ORIGINAL ARTICLE

PREVALENCE OF HEALTHCARE-ASSOCIATED CERVICITIS AND ANTIMICROBIAL RESISTANCE OF THE RESPONSIBLE PATHOGENS IN UKRAINE: RESULTS OF A MULTICENTER STUDY (2019-2021)

DOI: 10.36740/WLek202209202

Aidyn G. Salmanov[1,2], Irina M. Koctjuk[3], Olena K. Ihnatieva[1], Alla D. Vitiuk[1], Volodymyr Artyomenko[4], Ihor Paliga[5], Lidiya V. Suslikova[1]

[1]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE
[2]NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE, KYIV, UKRAINE
[3]NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSIA, UKRAINE
[4]ODESSA NATIONAL MEDICAL UNIVERSITY, ODESSA, UKRAINE
[5]ANDREI KRUPYNSKYI LVIV MEDICAL ACADEMY, LVIV, UKRAINE

ABSTRACT

The aim: To obtain the first estimates of the current prevalence of healthcare-associated cervicitis (HACs) and antimicrobial resistance of responsible pathogens in Ukraine.

Materials and methods: We conducted a retrospective multicentre cohort study was based on surveillance data from January 1st, 2019 to December 31st, 2021 in Ukraine. Antibiotic susceptibility testing was determined by Kirby–Bauer disc diffusion test according to the protocol of the European Committee on Antimicrobial Susceptibility Testing.

Results: Of the 6,885 participants in this study, 1746 women (25.5%) met the clinical definition of cervicitis. Prevalence of HACs and cervcits caused sexually transmitted pathogens were 12.7% and 8.3%, respectively. The incidence of HACs among women with a history of gynecological procedures was 25.4%. The main causes of HACs were legal induced abortions (28.8%), vaginal hysterectomy (23.9%), and postpartum instrumental examination (12.8%). The predominant pathogens of HACs were: *Escherichia coli*, *Enterobacter* spp., *Klebsiella* spp., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*. Methicillin-resistance was observed in 20.8% of *S. aureus* (MRSA). Vancomycin resistance was observed in 7.4% of isolated enterococci (VRE). Resistance to third-generation cephalosporins was observed in 13.1% *Klebsiella* spp. and *E.coli* 17.5% isolates. Carbapenem resistance was identified in 11.6% of *P.aeruginosa* isolates. The prevalence of ESBL production among *E. coli* isolates was significantly higher than in K. pneumoniae (33.5%, vs 8.7%). The overall proportion of extended spectrum beta-lactamases (ESBL) production among *Enterobacteriaceae* was 34.6%.

Conclusions: This study showed that the prevalence of healthcare-associated cervicitis in Ukraine is high, and many cases were caused by antibiotic-resistant pathogens.

KEY WORDS: pelvic inflammatory disease, healthcare-associated cervicitis, prevalence, risk factors, antimicrobial resistance, Ukraine

Wiad Lek. 2022;75(9 p2):2189-2197

INTRODUCTION

Reproductive tract infections in female are common worldwide and represent a major public health problem with high morbidity, mortality and cost implications [1-4]. One of these diseases is a cervicitis. Cervicitis is the inflammation of the cervix. Inflammation is localised mainly in the columnar epithelial cells of the endocervical glands, but it can also affect the squamous epithelium of the ectocervix [5]. Despite the fact that there are not many studies on cervicitis, it is estimated that it is a common condition, with prevalence's as high as 20–40% in women [6].

A significant association has been found between cervicitis and the risk of affect the upper genital tract, such as endometritis and pelvic inflammatory disease (PID), infertility and adverse effects in pregnancy and birth, including ectopic pregnancy, premature rupture of membranes, spontaneous abortion, premature birth, and childhood morbidity [7-10]. Approximately 40% of cases of spontaneous preterm birth (sPTB) are associated with ascending intrauterine infections [11]. Previous studies have established bacterial (i.e., chlamydia, gonorrhea, mycoplasma, etc.) and viral infections (i.e., herpesviruses and human papillomaviruses) as risk factors of PTB [11]. However, the exact mechanism leading to PTB is still unknown. It is also reported that chronic inflammation of the cervix could contribute to the development of cervical cancer [12], In addition, cervicitis is thought to play an important role in the transmission of HIV infection, by increasing susceptibility to HIV infection and increased HIV viral shedding [13].

Cervicitis is a frequently asymptomatic, inflammatory condition of the cervix. It is common with rates as high as 30–45% in some clinic populations [6, 8]. Cervicitis can persist or recur after completing one or several cycles of antibiotic treatment [14]. This raises concerns about the appropriateness of empirical treatments currently

used to treat women with cervicitis. A lack of consensus on definitive treatments for cervicitis treatment guidelines reflects these uncertainties, with the potential for over-use of antibiotics. The clinical significance of the finding of cervicitis, especially in asymptomatic, has been debated.

There are multiple agents, as infectious and non-infectious, potentially involved in cervicitis. Most research focuses on infectious agents that are sexually transmitted and other potentially involved genital tract microorganisms [5]. According to literature, organisms variably implicated in the pathogenesis of cervicitis include *Chlamydia trachomatis, Neisseria gonorrhoeae*, *Trichomonas vaginalis, Mycoplasma genitalium, Mycoplasma hominis, Ureaplasma parvum*, *Ureaplasma urealyticum*, bacterial vaginosis, *Herpes simplex virus* (HSV), *Cytomegalovirus* (CMV), and adenovirus [5, 15-17]. *Chlamydia* and *N.gonorrhoea* account for less than half of cervicitis cases, with a largely undefined aetiology in the remainder, referred to as nonchlamydial, nongonococcal cervicitis or nonspecific cervicitis. The etiology in a high percentage of women in whom none of the known pathogens are found is still unknown. At the same time, the role of opportunistic gram-positive and gram-negative organisms, which are the main pathogens of reproductive tract infections in female, in the pathogenesis of cervicitis has not been sufficiently studied.

The prevalence of cervicitis associated with gynecological surgery is still not well known, in part due to the lack of surveillance for these infections. The importance of detection cervicitis and correct treatment lies in the fact that silent infection can result in complications such as salpingitis, endometritis and PID and have severe consequences in pregnant women. However, wide variations of case definition, study populations and methods for pathogen isolation hinder the ability to draw conclusions on the aetiology, natural history and best management of cervicitis on a population basis [18]. Most prevalence studies have been carried out in risk populations, mainly in patients from sexually transmitted infections clinics, which imply a bias and limits the conclusions with respect to the frequency of cervicitis associated with gynecological surgery or other medical procedures in the general population. Similar studies have not been conducted in Ukraine.

THE AIM

The aim of this study was to obtain the first estimates of the current prevalence of healthcare-associated cervicitis and antimicrobial resistance of responsible pathogens in Ukraine.

MATERIALS AND METHODS

DESIGN AND STUDY POPULATION

We conducted a retrospective multicentre cohort study was based on surveillance data for reproductive tract infection in female from January 1st, 2019 to December 31st, 2021 in Ukraine. The study population comprised women 17–45 years of age who were seeking health care at 10 women's health clinics (located in Odessa, Ivano-Frankivsk, Vinnytsia, Volyn, Rivne, Chernivtsi, Lviv, Poltava, Cherkasy, Zhytomyr, Chernihiv, Dnipropetrovsk, and Kyiv, Ukraine) and a 6 clinics for the management of sexually transmitted diseases (located in Kyiv and Odessa, Ukraine). From each clinic, we studied a group of women referred for suspected mucopurulent cervicitis and a representative sample of other women attending the clinic. All participants in this study were local residents. Criteria for exclusion from the study included pregnancy, current menses, concomitant vulvovaginal candidiasis, use of intravaginal or systemic antimicrobials during the week before enrollment, and the presence of an intrauterine device.

DEFINITIONS

In this study healthcare-associated cervicitis are infections in women get while they are receiving health care for another reproductive tract condition. Cervicitis was defined as the presence of either mucopurulent (yellow) endocervical discharge and/or endocervical bleeding (graded as "moderate" or "severe," as defined by the clinician) induced by gentle passage of a cotton swab. In addition, cervical infection must occur 48 hours after gynecological procedures. Cervicitis can happen in any health care facility, including hospitals and ambulatory centers. From the clinical point of view, cervicitis among women was classified as acute or chronic. In our study 'Thin' means that Body Mass Index (BMI) is less than 18.5 kg/m^2. 'Normal' means 18.5 kg/m2≤ BMI < 24 kg/m^2. 'Overweight' means 24 kg/m^2≤ BMI < 28 kg/m^2. 'Obesity' means that BMI is more than 28 kg/m^2.

Table I. Distribution of healthcare-associated cervicitis by type of gynecological procedures in Ukraine (2019-2021)

Characteristics of procedure	Number of women (n)	Healthcare-associated cervicitis				95% CI
		No		Yes		
		n	%	n	%	
Legal induced abortions	2043	1455	71,2	588	28,8	28.0 – 29.6
Vaginal hysterectomy	961	732	76,1	229	23,9	23.2 – 24.6
Postpartum instrumental examination	438	382	87,2	56	12,8	12.2 – 13.4
Total	3442	2569	74,6	873	25,4	24.7 – 26.1

CI. Confidence interval

Table II. Characteristics of women with healthcare-associated cervicitis in Ukraine (2019-2021)

Characteristucs	All (n=3,442)	Healthcare-associated cervicitis				p-value
		No		Yes		
		n	%	n	%	
Age (years)						
17-21	1,.178	814	31.7	364	41.7	< 0.001
22-26	670	427	16.6	243	27.8	
27-31	428	320	12.5	108	12.4	
32-36	810	711	27.7	99	11.3	
37-41	197	148	5.8	49	5.6	
42-45	159	149	5.8	10	1.1	
Place of residence						
Urban	1,804	1,357	52.8	447	51.2	0.523
Rural	1,638	1,212	47.2	426	48.8	
Occupation						
Unemployed	468	333	13.0	135	15.5	0.517
Head of enterprises	486	356	13.9	130	14.9	
Professional worker	1,264	967	37.6	297	34.0	
Clerk	131	108	4.2	23	2.6	
Service worker	472	355	13.8	117	13.4	
Agricultural and related worker	90	63	2.5	27	3.1	
Operator	45	36	1.4	9	1.0	
Other	486	351	13.7	135	15.5	
Education						
Primary	486	338	13.2	148	17.0	0.374
High school	522	409	15.9	113	12.9	
Junior college degree	756	575	22.4	181	20.7	
Bachelor's degree and above	1,678	1,247	48.5	431	49.4	
Smoking						
No	45	36	1.4	9	1.0	0.564
No, secondhand smoke	801	598	23.3	203	23.2	
Yes	2,596	1,935	75.3	661	75.7	
Drinking						
No	400	333	13.0	67	7.7	0.072
Yes	3,042	2,236	87.0	806	92.3	
BMI (kg/m^2)						
Thin	248	176	6.9	72	8.2	0.454
Normal	2,173	1,651	64.3	522	59.8	
Overweight	778	562	21.9	216	24.7	
Obese	243	180	7.0	63	7.2	
Irregular menstruation						
No	2,362	1,786	69.5	576	66.0	0.218
Yes	1,080	783	30.5	297	34.0	
Married						
No	1,948	1,458	56.8	490	56.1	0.561
Yes	1,494	1,111	43.2	383	43.9	
Unmarried						

No	1,714	1,358	52.9	356	40.8	0.047
Yes	1,728	1,211	47.1	517	59.2	
History of PID						
No	3,091	2,394	93.2	697	79.8	< 0.001
Yes	351	175	6.8	176	20.2	
The presence of an intrauterine device						
No	1,300	913	35.5	387	44.3	0.009
Yes	2,142	1,656	64.5	486	55.7	
History of endometriosis						
No	3,348	2,515	97.9	833	95.4	0.041
Yes	94	54	2.1	40	4.6	
Bacterial vaginosis	3,442	2,569		873		
No	3,262	2,497	97.2	765	87.6	< 0.001
Yes	180	72	2.8	108	12.4	
Total	3,442	2,569	74.6	873	25.4	

BMI, Body Mass Index
PID, Pelvic Inflammatory Disease

Table III. Logistic multivariate regression analyses of risk factors for healthcare-associated cervicitis in Ukraine (2019-2021)

Characteristics	*p*-value	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)
Age (years)				
	< 0.001		< 0.001	
17–21		Ref		Ref
22-26	0.003	9.379 (2.165–40.619)	0.011	6.862 (1.557–30.247)
27–31	0.012	6.618(1.549–28.274)	0.031	5.036 (1.163–21.83)
32–36	0.025	5.577 (1.244–25.011)	0.109	3.49 (0.758–16.071)
37–41	0.035	5.50 (1.131–26.752)	0.174	3.096 (0.607–15.797)
42–45	0.269	2.297(0.515–10.249)	0.587	1.523 (0.335–6.943)
History of endometriosis				
No		Ref		Ref
Yes	0.041	5.53 (1.136–26.781)	0.173	3.093 (0.608–15.792)
The presence of an intrauterine device				
No		Ref		Ref
Yes	0.009	3.623 (2.231–5.841)	< 0.001	3.081 (1.816–5.157)
History of PID				
No		Ref		Ref
Yes	< 0.001	3.611 (2.234–5.831)	< 0.001	3.063 (1.819–5.158)
Bacterial vaginosis				
No		Ref		Ref
Yes	< 0.001	5.131 (2.662–9.878)	< 0.001	3.835 (1.908–7.712)
Constant			0.003	0.109

OR, Odd Ratio
PID, Pelvic Inflammatory Disease

DATA COLLECTION

This study includes interviews and questionnaires of women's, also analyses medical records. We formed a working group to conduce this research, which included obygyne specialists (nurses and physicians). After written, informed consent was obtained from each woman, the women were interviewed about their medical history. Women were approached face-to-face in medical clinics conversation to

Table IV. Antibiotic susceptibility of gram-positive bacteria isolated from women with healthcare-associated cervicitis in Ukraine (2019-2021)

Antibiotic	*S. aureus* (n=103)		*S.epidermidis* (n=52)		*Streptococcus* spp. (n=39)		*E. faecalis* (n=80)	
	S	R	S	R	S	R	S	R
PEN	28.3	71.7	30.7	69.3	35.2	64.8	72.9	27.1
AMP	81.7	18.3	89.2	10.8	48.3	51.7	88.1	11.9
SAM	88.9	17.1	78.6	21.4	94.1	5.9	38.8	61.2
OXA	79.2	20.8	81.3	18.7	NT	NT	NT	NT
CXM	68.8	31.2	81.5	18.5	86.2	13.8	NT	NT
CRO	81.5	18.5	86.2	13.8	94.1	5.9	NT	NT
EPM	NT	NT	NT	NT	NT	NT	100.0	0
GEN	87.4	12.6	91.5	8.5	91.2	8.8	81.1	18.8
AMK	92.4	7.6	100.0	0	95.9	4.1	76.8	23.2
CLI	83.5	16.5	78.8	21.2	89.8	16.2	11.9	88.1
AZM	65.9	34.1	71.6	28.4	68.8	31.2	84.9	15.1
VAN	100.0	0	100.0	0	NT	NT	92.6	7.4
CIP	78.3	21.7	NT	NT	NT	NT	91.1	8.9
LVX	83.7	16.3	74.2	25.8	87.2	12.8	92.8	7.2
LNZ	100.0	0	100.0	0	99.8	0.2	100.0	0

R, resistant isolates (%); S, susceptible isolates (%); NT, no tested; NT, no tested;
PEN, penicillin; AMP, ampicillin; SAM, ampicillin/sulbactam; OXA, oxacillin; CXM, cefuroxime; CRO, ceftriaxone; EPM, ertapenem; GEN, gentamicin; AMK, amikacin; CLI, clindamycin; AZM, azithromycin; VAN, vancomycin; CIP, ciprofloxacin; LVX, levofloxacin; LNZ, linezolid.

complete the standardised and structured questionnaire by trained interviewers. The next step was to complete the paper questionnaires, which contained a series of questions, including basic information, medical history, and personal lifestyle habits, under the guidance of this specialist. In our study adopted double entry mode of paper questionnaire data and were analysed anonymously. In addition, all patients underwent a standardized physical examination, including speculum examination and visual inspection and collection of endocervical fluid for cultural microbiological analysis. Current douching and smoking were defined as douching and smoking that occurred during the month before enrollment, and sexual practices were assessed by asking subjects to estimate the recent frequency of and the time to last occurrence of specific behaviors.

MICROBIAL ANALYSIS

Two endocervical and two vaginal swabs were collected and processed. Endocervical swab specimens were collected and used for aerobic and anaerobic cultures, as well as for antibiotic susceptibility testing. Swab specimens obtained for culture were immediately placed into Port-a-Cul anaerobic transport tubes (Becton Dickinson), which were held and transported at room temperature to the laboratory and were prepared for culture immediately on receipt. In this study species identification was performed with standard microbial methods. In this study bacterial species identification was performed with standard microbial methods. Antibiotic susceptibility testing of bacteria was determined by Kirby–Bauer disc diffusion test according to the protocol of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (http://eucast.org). Methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE) were defined by resistance to oxacillin and vancomycin respectively. Multidrug resistance (MDR) for *Acinetobacter* spp. and *Pseudomonas aeruginosa* was defined in accordance with published definitions, which were used in NHSN AMR report [19]. An isolate of *Acinetobacter* spp was defined as having MDR if it tested nonsusceptible to at least 1 drug in 3 of the following 6 antimicrobial agents/groups: piperacillin or piperacillin/tazobactam, extended-spectrum cephalosporins (cefepime or ceftazidime), aminoglycosides, ampicillin/sulbactam, carbapenems, and fluoroquinolones. For *P. aeruginosa* isolates, MDR was defined as testing nonsusceptible (ie, either resistant or intermediate) to at least 1 drug in 3 of the 5 following antimicrobial groups: piperacillin or piperacillin/tazobactam, extended-spectrum cephalosporins (cefepime or ceftazidime), fluoroquinolones, aminoglycosides, and carbapenems. Multi-drug resistance for *Klebsiella pneumoniae* and *Escherichia coli* was defined as being non susceptible to at least 1 drug in 3 antimicrobial agents/groups [20].

ETHICS

Ethical clearance for this study was obtained from the ethics committee of the Shupyk National Healthcare University of Ukraine. This study was performed in line with the principles

Table V. Antibiotic susceptibility of gram-negative bacteria isolated from women with healthcare-associated cervicitis in Ukraine (2019-2021)

Antibiotic	*E. coli* (n=548)		*Enterobacter* spp. (n=129)		*Klebsiella* spp. (n=105)		*Proteus* spp. (n=55)		*P. aeruginosa* (n=84)	
	S	R	S	R	S	R	S	R	S	R
AMX	65.2	34.8	NT	NT	NT	NT	70.4	29.6	NT	NT
AMC	78.1	21.9	39.8	60.2	85.2	14.8	84.3	15.7	NT	NT
TIC	69.9	30.1	92.7	7.3	NT	NT	86.5	13.5	81.9	18.1
TZP	96.3	3.7	96.5	3.5	100.0	0	100.0	0	77.2	22.8
CXM	63.8	36.2	77.4	22.6	87.6	12.4	NT	NT	NT	NT
CTX	87.1	12.9	96.1	3.9	88.3	11.7	98.8	1.2	NT	NT
CRO	72.2	27.8	65.9	34.1	73.9	26.1	NT	NT	NT	NT
CAZ	91.4	8.6	96.2	3.8	92.1	7.9	94.5	5.5	87.8	12.2
FEP	93.3	6.7	100.0	0	77.6	22.4	96.7	3.3	51.2	48.8
IPM	87.1	12.9	100.0	0	91.3	8.7	98.3	1.7	84.6	15.4
MEM	NT	NT	NT	NT	NT	NT	NT	NT	91.3	8.7
EPM	100.0	0	100.0	0	100.0	0	100.0	0	100.0	0
GEN	94.5	5.5	91,2	8.8	91.2	8.8	98.8	1.2	63.8	36.2
AMK	89.4	10.6	92.7	7.3	82.6	17.4	100.0	0	84.7	15.3
CIP	87.2	12.8	98.6	1.4	95.1	4.9	75.1	24.9	81.2	18.8
LVX	67.3	32.7	78.7	21.3	92.7	7.3	NT	NT	NT	NT
CFP	NT	NT	NT	NT	NT	NT	NT	NT	66.2	33.8

R, resistant isolates (%); S, susceptible isolates (%); NT, no tested; NT, no tested;
AMX, amoxicillin; AMC, amoxicillin/clavulanic acid; TIC, ticarcillin; TZP, piperacillin/tazobactam; CXM, cefuroxime; CTX, cefotaxime; CRO, ceftriaxone; CAZ, ceftazidime; FEP, cefepime; IPM, imipenem; MEM, meropenem; EPM, ertapenem; GEN, gentamicin; AMK, amikacin; CIP, ciprofloxacin; LVX, levofloxacin; CFP, cefoperazone.

of the Declaration of Helsinki. Informed consent was obtained from all subjects involved in the study. Participants' data were anonymised prior to the analysis, and each had a unique identification number assigned to protect their privacy.

STATISTICAL ANALYSIS

In this study all clinical and microbiological data were entered in an Excel (Microsoft Corp., Redmond, WA, USA) database for statistical analysis. Results are expressed as median (range), mean standard deviation for continuous variables, and number and corresponding percentage for qualitative variables. Proportions of total cervicitis cases meeting specific criteria were calculated, and characteristics of each category were compared by using Fisher exact test. Multivariable analysis was done including all the potential risk factors. Standard techniques for continuous variables and an unadjusted chi-square test for binary variables were used for the univariate analysis. All statistical analyses were 2-sided and significance was set at $p<0.05$.

RESULTS

PREVALENCE OF CERVICITIS

Between January 2019 and December 2021, 6852 women participated in the study. Of these, 1746 women (25.5%) met the clinical definition of cervicitis. Prevalence of healthcare-associated cervicitis and cervcits caused sexually transmitted pathogens were 12.7% [95% confidence interval (CI), 12.3-13.1] and 8.3% (95% CI, 8-8.6%), respectively. The etiology of 4.4% (301/6852) cases cervicitis was unknown. The incidence of healthcare-associated cervicitis among women with a history of gynecological procedures was 25.4% (95% CI, 24.7-26.1%). From data obtained, the main causes of healthcare-associated cervicitis were legal induced abortions (28.8%, 95% CI, 28.0-29.6), vaginal hysterectomy (23.9%, 95% CI, 23.2-24.6), and postpartum instrumental examination (12.8%, 95% CI, 12.2-13.4). The characteristics of these procedures are presented in Table I.

PATIENT CHARACTERISTICS AND RISK FACTORS

In this study the difference in the age, history of endometriosis, the presence of an intrauterine device, history of PID, and bacterial vaginosis between the two groups were statistically significant ($p < 0.05$). The healthcare-associated cervicitis rate rose initially and then decreased for every 4 years added to women's age. Women aged 17-21 years and 22-26 years had the highest healthcare-associated cervicitis rate. When the participants our study were grouped by age the healthcare-associated cervicitis rate increased as the age. It was found that among those women who had healthcare-associated cervicitis , more were from rural than

urban. Among healthcare-associated cervicitis women 67.3% went to clinc seeking medical help regardless of the outcome after treatment. Characteristics of women with healthcare-associated cervicitis and risk factors are presented in Table II.

In this study Table III showed the odds ratio (OR) and 95% confidence interval (CI) for the risk factors associated with cervicitis in logistic multivariate regression analyses. Healthcare-associated cervicitis was associated with age as shown in logistic regression analysis. Also, history of PID, bacterial vaginosis, the presence of an intrauterine device, and history of endometriosis was associated with healthcare-associated cervicitis. There were differences among factors associated with cervicitis. In our study the risk factors associated with cervicitis were age of women (< 0.001), history of PID (< 0.001), the presence of an intrauterine device (p= 0.009), bacterial vaginosis (< 0.001), and history of endometriosis (p=0.041).

RESPONSIBLE PATHOGENS AND ANTIMICROBIAL RESISTANCE

In this study a total of 1208 different bacterial strains were isolated from 873 women's with healthcare-associated cervicitis. Aerobic Gram-negative bacilli make up 77.5% and 22.5% Gram-positive cocci from of all isolates. The predominant pathogens were: *Escherichia coli* (45.4%), *Enterobacter* spp. (10.7%), *Klebsiella* spp. (8.7%), *Staphylococcus aureus* (8.5%), *Pseudomonas aeruginosa* (7%), *Enterococcus faecalis* (6.6%), *Proteus* spp. (4.6%), *Staphylococcus epidermidis* (4.3%), followed by *Streptococcus* spp. (3.2%) and *Acenetobacter* spp. (1.1%).

Antimicrobial susceptibility tests were performed on a total of 274 isolates of Gram-positive cocci and 934 Gram-negative organisms. In present study the antimicrobials used in antimicrobial susceptibility testing included those commonly used as therapeutic agents. Varying degrees of resistance to most antibiotics tested were found. The antibiotic susceptibility profiles of isolates from women's with healthcare-associated cervicitis are presented in Table IV and Table V.

In this study the overall proportion of methicillin-resistance was observed in 20.8% of *S. aureus* (MRSA). Vancomycin resistance was observed in 7.4% of isolated enterococci (VRE). Resistance to third-generation cephalosporins was observed in 13.1% *Klebsiella* spp. and *E.coli* 17.5% isolates. Carbapenem resistance was identified in 11.6% of *P.aeruginosa* isolates. The prevalence of ESBL production among *E. coli* isolates was significantly higher than in *K. pneumoniae* (33.5%, vs 8.7%). The overall proportion of extended spectrum beta-lactamases (ESBL) production among *Enterobacteriaceae* was 34.6%.

DISCUSSION

This study presents the first estimates data on prevalence of healthcare-associated cervicitis and antimicrobial resistance of responsible pathogens in Ukraine. I during study period was identified a high level of cervicitis (25.5%) in women. I during study period was identified a high level of cervicitis (25.5%) in women. Prevalence of healthcare-associated cervicitis and cervcits caused sexually transmitted pathogens were 12.7% and 8.3%, respectively. The etiology of 4.4% cases cervicitis was unknown. The incidence of healthcare-associated cervicitis among women with a history of gynecological procedures was 25.4%. The main causes of healthcare-associated cervicitis were legal induced abortions (28.8%), vaginal hysterectomy (23.9%), and postpartum instrumental examination (12.8%). In our study age of women (< 0.001), history of PID (< 0.001), the presence of an intrauterine device (p= 0.009), bacterial vaginosis (< 0.001), and history of endometriosis (p=0.041) were associated with a higher risk of contracting a healthcare-associated cervicitis. The risk factors identified in this study are consistent with previous studies [4].

The prevalence of healthcare-associated reproductive tract infection in women varies from country to country and ranges from 1.8% [21] to 48% [22]. However, the available literature does not contain data on the prevalence of healthcare-associated cervicitis in Ukraine and other countries. Therefore, we were unable to compare our results with other studies in other countries.

In this study the predominant pathogens of healthcare-associated cervicitis were: *E. coli, Enterobacter* spp., *Klebsiella* spp., *S. aureus, P. aeruginosa*, *E. faecalis*, *Proteus* spp. *S. epidermidis,* followed by *Streptococcus* spp. and *Acenetobacter* spp. Our results was coherent with reports other studies that focus on female healthcare-associated PID [4, 22-24].

In the past several years, the generally understanding of cervicitis has extended beyond the recognition of *C. trachomatis*, *N. gonorrhoeae*, *T. vaginalis*, HSV, *M.genitalium*, and bacterial vaginosis as the prime etiologic suspects. However, major gaps in our knowledge of this common condition remain. Putative etiologic agents have not been identified in many women with cervicitis. Moreover, cervicitis occurs in a relatively small proportion of women with chlamydia or gonorrhea [6]. Whereas *Chlamydia*, *N. gonorrhoea* and syphilis have been extensively examined, there remains a paucity of knowledge of healthcare-associated cervicitis, an arguably more prevalent but poorly characterized condition with uncertain clinical implications. In addition, scant research has addressed the clinical response of nonchlamydial and nongonococcal cervicitis to antibiotic therapy.

Increasing broad-spectrum antibiotic usage with associated emergence of antimicrobial resistance reinforces the need for targeted antibiotic therapies, including the management of cervicitis. However, a lack of consensus on definitive treatments for cervicitis treatment guidelines reflects uncertainties, with the potential for over-use of antibiotics. This raises concerns about the appropriateness of empirical treatments currently used to treat women with cervicitis.

In our study the overall proportion of methicillin-resistance was observed in 20.8% of *S. aureus* (MRSA). Vancomycin

resistance was observed in 7.4% of isolated enterococci (VRE). Resistance to third-generation cephalosporins was observed in 13.1% *Klebsiella* spp. and *E.coli* 17.5% isolates. Carbapenem resistance was identified in 11.6% of *P.aeruginosa* isolates. The prevalence of ESBL production among *E. coli* isolates was significantly higher than in *K. pneumoniae* (33.5%, vs 8.7%). The overall proportion of extended spectrum beta-lactamases (ESBL) production among *Enterobacteriaceae* was 34.6%.

Current international and most national guidelines for the management of pelvic inflammatory disease recommend the prescription of antibiotics for prophylactic and treatment [22, 25]. However, the appointment of an inadequate starting therapy decreases the effectiveness of treatment infection. Microbiological monitoring of the antimicrobial resistance of the responsible pathogens of healthcare associated cervicitis is necessary to enhance our knowledge of epidemiology. Therefore, this was the basis for this study.

Advances in surveillance will facilitate this process, but antibiotic susceptibility testing of responsible pathogenes should not replace clinical examination while cervicitis prevalence and significance is not yet established. A standardized approach to healthcare-associated cervicitis research, particularly with consensus of case definition, may facilitate outcomes that can be more generally applied in surveillance and clinical practice.

STRENGTHS AND LIMITATION

Strengths: This was a first multi-center study based on surveillance data and designed to evaluate the prevalence current prevalence of healthcare-associated cervicitis and antimicrobial resistance of responsible pathogens in Ukraine.

Limitation: The retrospective nature of this study. Despite this, important prevalence healthcare-associated cervicitis data were obtained that can be used for comparison between countries. In addition, these data will be useful for improving infection control activities and developing a new strategy for the control and prevention of HAIs.

CONCLUSIONS

This study showed that the prevalence of healthcare-associated cervicitis in Ukraine is high, and many cases were caused by antibiotic-resistant pathogens. As our understanding of the aetiology and significance of cervicitis, particularly healthcare-associated cervicitis, improves, management will be refined. New research into the etiology and antibiotic resistance of responsible pathogens, and natural history of this common condition is needed, especially in view of the well-established links between cervicitis and an increased risk of upper genital tract infection. To prevent the healthcare-associated cervicitis it is necessary to develop and implement advanced infection control measures that are based on surveillance data.

REFERENCES

1. Ruggeri M., Cannas S., Cubeddu M. et al. Bacterial agents as a cause of infertility in humans. New Microbiol. 2016;39(3):206-209.
2. Mascarenhas M.N., Flaxman S.R., Boerma T. et al. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med. 2012;9(12):e1001356. doi: 10.1371/journal.pmed.1001356.
3. Chayachinda C., Rekhawasin T. Reproductive outcomes of patients being hospitalised with pelvic inflammatory disease. J Obstet Gynaecol. 2017;37(2):228-232. doi: 10.1080/01443615.2016.1234439.
4. Salmanov A.G., Suslikova L.V., Pandei S.A. et al. Healthcare associated Deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine. Wiad Lek. 2021;74(3):406-412. doi: 10.36740/WLek202103105.
5. Ortiz-de la Tabla V., Gutiérrez F. Cervicitis: etiología, diagnóstico y tratamiento. Enferm Infecc Microbiol Clin. 2019;37(10):661–667. doi: 10.1016/j.eimc.2018.12.004.
6. Marrazzo J.M., Martin D.H. Management of women with cervicitis. Clin Infect Dis. 2007;44(3):S102-10. doi: 10.1086/511423.
7. Lis R., Rowhani-Rahbar A., Manhart L.E. Mycoplasma genitalium infection and female reproductive tract disease: a meta-analysis. Clin Infect Dis. 2015;61(3):418-26. doi: 10.1093/cid/civ312.
8. Manhart L.E. Mycoplasma genitalium: an emergent sexually transmitted disease? Infect Dis Clin North Am. 2013;27(4):779-92. doi: 10.1016/j.idc.2013.08.003.
9. Oakeshott P., Aghaizu A., Hay P. et al. Is Mycoplasma genitalium in women the 'New Chlamydia?' A community-based prospective cohort study. Clin Infect Dis. 2010;51(10):1160-6. doi: 10.1086/656739.
10. Rours G.I., Duijts L., Moll H.A. et al. Chlamydia trachomatis infection during pregnancy associated with preterm delivery: a population-based prospective cohort study. Eur J Epidemiol. 2011;26(6):493-502. doi: 10.1007/s10654-011-9586-1.
11. Tantengco O.A.G., Menon R., Tantengco O.A.G. et al. Breaking Down the Barrier: The Role of Cervical Infection and Inflammation in Preterm Birth. Front Glob Womens Health. 2022;2:777643. doi: 10.3389/fgwh.2021.777643.
12. Rosai J. Female reproductive system. Rosai and Ackerman's surgical pathology. 10th ed. St. Louis: Mosby. 2011, 1439 p.
13. McClelland R.S., Wang C.C., Mandaliya K. et al. Treatment of cervicitis is associated with decreased cervical shedding of HIV-1. AIDS. 2001;15(1):105-10. doi: 10.1097/00002030-200101050-00015.
14. Workowski K.A., Bachmann L.H., Chan P.A. et. al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. doi: 10.15585/mmwr.rr7004a1.
15. Clarivet B,, Picot E,, Marchandin H, et al. Prevalence of Chlamydia trachomatis, Neisseria gonorrhoeae and Mycoplasma genitalium in asymptomatic patients under 30 years of age screened in a French sexually transmitted infections clinic. Eur J Dermatol. 2014;24(5):611-6. doi: 10.1684/ejd.2014.2413.
16. Kletzel H.H., Rotem R., Barg M. et al. Ureaplasma urealyticum: the role as a pathogen in women's health, a systematic review. Curr Infect Dis Rep. 2018;20(9):33. doi: 10.1007/s11908-018-0640-y.
17. L, Cao G., Zhao Z. et al. High bacterial loads of Ureaplasma may be associated with non-specific cervicitis. Scan J Infect Dis. 2014;46(9):637–41. doi: 10.3109/00365548.2014.922696.
18. Svenstrup H.F., Dave S.S., Carder C. et al. A cross-sectional study of Mycoplasma genitalium infection and correlates in women undergoing population-based screening or clinic-based testing for Chlamydia infection in London. BMJ Open. 2014;4:e003947. doi:10.1136/bmjopen-2013-003947.

19. Weiner L.M., Webb A.K., Limbago B. et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011-2014. Infect Control Hosp Epidemiol. 2016 ;37(11):1288-1301. doi: 10.1017/ice.2016.174.
20. Magiorakos A-P., Srinivasan A., Carey R.B. et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012;18(3):268–81. doi:10.1111/j.1469-0691.2011.03570.x.
21. Salmanov A., Vozianov S., Kryzhevsky V. et al. Prevalence of healthcare-associated infections and antimicrobial resistance in acute care hospitals in Kyiv, Ukraine. J Hosp Infect. 2019;102(4):431-437. doi: 10.1016/j.jhin.2019.03.008.
22. Ross J. Antibiotic therapy for pelvic inflammatory disease. Cochrane Database Syst Rev. 2017;4(4):CD010285. doi: 10.1002/14651858.CD010285.pub2.
23. Salmanov A.G., Vitiuk A.D., Hrynchuk S.Ya. et al. Vaginal cuff infection after hysterectomy in Ukraine. Wiad Lek. 2021;74(2):196-201. doi:10.36740/WLek202102104.
24. Wójkowska-Mach J., Pomorska-Wesołowska M., Romanik M. et al. Prevalence and Antimicrobial Susceptibility Profiles of Microorganisms Associated with Lower Reproductive Tract Infections in Women from Southern Poland-Retrospective Laboratory-Based Study. Int J Environ Res Public Health. 2021;18(1):335. doi: 10.3390/ijerph18010335.
25. Savaris R.F., Fuhrich D.G. et al. Antibiotic therapy for pelvic inflammatory disease. Cochrane Database Syst Rev. 2020;8:CD010285. doi: 10.1002/14651858.CD010285.pub3.

We would like to thank all the nurses and physicians, and students who contributed to the prevalence surveys.
The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID and contributorship:
Aidyn G. Salmanov: 0000-0002-4673-1154 [A,C-F]
Irina M. Koctjuk: 0000-0001-6765-7267 [B-D, F]
Olena K. Ihnatieva: 0000-0001-9034-6010 [B-D, F]
Alla D. Vitiuk: 0000-0003-0550-1076 [B-D, F]
Volodymyr Artyomenko: 0000-0003-2490-375X [B-D, F]
Ihor Paliga: 0000-0001-8130-4185 [B-D, F]
Lidiya V. Suslikova: 0000-0002-3039-6494 [B, C, F]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Aidyn G. Salmanov
Shupyk National Healthcare University of Ukraine,
9 Dorohozhytska St., 04112 Kyiv, Ukraine
tel: +380667997631
e-mail: mozsago@gmail.com

Received: 25.05.2022
Accepted: 03.09. 2022

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article