ORIGINAL ARTICLE

VAGINAL CUFF INFECTION AFTER HYSTERECTOMY IN UKRAINE

DOI:10.36740/WLek202102104

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ABSTRACT

The aim: To obtain the first estimates of the current prevalence of vaginal cuff infection after hysterectomy and antimicrobial resistance of causing pathogens in Ukraine.

Materials and methods: We performed a retrospective multicenter cohort study was based on surveillance data. The study population consisted of women who had an abdominal, vaginal or laparoscopic hysterectomy from 2017 to 2019 in 7 women hospitals of Ukraine. Definitions of vaginal cuff infections were used from the Centers for Disease Control and Prevention's National Healthcare Safety Network, USA.

Results: Total 12.6% women's after hysterectomy had vaginal cuff infections. Of these cases, 20.3% after abdominal, 15.5% vaginal and 4.1% laparoscopic hysterectomy were identified. The predominant pathogens of VCUF infections were: *Escherichia coli* (18.6%), *Enterobacter* spp. (12.4%), *Staphylococcus aureus* (10.8%), *Streptococcus* spp. (9,7%), *Klebsiella pneumoniae* (8.2%), *Pseudomonas aeruginosa* (7.6%), *Enterococcus faecalis* (7,0%) and *Proteus* spp. (7.0%).

Methicillin-resistance was observed in 12.9% of S. *aureus* (MRSA) and 9.7% CoNS. Carbapenem resistance was identified in 7.3% of *P.aeruginosa* isolates. Resistance to third-generation cephalosporins was observed in 8.9% *K. pneumoniae* and *E.coli* 11.9% isolates. The overall proportion of extended spectrum beta-lactamases (ESBL) production among *Enterobacteriaceae* was 22.7%. The prevalence of ESBL production among *E. coli* isolates was significantly higher than in *K. pneumoniae* (32.6%, vs 12.3%).

Conclusions: Vaginal cuff infections in women after hysterectomy are common in Ukraine and most of these infections caused by antibiotic-resistant bacteria. The incidence of VCUF infections after hysterectomy differs depending on the type of surgical procedure.

KEY WORDS: Hysterectomy, abdominal, vaginal, laparoscopic, vaginal cuff infection, pathogens, antimicrobial resistance

Wiad Lek. 2021;74(2):196-201

INTRODUCTION

Hysterectomy is one of the most commonly performed gynecological surgeries, which can be carried out via a vaginal, abdominal or a laparoscopic approach for treatment adenomyosis, uterine prolapse, cervix, or ovaries and other diseases. Vaginal cuff (VCUF) infection remains a common complication after hysterectomy surgery in Ukraine and results in significant patient morbidity. However, studies of prevalence of VCUF – infection are scant.

According to literature, gynecologic surgical procedures pose a potential risk transmission of pathogenic microorganisms from the skin or vagina and endocervix may migrate to operative sites and can result in VCUF – infections [1]. Estimated, prior to the advent of routine antimicrobial prophylaxis, pelvic infection rates after hysterectomy were high as 33% [2]. Therefore, guidelines of many countries, including Ukraine, recommend the use of antibiotic prophylaxis for gynecological surgery. However, the effect of antibiotic prophylaxis for VCUF – infections after hysterectomy is not fully understood. The majority of patients typically present after hospital discharge with moderate purulent vaginal discharge [1].

Current guidelines for the treatment of infections recommend the immediate prescription of antimicrobial medicines as soon as the infection is diagnosed. Broad spectrum antimicrobials should be prescribed even before the culture results are known in order to cure the most probable infection agents [3-8]. However, the literature data on the etiology and resistance of pathogens caused Reproductive Tract Infections varies considerably [9, 10]. Inadequate therapy extends the duration of hospitalization and provokes a need for additional courses of antimicrobial therapy that makes treatment more expensive.

The epidemiologies of VCUF – infections after hysterectomy in Ukraine are not studied. The previous reports of Reproductive Tract Infections in Ukraine have been limited only to Endometritis [11] and Episiotomy infections [12].

THE AIM

The aim of this study was to obtain the current prevalence of VCUF – infections after hysterectomy and antimicrobial resistance of causing pathogens in Ukraine.

MATERIALS AND METHODS

STUDY DESIGN AND POPULATION

We performed a retrospective multicenter cohort study was based on surveillance data of Reproductive Tract Infections in women's. Our study included patients undergoing an elective abdominal, vaginal or laparoscopic hysterectomy for benign reasons in 7 women hospitals of Ukraine from January 1st, 2017 to December 31st, 2019 (Table I). In the current study, we included 1491 women's (less than 50 years of age or if over 50 still menstruating) who were local residents. However, 236 of these were excluded from this study. Exclusion criteria were preoperative antibiotic use within one month prior to surgery, surgery for malignant disease and operations that for other reasons required preoperative antibiotics. 43 patients were excluded for missing or inadequate vaginal smears, mostly due to interfering menstrual blood.

DEFINITION AND DATA COLLECTION

In our study the CDC/NHSN (Centers for Disease Control and Prevention/National Healthcare Safety Network) definition of VCUF – infections was used [13]. In study period were analyzed the inpatient data and ambulatory medical records to identify VCUF – infections. We collected the data using structured NHSN Reproductive Tract Infection (REPR) Checklist for VCUF – infections. Full-text ambulatory medical records and relevant hospital records were reviewed for the all women's. Additional data form was created to extract microbiology (isolated pathogens and antibiograms) from inpatient data and ambulatory medical records. The follow-up of each patient was during 1 month days after hysterectomy. VCUF – infections were classified as superficial incisional SSI as per CDC/NHSN criteria [13].

MICROBIOLOGICAL SAMPLING AND SUSCEPTIBILITY TESTING

A purulent sample were collected with sterile swab on stick from the vaginal cuff from women with clinical symptoms of VCUF – infections and transported to microbiology laboratory. Results were not considered for more than two clinical isolates obtained from the same patient and the sample was considered to be contaminated. Microbial isolates from patients were identified using standard microbiological techniques, including automated microbiology testing (Vitek-2; bioMe´rieux, Marcy l'Etoile, France). Antibiotic susceptibility testing was performed by using the disk diffusion method according to the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). In our study strains in the intermediate range were classified as resistant for data analysis.

ETHICS

The Shupyk National Medical Academy of Postgraduate Education (Kyiv, Ukraine) ethics committee approved the

Table I. Distribution of type hysterectomy in different women hospitals of Ukraine

Hospital	All patients No.	Type of hysterectomy		
		Abdominal No. of procedure	Vaginal No. of procedure	Laparascopic No. of procedure
A	174	25	69	80
B	180	43	78	59
C	185	38	79	68
D	175	41	80	54
E	184	49	79	56
F	176	43	74	59
G	181	37	83	61
Total	1255	276	542	437

Table II. Characteristics patients with VCUF infections after different type hysterectomy

Type of hysterectomy	All patients *n*	VCUF infections		95% CI*
		n	%	
Abdominal	276	56	20,3	17.9 – 22.7
Vaginal	542	84	15,5	14.0 – 17.0
Laparoscopic	437	18	4,1	3.2 – 5.1
Total	1255	158	12,6	11.7 – 13.5

Note

*CI-confidence interval

waiver of informed consent to participate in this study due to its retrospective design. All women's data were anonymised prior to the analysis.

STATISTICAL ANALYSIS

In our study prevalence of VCUF – infections was reported as the percentage of the total number of women who had been submitted to hysterectomy cases. We analyzed samples from women's in the context of a study about microbiology of VCUF infection and antimicrobial resistance of causing pathogens. 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. Comparisons were undertaken using Student's t-test and Fisher's exact test for categorical variables. Statistical significance was defined as $P<0.05$.

RESULTS

PREVALENCE OF VAGINAL CUFF INFECTIONS

During the study period (January 1st, 2017 and December 31st, 2019), of the 1,255 patients who underwent hysterectomy for benign indications, VCUF infections was diagnosed within 30 days in 158 (12.6%, 95% CI 11.7%, 13.5%, P<0.001). Incidence of VCUF infections after hysterectomy differed according to the surgery procedure types and women clinics. Of these cases, 20.3% (56/276) after abdominal, 15.5% (84/542) vaginal and 4.1% (18/437) laparoscopic hysterectomy were identified. Characteristics of patients with VCUF infections after different type hysterectomy are presented in Table II.

Prevalence of VCUF – infections was lower among women with adenomyosis who underwent laparoscopic hysterectomy compared with those who underwent abdominal hysterectomy for benign indications. Of the total cases VCUF – infections, 89.2% (141/158) were detected after hospital discharge. 94.3% (149/158) of patients with VCUF – infections did not return to the hospital for evaluation or treatment. These patients continued their treatment outside the hospital in outpatients.

ANTIBIOTIC PROPHYLAXIS

Routine antibiotic prophylaxis at gynecological surgery is standard practice in Ukraine, consistent with surgical guidelines internationally. Prophylactic antibiotic administration is generally timed to establish a bactericidal concentration in serum and tissue prior to surgical incision. Of 1255 women's, 89.9% were prescribed combination ceftriaxone and metronidazole pre-operative period. Ceftriaxone and metronidazole was also prescribed for 77.8% (123/158) participants meeting criteria for VCUF infections. Another 22.2% (35/158) were prescribed cefazoline and metronidazole. Overall, in this study 89.9% participants had a chart-documented prescription for β-lactam antibiotic prophylaxis, including 77.8% of women's with VCUF infections.

MICROORGANISMS CAUSING VCUF INFECTIONS

In this study, a total of 158 samples from women with VCUF infections after hysterectomy were analyzed. Among the 158 analyzed samples, 8.2% (13/158) did not show any microbial growth. The remaining 91.8% (145/158) samples were positive for pathogens with colony count higher than 10^5 CFU/mL and were included in the current study analysis. In this study, 84.9% VCUF infections were polymicrobial. A total 474 strains of microorganisms were identified. Among this isolates gram-negative bacilli make up 67.7% (321/474) and 32.3% (153/474) gram-positive cocci. The predominant pathogens of VCUF infections were: *Escherichia coli* (18.6%), *Enterobacter* spp. (12.4%), *Staphylococcus aureus* (10.8%), *Streptococcus* spp. (9,7%), *Klebsiella pneumoniae* (8.2%), *Pseudomonas aeruginosa* (7.6%), *Enterococcus faecalis* (7,0%), and *Proteus* spp. (7.0%). They are closely followed by *Klebsiella oxytoca* (4.6%), *Serratia* spp. (3.8%), Coagulase-negative staphylococci (3.2%), *Citrobacter* spp. (3.2%), *Acinetibacter* spp. (2.3%) and *Enterococcus faecium* (1.7%). Structure of the microorganisms differed according to the hysterectomy types. The distribution of microorganisms causing infections after different types of hysterectomy in Ukraine is shown in Table III.

Antimicrobial resistance of CAUSING pathogens

The staphylococcal isolates displayed a remarkable resistance to penicillin (84.7%) and erythromycin (69%), although there were some differences depending on the species. Staphylococcal isolates showed susceptibility to most of the other antimicrobials tested. No strains resistant to linezolid, teicoplanin, vancomycin, tigecycline, and fusidic acid were found. Methicillin-resistance was observed in 12.9% of *S. aureus* (MRSA) and 9.7% CoNS.

Streptococcal isolates demonstrated a noteworthy resistance against erythromycin (66.3%) and benzylpenicillin (53.1%), followed by ampicillin (32.7%) and tigecycline (18.4%). Most of the isolates were sensitive to rifampicin (87.3%), clindamycin (89.5%), gentamycin (91.1%), cefuroxime (94.3%), tobramycin (98.3%), and linezolid (99.4%).

Regarding the genus *Enterococcus*, *E. faecalis* isolates were not sensitive to those antibiotics to which they are intrinsically resistant (cefuroxime, clindamycin, and trimethoprim-sulfamethoxazole) and 78.7% of them were resistant to erythromycin. Approximately, 20% of the *E. faecalis* isolates displayed resistance to high levels of aminoglycosides (gentamycin, tobramycin) and around 8.2% was resistant to quinolones (ciprofloxacin and levofloxacin), and 4% to glycopeptides (vancomycin and teicoplanin).

The overall proportion of extended spectrum betalactamases (ESBL) production among Enterobacteriaceae was 22.7%. The prevalence of ESBL production among *E. coli*

Table III. Distribution of microorganisms, isolated from women with VCUF infections after different types of hysterectomy in Ukraine.

Microorganisms[(a)]	All isolates (n=474)	Type hysterectomy		
		Abdominal (No./% of isolates)	Vaginal (No./% of isolates)	Laparoscopic (No./% of isolates)
Gram-positive cocci	153	109 /7 1.2	31 /20.3	13 /8.5
Enterococcus faecalis	33	21 / 63.6	8 / 24.2	4 / 12.1
Enterococcus faecium	8	3 / 37.5	4 / 50.0	1 /12.5
Streptococcus spp.	46	23 / 50.0	17 / 37.0	6 / 13.0
CoNS[(b)]	15	13 / 86.7	0	2 / 13.3
Staphylococcus aureus	51	49 / 96.1	2 / 3.9	0
Gram-negative bacilli	321	176 / 54.8	127 / 39.6	18 / 5.6
Escherichia coli	88	62 / 70.5	23 / 26.1	3 / 3.4
Klebsiella pneumoniae	39	12 / 30.8	25 / 64.1	2 / 5.1
Klebsiella oxytoca	22	5 /2.7	13 / 59.1	4 / 18.2
Enterobacter spp.	59	28 / 47.5	28 / 47.5	3 / 5.1
Proteus spp.	33	20 / 60.6	13 / 39.4	0
Serratia spp.	18	11 / 61.1	6 / 33.3	1 / 5.6
Citrobacter spp.	15	6 / 40.0	9 / 60.0	0
Pseudomonas aeruginosa	36	27 / 75.0	7 / 19.4	2 / 5.6
Acinetobacter spp.	11	5 / 54.5	3 / 27.3	3 / 27.3

Notes:
(a) Used "The Bergey's Manual of Determinative Bacteriology" 9th Edition
(b) CoNS: Coagulase-negative staphylococci

isolates was significantly higher than in *K. pneumoniae* (32.6%, vs 12.3%, $p < 0.001$). *E. coli* was most sensitive (>90%) to ertapenem (100%), cefotaxime (99.1%), ceftazidime (99.4%), imipenem (98.9%), piperacillin/tazobactam (97.3%), and gentamycin (91.3%) but least susceptibility (<70%) was observed for moxifloxacin (54.2%), cefuroxime (61.8%), amoxicillin (65.2%), and levofloxacin (66.5%). Resistance to third-generation cephalosporins was observed in 11.9% *E.coli* isolates. No strains resistant to ertapenem were found.

Enterobacter spp. was most sensitive (>90%) to ciprofloxacin (97.3%), piperacillin/tazobactam (94.9%), cefotaxime (94.8%), ceftazidime (94.5%) and ticarcillin (91.5%). No strains resistant to cefepime, meropenem, imipenem, and ertapenem were found. *Enterobacter* spp. isolates ones exhibited a noticeable percentage of resistance against ampicillin/sulbactam (59.5%), ampicillin (52.1%), amoxicillin/clavulanic acid (51.4%), clindamycin (49.2%), ciprofloxacin (47.8%), gentamycin (43.5%), cefaperazon (41.3%) and ceftriaxon (31.5%).

K. pneumoniae isolates showed susceptibility to most of the other antimicrobials (meropenem, imipenem, levofloxacin, and gentamycin) tested, while these isolates ones exhibited a noticeable percentage of resistance against ampicillin (53.8%), amoxicillin/clavulanic acid (39.5%), ofloxacin (31.5%), and ciprofloxacin (28.8%). No strains resistant to piperacillin/tazobactam and ertapenem were found. Resistance to third generation cephalosporins was observed in 8.9% *K.pneumoniae* isolates. *Proteus* spp. was most sensitive (>90%) to imipenem (98.1%), gentamycin (97.5%), cefotaxime (93.6%), cefepime (91.5%), and ceftazidime (91.4%). No strains resistant to ertapenem piperacillin/tazobactam, and amikacin were found. In our study *P. aeruginosa* isolates demonstrated remarkable resistance to cefepime (47.1%), gentamycin (36.2%), and cefoperazone (33.5%), and was most sensitive to meropenem (97.2%), imipenem (88.6%), piperacillin/tazobactam (87.8%), ceftazidime (88.1%), amikacin (85.1%), ticarcillin (81.9%), ciprofloxacin (81.9%). No strains resistant to ertapenem were found. Carbapenem resistance was identified in 7.3% of *P.aeruginosa* isolates.

DISCUSSION

Results of our study have shown that cuff infection is an important problem for women after hysterectomy in Ukraine. During the study period (2016-2018) the prevalence of VCUF infection after hysterectomy was 12.6%. Of these cases, 20.3% after abdominal, 15.5% vaginal and 4.1% laparoscopic hysterectomy were identified. Hysterectomy is one of the most common major surgical procedures for women with benign gynecological diseases in Ukraine. This surgery may be done for different reasons, including adenomyosis, uterine prolapse and other problems. However, there are limited numbers of study that report VCUF – infection after hysterectomy.

The VCUF – infections were classified as superficial incisional SSI as per CDC/NHSN criteria [13]. In literature

reported Incidence rate of SSI after hysterectomy have ranged from 1.7 to 11% [14-19], while VCUF – infection ranged from 3.1 to 4.8%. [17-19]. In our study incidence rate of VCUF infections was lower among women with adenomyosis who underwent laparoscopic hysterectomy compared with those who underwent abdominal hysterectomy for benign indications. These findings are in parallel with previous reports that showed that minimally invasive hysterectomy is associated with more favorable perioperative outcomes and fewer postoperative complications, including SSI [20, 21].

Incidence rate of VCUF – infections vary depending on the whether or not post-discharge surveillance was used to identify infections. Reilly et al. [22] reported that the incidence of SSI after hysterectomy doubled when patients completed questionnaires after hospital discharge. In this study the CDC/NHSN criteria [13] were used for diagnosing VCUF – infections after hysterectomy. During the surveillance period VCUF infections was diagnosed within 30 days in 158 patients. Of these cases, 89.2% of VCUF infections were detected in post-discharge surveillance period.

Gynecologic procedures, including laparoscopy or laparotomy pose a potential risk transmission of pathogenic microorganisms from the skin or vagina and endocervix may migrate to surgical sites after hysterectomy and can result in VCUF – infections [1, 10, 23]. In vaginal surgery or hysterectomy, the endogenous flora of the genital tract the likely cause will be polymicrobial, consisting of anaerobes, Gram-negative aerobes and Gram-positive cocci [10]. In our study, 84.9% VCUF infections were polymicrobial and gram-negative bacilli make up 67.7%, and 32.3% gram-positive cocci from of all isolates. The predominant pathogens of VCUF infections were: *E. coli*, *Enterobacter* spp., *S. aureus*, *Streptococcus* spp., *K. pneumoniae*, *P. aeruginosa*, *E. faecalis*, and *Proteus* spp. Structure of the microorganisms differed according to the hysterectomy types (Table III).

Although current guidelines of many countries recommend the use of antibiotic prophylaxis for gynecological surgery, postoperative infections still occur [24, 25]. Clinical and therapeutic decisions are influenced by numerous factors, including antimicrobial resistance of the causative agents of VCUF infections. Optimally, the given antibiotic should be selected depending on the safety profile and local drug susceptibility. However, in Ukraine, there is no national network for the antimicrobial resistance surveillance. Our study showed that higher incidence rate of VCUF infections after hysterectomy in Ukraine was significantly associated with pathogens resistant to antibiotics. Antimicrobial resistance in the isolates associated with VCUF – infections showed, proportion of extended spectrum beta- lactamases (ESBL) production among *Enterobacteriaceae* was 22.7%. The prevalence of ESBL production among *E. coli* isolates was significantly higher than in *K. pneumoniae* (32.6%, vs 12.3%). Among the gram-negative bacteria, third-generation cephalosporins resistance was found in 8.9% of *K. pneumoniae* and in 11.9% of *E.coli* isolates. Carbapenem resistance was reported in 7.3% of *P. aeruginosa* isolates. Methicillin resistance was reported in 12.9% of *S.aureus* isolates.

STRENGTHS AND LIMITATION

Our study is the first study reporting the prevalence of VCUF – infections in women after hysterectomy and antimicrobial resistance of causing pathogens in Ukraine. The absence of national surveillance data for VCUF – infections in Ukraine compelled us to rely entirely on data from the only existing study. The strengths of the study lie in the application of CDC/NHSN methodology. The CDC/NHSN criteria [13] were used for diagnosing VCUF – infections after hysterectomy. The follow-up of each patient was during 1 month days after hysterectomy. The screening of hospital and ambulatory records was a sensitive surveillance method for identifying VCUF – infections. The limitations of this study include its retrospective design and conduct at a in seven hospitals in Ukraine. Therefore, the results this study not be representative of other hospitals of Ukraine with different distributions of antimicrobial resistance of causing pathogens of VCUF – infections. However, this study provides valuable data as a first study for national surveillance of VCUF – infections and potential comparison with data from other countries.

CONCLUSIONS

The study showed that VCUF – infections after hysterectomy in Ukraine is a common occurrence and many cases are caused by pathogens that are resistant to antibiotics. Incidence of VCUF infections after hysterectomy differed according to the surgery procedure types. Minimally invasive (Laparoscopic) hysterectomy has lower infection rates than abdominal and vaginal hysterectomy. Given of the rapidly developing antimicrobial resistance, the policy of antibiotic use for prophylactic or treatment of VCUF infections in each region should be determined depending on local data on resistance to antimicrobials. Strategic planning and implementation of Reproductive tract infections in women surveillance is required.

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Acknowledgements:
We would like to thank all the nurses and physicians who contributed to the prevalence surveys.

Funding:
This work is a fragment of a research study of the Scientific Research Laboratory of Shupyk National Medical Academy of Postgraduate Education (Kyiv, Ukraine). Title: The scientific justification for measures to combat the resistance of microorganisms to antimicrobial drugs in Ukraine on the "One Health" approaches. State Registration Number: 0120U101440. Study period: 2020-2022. This work was funded by the Ministry of Health of Ukraine according to the plan of that research study. The authors did not receive any financial support from the manufacturers of medical instruments and drugs.

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

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Received: 11.08.2020
Accepted: 04.01.2021

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