNTNT88.974.4NTNTFOS10010010010099.6SXTNTNT95.175.2NTNT	VAN	100	100	88.5	77.1	100	100
MFX 86.3 85.6 96.7 88.9 67.8 33.3 LVX NT NT 98.2 95.3 81.1 68.1 CHL NT NT 88.9 74.4 NT NT FOS 100 100 100 100 99.6 SXT NT NT 95.1 75.2 NT NT	CIP	NT	NT	100	100	77.8	48.1
LVXNTNT98.295.381.168.1CHLNTNT88.974.4NTNTFOS10010010010010099.6SXTNTNT95.175.2NTNT	PEF	100	88.9	80.6	40.2	NT	NT
CHL NT NT 88.9 74.4 NT NT FOS 100 100 100 100 99.6 SXT NT NT 95.1 75.2 NT NT	MFX	86.3	85.6	96.7	88.9	67.8	33.3
FOS 100 100 100 100 99.6 SXT NT NT 95.1 75.2 NT NT	LVX	NT	NT	98.2	95.3	81.1	68.1
SXT NT NT 95.1 75.2 NT NT	CHL	NT	NT	88.9	74.4	NT	NT
	FOS	100	100	100	100	100	99.6
LNZ NT NT 100 98.7 100 99.7	SXT	NT	NT	95.1	75.2	NT	NT
	LNZ	NT	NT	100	98.7	100	99.7

Table IV. Antibiotic susceptibilities (% susceptible) of aerobic Gram-positive bacteria isolated from patients with endometritis after cesarean section (CS) and vaginal deliveries (VD) in Ukrainian woumen's hospitals (2015-2017).

Notes:

NT, no tested; PEN, penicillin; AMP, ampicillin; SAM, ampicillin/sulbactam; AMC, amoxicillin/clavulanic acid; AMX, amoxicillin; OXA, oxacillin; CRO, ceftriaxone; EPM, ertapenem; TEC, teicoplanin; AMK, amikacin; NET, netilmicin; GEN, gentamicin; CLI, clindamycin; LIN, lincomycin; AZM, azithromycin; VAN, vancomycin; CIP, ciprofloxacin; MFX, moxifloxacin; PEF, pefloxacin; LVX, levofloxacin; CHL, chloramphenicol; FOS, fosfomycin; SXT, trimethoprim/ sulfamethoxazole; LNZ, linezolid.

The predominant pathogens were: *Escherichia coli* (32.7%), *Enterococcus faecalis* 13.0%), *Streptococcus* spp. (12.1%), *Klebsiella* spp. (10.4%), *Enterobacter* spp. (10%), *Staphylococcus aureus* (4.8%), *Proteus mirabilis* (3.9%) and *Pseudomonas aeruginosa* (3.3%). The distribution of the microorganisms differed according to the after cesarean section or after vaginal deliveries of the infection (Table II).

In cesarean section patients, increased proportions of aerobic bacteria were observed with increased proportions of *Staphylococcus aureus* (12.5% vs. 2.3% in vaginal deliveries patients; P<0.01) and *Pseudomonas aeruginosa* strains (8.7% vs. 1.5% in vaginal deliveries patients; P<0.01), and *Enterococcus faecium* (7.1% vs. 1.0% in vaginal deliveries patients; P<0.02). Conversely, decreased proportions of *Klebsiella* spp. (5.3% vs. 12.0% in cesarean section patients,

P<0.05) and *Streptococcus* spp. were observed in cesarean section patients (6.9% vs. 13.8% in vaginal deliveries infection, P<0.01) and *Bacteroides* spp. were observed in cesarean section patients (1.2% vs. 5.7% in vaginal deliveries infection, P<0.02). When taking into account prior antibiotic therapy, we did not observe any change in the type or proportion of the cultured organisms, whatever the type of infection.

ANTIMICROBIAL RESISTANCE OF RESPONSIBLE PATHOGENS

Among the antimicrobial agents tested, the carbapenems (ertapenem) and piperacillin/tazobactam, and cefotaxim were the most consistently active in vitro against Enterobacteriaceae in both vaginal deliveries and after cesarean section infections (Table 3). The overall proportion of extended spectrum beta-lactamase (ESBL) production among Enterobacteriaceae was 22.8% and of methicil-lin-resistance in *S. aureus* (MRSA) 15.4%.

Against *P. aeruginosa*, the carbapenems (meropenem, ertapenem, imipenem), trimethroprim/sulfamethoxazole, amikacin and ticarcillin were the most active agents in vaginal deliveries infections, while meropenem, ertapenem, and trimethroprim/sulfamethoxazole were the most active agents in cesarean section infection cases (Table III). No vancomycin-resistance *E. faecalis* (VRE) strains were cultured. When taking into account the global activity against the Gram-positive bacteria, vancomycin, teicoplanin, linezolid and fosfomycin, were the most consistently active in vitro in both vaginal deliveries and cesarean section infections, due to the strains of *E. faecalis* (Table IV).

DISCUSSION

To our knowledge, this is the first national postpartum infections surveillance multicenter study in Ukraine, which describes prevalence of postpartum endometritis and antimicrobial resistance of responsible pathogens in Ukrainian hospitals. This study, performed over a short period of time (2015-2017), investigated the epidemiology endometritis in a mixed group of patients with endometritis after cesarean section and vaginal delivery infections. We assume that this descriptive study reflects 'real-life' conditions. The principal results of this study were a high incidence of postpartum endometritis, diversity of microorganisms isolated in cesarean section infections and decreased susceptibility among these strains. The results of antibiotic sensitivity test in our study indicated that he carbapenems (ertapenem) and piperacillin/tazobactam, and cefotaxim were the most consistently active in vitro against Enterobacteriaceae in both vaginal deliveries and after cesarean section infections. The overall proportion of extended spectrum beta-lactamase (ESBL) production among Enterobacteriaceae was 22.8% and of MRSA strains 15.4%. Against P.aeruginosa, the carbapenems (meropenem, ertapenem, imipenem), rimethroprim/ sulfamethoxazole, amikacin and ticarcillin were the most active agents in vaginal deliveries infections, while meropenem, ertapenem, and trimethroprim/sulfamethoxazole were the most active agents in cesarean section infection cases. Against the Gram-positive bacteria, vancomycin, teicoplanin, linezolid and fosfomycin, were the most consistently active in vitro in both vaginal deliveries and cesarean section infections, due to the strains of *E. faecalis*.

The estimates, postpartum endometritis occurs following 1-3% of vaginal births [3] and up to 30% of caesarean sections [3-9]. In a Cochrane review [4], the mean incidence of postpartum endometritis following elective cesarean section was 7% and after non-elective or emergency operations was 30%. In our study 9.7% patients were found to have postpartum endometritis. The postpartum endometritis rates were 7.6% after vaginal delivery and 16.4% after

cesarean section. Incidence of postpartum endometritis after cesarean section is affected by the mode of delivery deliveries and amounted to 13.8% after the planned cesarean section and 22.5% of unscheduled cesarean section.

According to the literature, the most common pathogenic organisms associated with postpartum endometritis include *Streptococcus* spp., *Staphylococcus* spp. (*S.aureus*, *S.epidermidis*), Gram-negative bacteria such as *E.coli*, *Klebsiella* spp., and *Proteus* spp., *Enterobacter* spp., and finally, anaerobes such as *Bacteroides* spp. [3, 18]. In our study the bacterial spectrum observed in patients with postpartum endometritis matches the previous reports.

Antibiotics are always indicated for endometritis [3]. Cochrane reviews and recommendations from the World Health Organization (WHO) support a combination of clindamycin and gentamicin as the optimal first-line antibiotic treatment [2, 3]. In our study, resistance of responsible pathogens in Ukrainian hospitals to clindamycin and gentamicin was 24.6% and 29.8%, respectively. Recommendations of Ukrainian Ministry of Health support a combination ceftriaxone and metronidazole for antibiotic treatment. During the study period, resistance to ceftriaxone was 36.4% (39.6% Gram-negative and 33.2% Gram-positive isolates). Therefore, the results of our study show that it is necessary to revise the recommendations for the use of clindamycin, gentamicin and ceftriaxone due to the high resistance of responsible pathogens of postpartum endometritis. Further research should address when and where antibiotic-resistant bacteria are acquired, infection outcomes, and local challenges in guideline implementation.

STRENGTHS AND LIMITATIONS

Strengths of our study include the cohort design, capturing all women's admitted to hospitals for delivery or postpartum care within the study period, and near-complete microbiologic evaluation of clinical endometritis using a reliable microbiology laboratory. The limitations of this study include its retrospective design and conduct at a 58.3% region (14 from 24) in Ukraine. The results may not be representative of other regions of Ukraine with different distributions of antimicrobial resistance of responsible pathogens of postpartum endometritis. However, there are no national surveillance data in Ukraine, which compelled us to rely entirely on data from the only existing national retrospective study of postpartum endometritis. This investigation provides valuable data as a first study for national surveillance of postpartum infections and potential comparison with data from other countries.

CONCLUSION

Postpartum endometritis and antimicrobial resistance of responsible pathogens presents a significant burden to the Ukraine hospital system. Optimizing the management and empirical antimicrobial therapy may reduce the burden of postpartum endometritis, but prevention is the key element. Knowledge about local data of resistance may contribute to limiting resistance and may have a significant role in designing effective antimicrobial stewardship policies. Strategic planning and implementation of postpartum infections surveillance is required in all women's hospitals.

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Conflict of interest:

The Authors declare no conflict of interest

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