

ORIGINAL ARTICLE

HEALTHCARE ASSOCIATED DEEP PELVIC TISSUE INFECTION AND OTHER INFECTIONS OF THE FEMALE REPRODUCTIVE TRACT IN UKRAINE

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ABSTRACT

The aim: To obtain the first estimates of the current prevalence of healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract (vagina, ovaries, uterus) including chorioamnionitis, and antimicrobial resistance of causing pathogens in Ukraine.

Materials and methods: We performed a retrospective multicenter cohort study based on surveillance data. The study population included 3,053 women's who underwent gynecological surgery or other procedures from 2017 to 2019 in 7 women hospitals in Ukraine. Definitions of healthcare-associated reproductive tract infection were used from the CDC/NHSN.

Results: The prevalence of healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract was 26.3%. Incidence of infection was: 13.3% Pelvic abscess or cellulitis, 14.6% Adnexa utery, 9.5% Salpingitis, 7.1% Oophoritis, 12.2% Parametritis, 4.6% Chorioamnionitis, and 38.8% Bacterial Vaginitis. The predominant pathogens were: *Escherichia coli* (25.6%), *Enterobacter* spp. (11.4%), *Klebsiella pneumoniae* (10.6%), *Staphylococcus aureus* (8.5%), *Enterococcus faecalis* (7.2%) and *Pseudomonas aeruginosa* (7.1%). Methicillin-resistance was observed in 14.3% of *S. aureus* (MRSA). The overall proportion of extended spectrum beta-lactamases (ESBL) production among *Enterobacteriaceae* was 20.8%. The prevalence of ESBL production among *E. coli* isolates was 24.7% and among *K. pneumoniae* 11.9%. Resistance to third-generation cephalosporins was observed in 12.8% *E. coli* and 9.2% *K. pneumoniae* isolates.

Carbapenem resistance was identified in 8.5% of *P.aeruginosa* isolates.

Conclusions: Healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine is a common occurrence and many cases are caused by pathogens that are resistant to antibiotics.

KEY WORDS: Healthcare-associated infection, deep pelvic tissue infection, female, vagina, ovaries, uterus, chorioamnionitis, pathogens, antimicrobial resistance

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INTRODUCTION

Healthcare-associated reproductive tract infection (HARTI) in female is a major problem for public health care in worldwide, causing increased morbidity and mortality in women. These infections may result in infertility, ectopic pregnancy and chronic pelvic pain and other disease [1-4]. The prevalence of RTIs in women varies from country to country and ranges from 1.8% [5] to 48% [6,7]. In the United States, 1 million women are diagnosed with RTI each year and the cost of their treatment is estimated at \$ 4.2 billion [8]. Many studies show that despite the introduction into medical practice of new diagnostic technologies for diagnosis and treatment, as well as broad-spectrum antibiotics, the number of healthcare-associated infections is not decreasing.

HARTIs in female include Endometritis, Episiotomy, Vaginal cuff infections and other infections of the female reproductive tract [9]. Other infection of the female reproductive tract involves the Deep pelvic tissue infection or other infection of the female reproductive tract (for example, vagina, ovaries, uterus) including chorioamnionitis,

but excluding Endometritis or Vaginal cuff infections [9]. In the available literature, there are many studies devoted to Endometritis or Vaginal cuff infections. However, there are a limited number of studies on other reproductive tract infection in female.

One of the reasons for healthcare-associated infections is the wide spread of conditionally pathogenic microorganisms in Ukraine that are resistant to antibiotics [10,11]. The emergence and spread of antimicrobial resistance has become a major public health threat in Ukraine, and the number of infections caused by resistant pathogens causing of HARTIs continues to increase [12,13].

Antimicrobial resistance creates obstacles for effective prevention and treatment of patients with infections. Every year resistant healthcare-associated infection is becoming more and more pressing for medical specialists in Ukraine. Microbiological monitoring of the prevalence of etiologic agents of HARTIs and antimicrobial resistance is necessary to enhance our knowledge of its epidemiology. To our knowledge, the prevalence of and causative agents of most HARTIs (besides Endometritis and Episiotomy infections)

among female in-patients and out patients have not been studies in Ukraine. This was the basis for our study.

THE AIM

The aim of this study was to obtain the first estimates of the current prevalence of infection of the female reproductive tract involves the Deep pelvic tissue infection or other infections of the female reproductive tract including Chorioamnionitis, but excluding Endometritis or Vaginal cuff infections and antimicrobial resistance of responsible pathogens in Ukraine.

MATERIALS AND METHODS

SETTING

We performed a retrospective multicenter cohort study was based on surveillance data of Reproductive Tract Infections in women's from January 1st, 2017 to December 31st, 2019 in 7 regional (tertiary) women hospitals of Ukraine. The hospitals had 1250 beds. They are similar in terms of medical equipment, staff and number of 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.

PARTICIPANTS

Inclusion criteria: This study included 3,053 women's aged 16-55 years admitted to hospitals with the diagnosis of acute pelvic inflammatory disease (PID). All women were local residents. Diagnosis of acute PID was based on criteria from the Centers for Disease Control and Prevention (CDC) [4].

Exclusion criteria: endometritis or vaginal cuff infections; current pregnancy; positive serological test for syphilis or other sexually transmitted infections; inflammatory bowel disease or significant renal or hepatic disease; had a history of colitis; neoplasms or haematological malignancy.

DEFINITIONS OF HARTI

Diagnosis of Deep pelvic tissue infection or other infection of the female reproductive tract (vagina, ovaries, uterus) including chorioamnionitis was based on criteria from the CDC/NHSN Surveillance Definitions for Specific Types of Infections [9]. Women had uterine curettage, or delivery, abortion, instrumentation of the upper genital tract, pelvic or abdominal surgery within the last month (30 days) prior to admission.

DATA COLLECTION

In this study, we analyzed the inpatient data and ambulatory medical records to identify deep pelvic tissue infection or other infections of the female reproductive tract including chorioamnionitis. We collected the data using structured

NHSN Reproductive Tract Infection (REPR) Checklist. Full-text ambulatory medical records and relevant hospital records were reviewed for the all women's. Additional data form was created to extract demographic and clinical data, microbiology (isolated pathogens and antibiograms) and outcome information from inpatient data and ambulatory medical records.

MICROBIOLOGICAL METHODS

All samples were obtained from women with clinical symptoms of PID. Microbial isolates 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 (Kirby – Bauer antibiotic testing) according to the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Strains in the intermediate range were classified as resistant for data analysis.

ETHICS

The Shupyk National Medical Academy of Postgraduate Education of Ukraine ethics committee approved the waiver of informed consent to participate in this study due to its retrospective design. All pregnant women's data were anonymised prior to the analysis.

STATISTICAL ANALYSIS

Prevalence of healthcare-associated deep pelvic tissue infection or other infections of the female reproductive tract was reported as the percentage of the total number of women who had been submitted to PID cases. We analyzed samples from women's in the context of a study about microbiology of HARTI and antimicrobial resistance of responsible pathogens. The analysis of statistical data was performed using Excel. 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 AND TYPE OF INFECTION

During the study period (from 2017 to 2019), 804 of 3,053 patients were found to have healthcare-associated infections (HAI). The prevalence of healthcare-associated deep pelvic tissue infection and other infections ($n=804$) of the female reproductive tract in women hospitals in Ukraine was 26.3% [95% confidence interval (CI) 25.5-27.1]. Of these cases, 13.3% Pelvic abscess or cellulitis, 14.6% Adnexa utery, 9.5% Salpingitis, 7.1% Oophoritis, 12.2% Parametritis, 4.6% Chorioamnionitis, and 38.8% Bacterial Vaginitis

were identified (Table I). Of 804 cases healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract, 78.6% were detected after hospital discharge. None of the patients died as a result of these infections. The prevalence of healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract in women differed according to the procedure types. Gynecologic patients had a higher incidence of healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract compared with pregnant women. The largest number of cases were identified after Abortion (35.8%, 95% CI 34,1 – 37.5), Instrumentation of the upper genital tract (20.1%, 95% CI 18,7 – 21.5) and vaginal surgery (19.4%, 95% CI 18,0 – 20.8). The incidence of HAI was 10.9% after abdominal surgery, 8.3% after laparoscopic surgery, and 5.3% after delivery (Table II). Vaginal delivery represented a low risk of HAIs compared cesarean delivery.

A total of 3053 women in reproductive age (16 – 55 years) participated in the study. The median age of the women was 28 years. The proportion of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract was higher in divorced (37.9 %) than married women (14.4 %). Demographic and Social characteristics of patients with healthcare associated deep

pelvic tissue infection and other infections of the female reproductive tract in Ukraine are presented in Table III.

ANTIBIOTIC PROPHYLAXIS

For Ukraine antibiotic prophylaxis at surgery and gynecological procedure is standard practice. In this study of 3,053 patients with PID who underwent chart review, 3,012 (98.7%) were prescribed Ceftriaxone (75%) or Cefotaxime (25%). However, 804 (26.3%) of 3,053 patients developed infections of the reproductive tract.

RESPONSIBLE PATHOGENS

In this study, a total of 1857 pathogens isolated from 804 women with healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine were analyzed using culture based methods. Of these pathogens, gram-negative bacilli make up 73.6% (1367/1857) and 26.4% (490/1857) gram-positive cocci from of all isolates. The predominant pathogens of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract were: *Escherichia coli* (25.6%), *Enterobacter* spp. (11.4%), *Klebsiella pneumoniae* (10.6%), *Staphylococcus aureus* (8.5%), *Enterococcus faecalis*

Table I. Types of healthcare-associated deep pelvic tissue infection and other infections (n=804) of the female reproductive tract in Ukraine (P < 0.05)

HAI ^a type	Cases of HAI ^a		95% CI ^b
	n	%	
A pelvic abscess or cellulitis	107	13.3	12.1 – 14.5
Infection of the uterine appendages (Adnexa utery)	117	14.6	13.4 – 15.8
Infection of the Fallopian tubes (Salpingitis)	76	9.5	8.5 – 10.5
Infection of the ovaries (Oophoritis)	57	7.1	6.2 – 8.0
Infection of the supporting ligaments (Parametritis)	98	12.2	11.1 – 13.3
Chorioamnionitis	37	4.6	3.9 – 5.3
Infection of the Vagina (Bacterial Vaginosis)	312	38.8	37.1 – 40.5

Note

^aHAI, healthcare-associated infection

^bCI, confidence interval.

Table II. Distribution of type procedure associated deep pelvic tissue infection and other infections (n=804) of the female reproductive tract in Ukraine

Type of procedure	Cases of HAI ^a		95% CI ^b
	n	%	
Surgery			
Abdominal	88	10,9	9,8 – 12.0
Vaginal	156	19,4	18,0 – 20.8
Laparoscopic	67	8,3	7,3 – 9.3
Delivery (vaginal and cesarean delivery)	43	5,3	4,5 – 6.1
Abortion	288	35,8	34,1 – 37.5
Instrumentation of the upper genital tract	162	20,1	18,7 – 21.5

Note

^aHAI, healthcare-associated infection

^bCI, confidence interval.

Table III. Demographic and Social characteristics of patients with healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine (P < 0.05)

Variables	Number of participants <i>n</i>	HAI ^a		95% CI ^b
		<i>n</i>	%	
Age of participants				
16–20	117	16	13,7	13,1 – 14,3
21–25	338	71	21,0	20,3 – 21,7
26–30	417	162	38,8	37,9 – 39,7
31–35	374	137	36,6	35,7 – 37,5
36–40	596	144	24,2	23,4 – 25,0
41–45	488	87	17,8	17,1 – 18,5
46–50	402	76	18,9	18,2 – 19,6
51–55	321	111	34,6	33,7 – 35,5
Marital status				
Single	1578	461	29,2	28,4 – 30,0
Married	918	132	14,4	13,8 – 15,0
Divorced	557	211	37,9	37,0 – 38,8
Residence				
Rural	857	112	13,1	12,5 – 13,7
Urban	2196	692	31,5	30,7 – 32,3
Educational status				
College and above	618	137	22,2	21,5 – 22,9
High school	2435	667	27,4	25,6 – 28,2
Occupational status				
Employed	633	151	23,9	23,1 – 24,7
Merchant	675	163	24,1	23,3 – 24,9
Students	421	112	26,6	25,8 – 27,4
Unemployed	1324	378	28,5	27,7 – 29,3
Total	3053	804	26,3	25,5 – 27,1

Note^aHAI, healthcare-associated infection^bCI, confidence interval.

(7.2%), *Pseudomonas aeruginosa* (7.1%). The distribution of microorganisms causing deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine is shown in Table IV.

ANTIMICROBIAL RESISTANCE

Staphylococcal strains displayed a most resistance to penicillin (78.1%) and erythromycin (58.7%). In this study methicillin-resistance was observed in 12.9% of *S. aureus* (MRSA). However, Staphylococcal isolates showed susceptibility to most of the other antimicrobials tested. No strains resistant to linezolid, teicoplanin, vancomycin, tigecycline, and fusidic acid were found.

Streptococcal isolates demonstrated a noteworthy resistance against erythromycin (54.7%) and benzylpenicillin (42.3%), followed by ampicillin (29.8%). Most of

the Streptococcal strains were sensitive to clindamycin (89.1%), gentamycin (93.2%), cefuroxime (95.1%), and linezolid (100%).

E. faecalis isolates were not sensitive to cefuroxime, clindamycin, and trimethoprim-sulfamethoxazole. Approximately, 20% of the *E. faecalis* isolates displayed resistance to aminoglycosides and 11.4% was resistant to quinolones.

The overall proportion of extended spectrum betalactamases (ESBL) production among Enterobacteriaceae was 20.8%. The prevalence of ESBL production among *E. coli* isolates was 24.7%. *E. coli* was most sensitive (>90%) to ertapenem, cefotaxime, ceftazidime, imipenem, piperacillin/tazobactam and high (>60%) resistance to cefuroxime, amoxicillin, and levofloxacin. Antimicrobial resistance to third-generation cephalosporins was observed in 12.8% *E. coli* isolates.

Isolates of *Enterobacter* spp. was most sensitive (>90%) to ciprofloxacin, cefotaxime, piperacillin/tazobactam,

Table IV. Types of microorganisms (n=1857) isolated from 804 patients with healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine

Microorganism ^a	All isolates	
	n	%
Gram-positive cocci	490	26.4
<i>Staphylococcus aureus</i>	157	8.5
<i>Enterococcus faecalis</i>	134	7.2
<i>Streptococcus spp.</i>	112	6.0
<i>Staphylococcus epidermidis</i>	73	3.9
<i>Enterococcus faecium</i>	14	0.8
Gram-negative bacilli	1367	73.6
<i>Escherichia coli</i>	476	25.6
<i>Enterobacter spp.</i>	211	11.4
<i>Klebsiella pneumoniae</i>	197	10.6
<i>Pseudomonas aeruginosa</i>	132	7.1
<i>Proteus mirabilis</i>	112	6.0
<i>Acinetibacter spp.</i>	103	5.5
<i>Serratia spp.</i>	77	4.1
<i>Citrobacter spp.</i>	43	2.3
<i>Klebsiella oxytoca</i>	16	0.9

Note:

^aUsed "The Bergey's Manual of Determinative Bacteriology" 9th Edition

ceftazidime and ticarcillin. No strains of *Enterobacter* spp. resistant to cefepime, meropenem, imipenem, and ertapenem were found. *Enterobacter* spp. strains were high (>50%) resistance to ampicillin/sulbactam, ampicillin, amoxicillin/clavulanic acid, clindamycin, ciprofloxacin, and high percentage resistance to gentamycin (41.2%), cefaperazon (38.5%) and ceftriaxon (29.2%).

K. pneumoniae isolates showed high susceptibility to piperacillin/tazobactam, ertapenem, meropenem, imipenem, levofloxacin, and gentamycin. However, these strains while ones exhibited a noticeable percentage (>30%) of resistance to ampicillin, amoxicillin/clavulanic acid, ofloxacin, and ciprofloxacin. The prevalence of ESBL production among *K. pneumoniae* isolates was 11.9%. Resistance of *K. pneumoniae* strains to third generation cephalosporins was observed in 9.2%.

P. aeruginosa isolates demonstrated remarkable resistance (>35%) to cefepime, gentamycin, and cefoperazone. This isolates was most sensitive (>90%) to meropenem, imipenem, piperacillin/tazobactam, and ceftazidime. Carbapenem resistance was identified in 8.5% of *P.aeruginosa* isolates.

DISCUSSION

This study presents the first estimates of the current prevalence of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract and antimicrobial resistance of responsible pathogens in Ukrainian women hospitals. The prevalence of healthcare

associated deep pelvic tissue infection and other infections of the female reproductive tract was 26.3%. The incidence of infection was: 13.3% Pelvic abscess or cellulitis, 14.6% Adnexa utery, 9.5% Salpingitis, 7.1% Oophoritis, 12.2% Parametritis, 4.6% Chorioamnionitis, and 38.8% Bacterial Vaginitis. Gynecologic patients had a higher incidence of HAIs compared with pregnant women. Of these cases, 78.6% were detected after hospital discharge. The prevalence of HAIs in women differed according to the procedure types. In our study gynecologic patients had a higher incidence of HAIs compared with pregnant women. Vaginal delivery represented a low risk of the female reproductive tract infection compared cesarean delivery. Available literatures there are no epidemiologic studies (prevalence or incidence) of different types of healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract. Therefore, we were unable to compare our results with other studies in other countries.

Microbiological monitoring of the prevalence of etiologic agents of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract and antimicrobial resistance is necessary to enhance our knowledge of its epidemiology. Therefore, this was the basis for this study. In present study, the predominant pathogens of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract were *E.coli*, *Enterobacter* spp., *K. pneumoniae*, *S.aureus*, *E.faecalis*, *P.aeruginosa*. Our results was coherent with reports other studies [7, 14, 15].

Current international guidelines for the management of pelvic inflammatory disease recommend the prescription of antibiotics for prophylactic and treatment [16-18]. According to the literature, the appointment of an inadequate starting therapy decreases the effectiveness of treatment [19, 20]. In our study, 26.3% of patients who were prescribed antibiotics developed reproductive tract infections. Possibly, this is due to the high levels of antimicrobial resistance of causing pathogens of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine. In present study, overall proportion of extended spectrum betalactamases (ESBL) production among *Enterobacteriaceae* was 20.8%. The prevalence of ESBL production among *E. coli* isolates was 24.7% and among *K. pneumoniae* isolates was 12.8%. Antimicrobial resistance to third-generation cephalosporins was observed in 12.8% *E. coli* isolates and in 9.2% *K. pneumoniae* isolates. Carbapenem resistance was identified in 8.5% of *P.aeruginosa* isolates. Methicillin-resistance was observed in 12.9% of *S. aureus* (MRSA). There is therefore need the treatment and prevention of pelvic infection and other infections of the female reproductive tract with Gram negative bacteria needs to be changed in Ukraine. However, the data are limited and more studies are needed to guide a change in first-line antibiotic treatment or prophylactics.

STUDY LIMITATIONS

The absence of national surveillance data in Ukraine compelled us to rely entirely on data from the only study prevalence of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract. The strengths of the study lie in the application of CDC/NHSN methodology. Indicators of HAIs provided by surveillance activities require comparison with adequate reference data to stimulate further infection control actions and to enhance quality of health care. The limitations of this study include in conduct at a in seven (29.2%) regional women hospitals in Ukraine. Therefore, the results present study not is representative of other hospitals of Ukraine.

CONCLUSIONS

Healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract in Ukraine is a common occurrence and many cases are caused by pathogens that are resistant to antibiotics. Results this study suggest that the prevention and treatment of pelvic infection and other infections of the female reproductive tract in Ukraine needs to be changed. However, the data are limited and more studies are needed. The present study provides valuable data as a first study for national surveillance of healthcare associated deep pelvic tissue infection and other infections of the female reproductive tract and potential for comparison with data from other countries.

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Conflict of interest:

The Authors declare no conflict of interest

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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