

# POSTPARTUM MASTITIS IN THE BREASTFEEDING WOMEN AND ANTIMICROBIAL RESISTANCE OF RESPONSIBLE PATHOGENS IN UKRAINE: RESULTS A MULTICENTER STUDY

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## ABSTRACT

**The aim:** To obtain the prevalence of mastitis in the breastfeeding women and antimicrobial resistance of responsible pathogens in Ukraine.

**Materials and methods:** A retrospective multicenter cohort study was based on surveillance data for Postpartum Mastitis and included 18,427 breastfeeding women's who gave birth in 11 regional hospitals of Ukraine.

**Results:** 22.6% breastfeeding women's were found to have breast infections. Among these patients, 11.6% breast abscess and 88.4% mastitis were observed. Of the total cases breast infections, 74.8% were detected after hospital discharge. The rate of healthcare-associated mastitis was 8.6%. The predominant pathogens were: *Staphylococcus aureus* (23.6%), *Escherichia coli* (19.4%), *Enterobacter* spp. (11.9%), *Staphylococcus epidermidis* (10.7%), *Klebsiella* spp. (8.7%), *Pseudomonas aeruginosa* (4.8%), *Enterococcus faecalis* (4.8%), and *Proteus mirabilis* (4.6%). The overall proportion of methicillin-resistance was observed in 27.9% of *S. aureus* (MRSA) and 24.3% of *S. epidermidis* (MRSE). Of the total methicillin-resistance strains, 74.8% of MRSA and 82.1% of MRSE is community-acquired, were detected after hospital discharge. Vancomycin resistance was observed in 9.2% of isolated enterococci. Carbapenem resistance was identified in 7.3% of *Paeruginosa* isolates. Resistance to third-generation cephalosporins was observed in 8.8% *Klebsiella* spp. and *E.coli* 9.1% isolates.

**Conclusions:** Mastitis in the breastfeeding women in Ukraine requires medical attention it is common, and a lot of cases are caused by pathogens resistant to antibiotics. Optimizing the management and empirical antimicrobial therapy may reduce the burden of mastitis, but prevention is the key element.

**KEY WORDS:** breastfeeding women; postpartum mastitis; breast abscess; pathogens; antimicrobial resistance

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## INTRODUCTION

Postpartum mastitis is one of the most common pyoinflammatory infections that occur in the breastfeeding women, and can progress from the infective mastitis to a breast abscess [1, 2]. In breastfeeding women's, mastitis or breast abscess is one of the main medical causes of early weaning [1-4], and is one of the diseases with highest economic impact and, a major welfare concern [5].

Guidelines for treatment recommend appropriate antibiotic therapy of breast abscesses [1, 6, 7]. Early treatment with an appropriate antibiotic is necessary to prevent complications of infection [8]. Knowledge on the antimicrobial susceptibility status of responsible pathogens is

important for better management of postpartum infections [4]. The lack of this information prompts the empiric use of broad-spectrum antibiotics giving rise to a frequent therapeutic failure.

To identify postpartum mastitis prevention targets and reduce thus disparities between countries, ongoing surveillance is necessary. However, the epidemiology of mastitis in breastfeeding women in Ukraine and associated treatment outcomes are not well studied. National network for the surveillance of antimicrobial resistance is not in Ukraine [9, 10]. Postpartum mastitis problems experienced by Ukrainian breastfeeding women's have not been reported previously.

## THE AIM

The aim of this study was to obtain the prevalence of mastitis in the breastfeeding women and antimicrobial resistance of responsible pathogens in Ukraine.

## MATERIALS AND METHODS

A retrospective cohort study was based on surveillance data for Postpartum Mastitis and included 18,427 breastfeeding women's who gave birth (vaginal delivery or cesarean section) in 11 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 2,108,241 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 1236 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 30 days (1 month).

Breast infections (breast abscess or mastitis) based on the definition used by the Centers for Disease Control and Prevention's National Nosocomial Infection Surveillance system (CDC/NHSN) [11]. A breast abscess or mastitis must meet at least 1 of the following criteria: (1) Patient has a positive culture of affected breast tissue or fluid obtained by incision and drainage or needle aspiration; (2) Patient has a breast abscess or other evidence of infection seen during a surgical operation or histopathologic examination; (3) Patient has fever ( $>38^{\circ}\text{C}$ ) and local inflammation of the breast and physician diagnosis of breast abscess. Cases of breast abscesses or mastitis were classified into mutually exclusive groups comprised of either community-acquired or healthcare-associated infection. Cases of breast abscesses or mastitis that occurs within 7 days after childbirth considered health care associated.

The WHO's breastfeeding definitions were used in this study. Exclusive breastfeeding was defined as "breast milk (including milk expressed or from a wet nurse), oral rehydration

salt (ORS), drops, and syrups (vitamins, minerals, medicines)". Predominant breastfeeding was defined as "breast milk (including milk expressed or from a wet nurse) as the predominant source of nourishment and certain liquids (water and water-based drinks, fruit juice), ritual fluids and ORS, drops or syrups (vitamins, minerals, medicines)".

In this study, we analyzed the inpatient data and ambulatory medical records to identify postpartum mastitis and describe the epidemiology of these infections. To be included in the study, women must have chosen to breastfeed (with or without food supplements). Breastfeeding women's who were local residents, had living infants, were within 1 month postpartum, and had a singleton child were recruited into the study. Women's who were local residents, had living infants, were within 1 month postpartum, and had a singleton child were recruited into the study. Mothers were excluded if they

were not a local resident of the selected regions. Participants were followed up during the 30 days postpartum. Information on infant feeding practices was collected at baseline and each follow-up visit. Full-text ambulatory medical records and relevant hospital records were reviewed for the 30-day postpartum period for a breastfeeding women's. All free-text notes were reviewed, and encounters for which the principal focus was the postpartum infection were identified. 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. Trained nurses and infection control professionals collected the data using structured questionnaires adapted from based on the definition used by CDC/NHSN on breast abscesses or mastitis. The data were conducted during 1 month (the first 4 weeks) postpartum, and information on were conducted during 1 month (the first 4 weeks) postpartum, and information on sociodemographic characteristics and lactation problems was collected at this time.

Infection rates for the entire study population of postpartum women were extrapolated by standard methods from the estimated infection rates for the sample of individual medical records and microbiologic laboratory records of specimens obtained from the breast.

We analyzed breast milk samples from breastfeeding women's in the context of a study about microbiology of postpartum mastitis and antimicrobial resistance of responsible pathogens. Milk samples were obtained from women with clinical symptoms of infectious mastitis. Breastmilk culture was obtained by manually collecting a clean catch sample in a sterile container (i.e. a small amount of initially expressed milk is discarded to avoid contamination of the sample with skin flora, and subsequent milk is expressed in a sterile container, being careful not to touch the inside of the container). The nipple was cleaned before to collection may further reduce skin contamination and minimise false-positive culture results.

All isolates from breast abscesses or mastitis cases was sent to microbiology laboratory for identification and antimicrobial resistance testing. Microbial isolates were identified using standard microbiological techniques, including automated microbiology testing (Vitek-2; bioMérieux, Marcy l'Etoile, France), and antibiotic susceptibility testing was performed by using the disk diffusion method (Kirby – Bauer antibiotic testing). Isolates were categorized as susceptible or resistant by Clinical and Laboratory Standards Institute criteria (CLSI). Strains in the intermediate range were classified as resistant for data analysis.

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.

The Prevalence of postpartum mastitis was reported as the percentage of the total number of breastfeeding women's. Cases of postpartum mastitis were analysed by type of infection (community-acquired and healthcare-associated

**Table 1.** Characteristics of breastfeeding women with mastitis in Ukraine ( $P < 0.05$ ).

Characteristics	Total cohort (n=18,427)		Mastitis (n=4172)		Incidence of mastitis [95% CI] <sup>a</sup>
	n	%	n	%	
Age (years, mean, SD) <sup>b</sup>	25.2		23.1		
Age category <sup>c</sup>					
≤18	872	4.7	321	36.8	35.2 – 38.4
18-24	7921	43.0	1732	21.9	21.4 – 22.4
25-34	6788	36.8	1286	18.9	18.4 – 19.4
35-44	2381	12.9	677	28.4	27.5 – 29.3
≥ 45	465	2.7	156	33.5	31.3 – 35.7
Mode of delivery					
Vaginal	15,588	84.6	2359	15.1	14.8 – 15.4
Cesarean	2839	15.4	1813	63.9	63.0 – 64.8
Time of initiation of first breastfeeding <sup>c</sup>					
After 1 hour	10,788	58.5	2518	23.3	22.9 – 23.7
Within first hour	7639	41.5	1654	21.7	21.2 – 22.2
Feeding infant					
Exclusive breastfeeding	12,752	69.2	1877	14.7	14.4 – 15.0
Predominant breastfeeding	5675	30.8	2295	40.4	39.7 – 41.1
Total	18,427	100.0	4172	22.6	22.3 – 22.9

Note:

a – Confidence interval;

b – Standard deviation;

c – Data missing for some participants.

infection), which were mutually exclusive. 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 end point was the epidemiology of the postpartum mastitis. Comparisons were undertaken using Student's t-test and Pearson's chi-squared test or Fisher's exact test for categorical variables as appropriate. Statistical significance was defined as  $P < 0.05$ .

## RESULTS

During the study period (January 1st, 2015 and December 31st, 2017), 4,172 of 18,427 breastfeeding women's were found to have breast infections. The incidence of postpartum mastitis was 22.6% [95% CI 22.3%, 22.9%]. Among these patients, 11.6% (484/4,172) breast abscess and 88.4% (3,688/4,172) mastitis were observed.

The postpartum mastitis rates were 91.4% (3,813/4,172) is community-acquired and 8.6% (359/4,172) health-care-associated infection. Healthcare-associated breast abscess was not been identified. Of the total cases breast infections, 74.8% (3,122/4,172) were detected after hospital discharge. For these post-discharge infections, 75.8% of patients did not return to the hospital where they delivered for evaluation or treatment.

The age of the patients was ≤18 to ≥ 45 years. Mean cohort age was 25.2 years (standard deviation (SD) 5.5 years), 37.4% (6,892/18,427) were primiparous. Postpartum mastitis rate was highest in the age group of ≤18 years (36.8%; 321/872) followed by those in the age group of ≥ 45 years (33.5%; 156/465) (Table 1). All of the mothers were breastfeeding at recruitment, and 30.8% reported providing prelacteal feeds to their newborn infants. Table 1 shows the characteristics data of patients with postpartum mastitis. A total of 22.6% [95% CI, 22.3%, 22.9%] breastfeeding women detected at least one episode of mastitis were observed in the postpartum period. In addition, 33.8% (6,231/18,427) reported cracked nipples. Findings from logistic regression after accounting for duration of exposure showed that those women who provided prelacteal feeds to their newborn infants and who had delivered by cesarean section had a higher likelihood of mastitis.

In this study, a total of 4,172 milk samples from women suffering infectious mastitis were analyzed using culture-based methods. A total of 4,758 isolates from the mastitis milk samples were identified. In the present study, 1.3% (55/4,172) samples did not show any microbial growth. Aerobic gram-negative bacilli make up 50.5% (2,405/4,758) and 42.7% (2,033/4,758) gram-positive cocci from of all isolates. In this study, 12.3% breast infections were polymicrobial. The predominant pathogens were:

**Table II.** Distribution of pathogens, detected of milk samples from breastfeeding women with mastitis in Ukraine (2015-2017)

Microorganism	All isolates (n = 4758)		Type of breast infections			
			Mastitis		Breast abscess	
	n	%	n	%	n	%
Aerobes	4438	93.3	3814	92.8	624	96.6
Gram-positive cocci	2033	42.7	1718	41.8	315	48.8
Staphylococcus aureus	1121	23.6	910	22.1	211	32.7
Staphylococcus epidermidis	510	10.7	488	11.9	22	3.4
Streptococcus spp.	124	2.6	106	2.6	18	2.8
Enterococcus faecalis	230	4.8	169	4.1	61	9.5
Enterococcus faecium	48	1.0	45	1.1	3	0.5
Gram-negative bacilli	2405	50.5	2096	51.0	309	47.8
Escherichia coli	922	19.4	870	21.2	52	8.0
Enterobacter spp.	566	11.9	486	11.8	80	12.4
Klebsiella spp.	416	8.7	324	8.3	92	14.2
Proteus mirabilis	220	4.6	152	3.7	68	10.5
Pseudomonas aeruginosa	228	4.8	216	5.3	12	1.9
Acinetibacter spp.	53	1.1	48	1.2	5	0.8
Anaerobes	198	4.2	185	4.5	13	2.0
Bacteroides spp.	124	2.6	115	2.8	9	1.4
Other	74	1.6	70	1.7	4	0.6
Fungi	122	2.6	118	2.9	4	0.6
Candida albicans	95	2.0	91	2.2	4	0.6
Other	27	0.6	27	0.7	0	0
Total microorganisms	4758	100.0	4112	100.0	646	100.0

*Staphylococcus aureus* (23.6%), *Escherichia coli* (19.4%), *Enterobacter* spp. (11.9%), *Staphylococcus epidermidis* (10.7%), *Klebsiella* spp. (8.7%), *Pseudomonas aeruginosa* (4.8%), *Enterococcus faecalis* (4.8%), and *Proteus mirabilis* (4.6%). They are closely followed by streptococci (2.6%), *Bacteroides* spp. (2.6%), *Candida albicans* (2.0%), *Acinetibacter* spp. (1.1%), and *Enterococcus faecium* (1.0%). The distribution of the microorganisms differed according to the breast abscess or mastitis (Table 2).

In mastitis patients, increased proportions of aerobic bacteria were observed with increased proportions of *E. coli* (19.4% vs. 8.0% in breast abscess patients;  $P < 0.01$ ), *S. epidermidis* (11.9% vs. 3.4% in breast abscess patients;  $P < 0.01$ ), and *P. aeruginosa* strains (5.3% vs. 9% in breast abscess patients;  $P < 0.01$ ). Conversely, decreased proportions of *Klebsiella* spp. (8.3% vs. 14.2% in breast abscess infection,  $P < 0.05$ ) and *P. mirabilis* were observed in mastitis patients (3.7% vs. 10.5% in breast abscess infection,  $P < 0.01$ ), and *E. faecalis* were observed in mastitis patients (4.1% vs. 9.5% in breast abscess 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. The predominant pathogens in healthcare-associated mastitis were: *S. aureus*, *E. coli*, *Enterobacter* spp., *Klebsiella* spp., *P. aeruginosa*, and *E. faecalis*.

The antibiotic susceptibility profiles of isolates from the infectious mastitis milk samples are presented in Table 3 and Table 4. The staphylococcal isolates displayed a remarkable resistance to penicillin (87.3%) and erythromycin (68.6%), although there were some differences depending on the species (Table 3).

*S. aureus* isolates showed susceptibility (> 90%) to most of the other antimicrobials (tobramycin, nitrofurantoin, chloramphenicol, fosfomicin, levofloxacin, ciprofloxacin, gentamycin) tested, while these isolates ones exhibited a noticeable percentage of resistance against benzylpenicillin (81.7%), erythromycin (65.7%), ceftriaxone (26.6%), and cefoxitin (26.3%). No strains resistant to linezolid, teicoplanin, vancomycin, tigecycline, and fusidic acid were found. Methicillin-resistance was observed in 27.9% of *S. aureus* (MRSA). Of the total MRSA strains, 74.8% is community-acquired, were detected after hospital discharge. *S. epidermidis* isolates demonstrated remarkable resistance to benzylpenicillin (92.9%) and erythromycin (71.5%), and moderate resistance to fusidic acid (41.4%), mupirocin (28.7%), cefoxitin (23.6%). Most of this species isolates were susceptible to the rest of the antimicrobials. Methicillin-resistance was observed in 24.3% of *S. epidermidis* (MRSE). Of the total methicillin-resistance strains, 82.1% of MRSE is community-acquired, were detected after hospital discharge. Antimicrobial susceptibility tests were

**Table III.** Antibiotic susceptibility (%) of aerobic Gram-positive bacteria isolated from milk samples from breastfeeding women with mastitis in Ukraine (2015-2017).

Antibiotic	<i>S. aureus</i> (n = 140)		<i>S. epidermidis</i> (n = 140)		<i>Streptococcus spp.</i> (n = 220)		<i>E. faecalis</i> (n = 112)	
	S	R	S	R	S	R	S	R
Penicillin	18.6	81.7	7.1	92.9	36.3	63.7	82.9	17.1
Ampicillin	89.9	10.1	97.1	2.9	48.5	51.5	92.3	7.7
Oxacillin	72.1	27.9	75.7	24.3	NT	NT	NT	NT
Cefuroxime	89.9	16.1	78.6	21.4	95.2	4.8	0	100.0
Cefotaxime	81.4	18.6	89.9	10.1	85.2	14.8	NT	NT
Ceftriaxone	73.4	26.6	80.4	19.6	86.3	13.7	NT	NT
Imipenem	NT	NT	NT	NT	NT	NT	100.0	0
Gentamycin	90.9	9.1	94.7	5.3	94.1	5.9	83.3	16.7
Tobramycin	98.6	1.4	100.0	0	98.9	1.9	76.9	23.1
Ciprofloxacin	94.8	15.2	NT	NT	NT	NT	92.3	7.7
Levofloxacin	98.6	1.4	94.1	5.9	88.0	12.0	92.9	7.1
Erythromycin	34.3	65.7	28.5	71.5	31.3	68.7	15.1	84.9
Clindamycin	89.9	10.1	78.6	21.4	89.9	16.1	7.3	92.7
Linezolid	100.0	0	100.0	0	99.8	0.2	100.0	0
Teicoplanin	100.0	0	97.7	2.3	NT	NT	92.9	7.1
Vancomycin	100.0	0	99.5	0.5	NT	NT	91.3	8.7
Tigecycline	100.0	0	95.2	4.8	69.2	30.8	100.0	0
Nitrofurantoin	98.9	1.9	100.0	0	NT	NT	92.3	7.7
Chloramphenicol	98.6	1.4	97.5	2.5	NT	NT	100.0	0
Fosfomycin	97.1	2.9	93.1	6.9	NT	NT	NT	NT
Fusidic acid	100.0	0	58.6	41.4	NT	NT	NT	NT
Mupirocin	86.3	13.7	71.3	28.7	NT	NT	NT	NT
Rifampicin	81.4	18.6	99.8	0.2	86.3	13.7	87.5	12.5
TMP-SMZ	88.9	11.1	86.3	13.7	NT	NT	1.4	98.6
Cefoxitin	73.7	26.3	76.4	23.6	NT	NT	NT	NT

Note:

R, resistant isolates (%); S, susceptible isolates (%); NT, no tested; TMP-SMZ, trimethoprim-sulfamethoxazole.

performed on a total of 220 streptococcal isolates and the results are summarized in Table 3. Streptococcal isolates demonstrated a noteworthy resistance against erythromycin (68.7%) and benzylpenicillin (63.7%), followed by ampicillin (51.5%) and tigecycline (30.8%). Most of the isolates were sensitive to rifampicin (86.3%), clindamycin (89.9%), gentamycin (94.1%), cefuroxime (95.2%), tobramycin (98.9%), and linezolid (99.8%). Regarding the genus *Enterococcus*, *E. faecalis* isolates (n = 112) were not sensitive to those antibiotics to which they are intrinsically resistant (cefuroxime, clindamycin, and trimethoprim-sulfamethoxazole) (Table 3) and 84.9% of them were resistant to erythromycin. Approximately, 20% of the *E. faecalis* isolates displayed resistance to high levels of aminoglycosides (gentamycin, tobramycin) and around 7.5% was resistant to quinolones (ciprofloxacin and levofloxacin), and 8% to glycopeptides (vancomycin and teicoplanin). Vancomycin

resistance was observed in 8.7% of isolated enterococci (VRE). Antimicrobial susceptibility tests were performed on a total of 922 *E. coli* isolates. *E. coli* was most sensitive (>90%) to ertapenem (100%), cefotaxime (99.1%), ceftazidime (99.4%), cefepime (99.3%), fosfomycin (98.7%), imipenem (98.9%), piperacillin/tazobactam (97.3%), and gentamycin (94.5%) but least susceptibility (<70%) was observed for moxifloxacin (54.2%), cefuroxime (61.8%), amoxicillin (65.2%), and levofloxacin (67.3%). Resistance to third-generation cephalosporins was observed in 9.1% *E. coli* isolates. No strains resistant to ertapenem were found. *Enterobacter* spp. was most sensitive (>90%) to ciprofloxacin (98.6%), piperacillin/tazobactam (96.5%), cefotaxime (96.1%), ceftazidime (96.2%), ticarcillin (92.7%), fosfomycin (92.6%), amikacin (92.7%), and gentamycin (92.7%). No strains resistant to cefepime, imipenem, and ertapenem were found. *Enterobacter* spp. isolates ones



**Table IV.** Antibiotic susceptibility (%) of aerobic Gram-negative bacteria isolated from milk samples from breastfeeding women with mastitis in Ukraine (2015-2016).

Antibiotic	<i>E. coli</i> (n=922)		<i>Enterobacter spp.</i> (n=566)		<i>Klebsiella spp.</i> (n=416)		<i>P. mirabilis</i> (n=220)		<i>P. aeruginosa</i> (n=228)	
	S	R	S	R	S	R	S	R	S	R
Amoxicillin	65.2	34.8	NT	NT	NT	NT	71.4	28.6	NT	NT
AMC	78.1	21.9	39.8	60.2	85.2	14.8	84.3	15.7	NT	NT
SAM	NT	NT	38.1	61.9	68.7	31.3	NT	NT	NT	NT
Ticarcillin	69.9	30.1	92.7	7.3	NT	NT	86.5	13.5	81.9	18.1
TZP	97.3	2.7	96.5	3.5	100.0	0	100	0	88.2	11.8
Cefuroxime	61.8	38.2	77.4	22.6	88.7	11.3	NT	NT	NT	NT
Cefotaxime	99.1	0.9	96.1	3.9	97.3	2.7	98.8	1.2	NT	NT
Ceftriaxone	74.2	25.8	65.9	34.1	78.9	21.1	NT	NT	NT	NT
Ceftazidime	99.4	0.6	96.2	3.8	97.5	2.5	94.5	5.5	87.8	12.2
Cefepime	99.3	0.7	100.0	0	77.6	22.4	96.7	3.3	51.2	48.8
Imipenem	98.9	1.1	100.0	0	94.7	5.3	99.3	0.7	88.6	11.4
Meropenem	NT	NT	NT	NT	NT	NT	NT	NT	96.8	3.2
Ertapenem	100.0	0	100.0	0	100	0	100	0	100.0	0
Gentamycin	94.5	5.5	91.2	8.8	91.2	8.8	98.8	1.2	63.8	36.2
Amikacin	89.4	10.6	92.7	7.3	82.6	17.4	100.0	0	84.7	15.3
Ciprofloxacin	87.2	12.8	98.6	1.4	95.1	4.9	75.1	24.9	81.2	18.8
Levofloxacin	67.3	32.7	78.7	21.3	92.7	7.3	NT	NT	NT	NT
Moxifloxacin	54.2	45.8	87.4	12.6	46.3	53.7	NT	NT	NT	NT
Cefoperazone	NT	NT	NT	NT	NT	NT	NT	NT	66.2	33.8
Fosfomycin	98.7	1.3	92.6	7.4	88.2	11.8	NT	NT	78.1	21.9

Note:  
R, resistant isolates (%); S, susceptible isolates (%); NT, no tested; AMC, amoxicillin/clavulanic acid; SAM, ampicillin/sulbactam; TZP, piperacillin/tazobactam.

exhibited a noticeable percentage of resistance against ampicillin/sulbactam (61.9%), amoxicillin/clavulanic acid (60.2%), and ceftriaxon (34.1%). *Klebsiella spp.* isolates showed susceptibility > 90% to most of the other antimicrobials (cefotaxime, ceftazidime, imipenem, levofloxacin, ciprofloxacin, gentamycin) tested, while these isolates ones exhibited a noticeable percentage of resistance against moxifloxacin (53.7%), ampicillin/sulbactam (31.3%), cefepime (22.4%), and ceftriaxone (21.1%). No strains resistant to piperacillin/tazobactam and ertapenem were found. Resistance to third-generation cephalosporins was observed in 8.8% *Klebsiella spp.* isolates. *P. mirabilis* was most sensitive (>90%) to imipenem (99.3%), gentamycin (98.8%), cefotaxime (98.8%), cefepime (96.7%), and ceftazidime (94.5%). No strains resistant to piperacillin/tazobactam, ertapenem, and amikacin were found. *P. aeruginosa* isolates demonstrated remarkable resistance to cefepime (48.8%), gentamycin (36.2%), and cefoperazone (33.8%), and was most sensitive to meropenem (96.8%), imipenem (88.6%), piperacillin/tazobactam (88.2%), ceftazidime (87.8%), amikacin (84.7%), ticarcillin (81.9%), ciprofloxacin (81.9%). Carbapenem resistance was identified in 7.3% of *P.aeruginosa* isolates. No strains resistant to ertapenem were found.

## DISCUSSION

To our knowledge this is the first epidemiological study for postpartum infectious mastitis among lactating women in Ukraine. During the study period, 22.6% breastfeeding women's were found to have breast infections. Among these patients, 11.6% breast abscess and 88.4% mastitis were observed. Of the total cases breast infections, 74.8% were detected after hospital discharge. The rate of healthcare-associated mastitis was 8.6%. Healthcare-associated breast abscess was not been identified. In this study, 12.3% breast infections were polymicrobial. The predominant pathogens were: *S. aureus* (23.6%), *E. coli* (19.4%), *Enterobacter spp.* (11.9%), *S. epidermidis* (10.7%), *Klebsiella spp.* (8.7%), *P. aeruginosa* (4.8%), *E. faecalis* (4.8%), and *P. mirabilis* (4.6%). The overall proportion of methicillin-resistance in *S. aureus* (MRSA) was 27.9%. Of the total MRSA strains, 74.8% is community-acquired, were detected after hospital discharge. Vancomycin resistance was observed in 9.2% of isolated enterococci (VRE). Carbapenem resistance was identified in 7.3% of *P.aeruginosa* isolates. Resistance to third-generation cephalosporins was observed in 8.8% *Klebsiella spp.* and *E.coli* 9.1% isolates.

Postpartum infectious mastitis is a common condition of women during lactation, although its incidence may be

underestimated because of differences in case definition and reporting [6, 12-14]. Previous studies have reported the incidence of postpartum mastitis to be as high as 33% in lactating women [2, 6-14]. The majority of cases occur in the first eight weeks (two months) postpartum, but mastitis can occur at any time during breastfeeding [2, 13-16]. The time of occurrence is an important consideration when measuring the incidence of mastitis, and several studies have reported that the incidence is highest in the first few weeks postpartum [14, 15] and that rates decline thereafter. In our study the follow-up of each breastfeeding women was continued 1 month (the first 4 weeks). During these period 22.6% infectious mastitis were observed.

Infective mastitis that is usually associated with lactation can progress to a breast abscess [1, 2]. Estimates, incidence of breast abscess may vary between 3% [2, 8] and 11% [13, 17], depending on the definition and length of postpartum follow-up. In our study 11.6% breast abscess were observed. All cases of breast infections were detected after hospital discharge.

Breast infections (and up to 40% of breast abscesses) may be polymicrobial, with isolation of aerobes (Gram-positive cocci and Gram-negative bacilli) and anaerobes [18, 19]. In our study the bacterial spectrum observed in patients with postpartum mastitis matches the previous reports. Infectious mastitis is a common reason for antibiotic treatment in lactating women [4]. Previous studies have reported high rates of antibiotic prescriptions for mastitis [13, 14]. In the absence of antimicrobial susceptibility testing, the antibiotic treatment, leading to the increase of antimicrobial resistance among mastitis-causing agents [7, 20].

The estimates, *Staphylococci* are the most common pathogens causing agents of mastitis in breastfeeding women's [2, 4, 5, 18, 21]. However, there are limited studies reporting the antimicrobial susceptibility of *Staphylococci* isolates recovered from milk of women suffering mastitis [4]. The majority of staphylococci isolates are now methicillin-resistant [5, 19, 21]. In our study the overall proportion of methicillin-resistance was observed in 27.9% of *S. aureus* (MRSA) and 24.3% of *S. epidermidis* (MRSE). Of the total methicillin-resistance strains, 74.8% of MRSA and 82.1% of MRSE is community-acquired, were detected after hospital discharge. This finding parallels the local and national increases in MRSA reported in other infections.

The increasing resistance of *Streptococcus* spp. against penicillin, erythromycin and tetracycline has become a concerning issue in the clinical practice [22, 23]. In our study streptococcal isolates demonstrated a noteworthy resistance against erythromycin (68.7%) and penicillin (63.7%), followed by ampicillin (51.5%) and tigecycline (30.8%). Marín M. et al. [4] showed high level resistance *Enterococcus* to aminoglycosides exhibited by about 20% of isolates, as well as the remarkable resistance to erythromycin (86%), is in concordance with previous studies [24, 25]. It must also be addressed that about 7% of the *E. faecalis* isolates obtained in this study showed resistance to quinolones and vancomycin [4]. In our

study, *Enterococcus* isolates were not sensitive to those antibiotics to which they are intrinsically resistant and 84.9% of them were resistant to erythromycin. Approximately, 20% of the *E. faecalis* isolates was resistance to high levels of aminoglycosides and around 7.5% was resistant to quinolones, and 8% to glycopeptides, is in concordance with previous studies [4]. Vancomycin resistance was observed in 8.7% of isolated enterococci (VRE). In the literature, the antimicrobial susceptibility patterns of aerobic Gram-negative bacteria isolated from milk samples from women with infectious mastitis have not been reported to date. In our study the predominant pathogens were *E. coli*, *Enterobacter* spp., *Klebsiella* spp., *P.aeruginosa*, and *P.mirabilis*. Carbapenem resistance was identified in 7.3% of *P.aeruginosa* isolates. Resistance to third-generation cephalosporins was observed in 8.8% *Klebsiella* spp. and *E.coli* 9.1% isolates.

The WHO recommends emptying the breast by frequent breastfeeding or expressing, and our study found that most of the women's had received advice to this effect, which they were following. However, a small proportion of women had stopped breastfeeding as a result of their mastitis. We found that women's who reported providing prelacteal feeds to their newborn infants and who had delivered by cesarean section were more at risk of having an episode of mastitis (Table 1).

Our study is the first study reporting the incidence of postpartum mastitis in Ukraine. Strengths of our study include the cohort design, capturing all breastfeeding women's the study period, and near-complete microbiologic evaluation of clinical mastitis and antimicrobial testing of responsible pathogens. In our study population, the screening of hospital and ambulatory records was a sensitive surveillance method for identifying postpartum mastitis.

The limitations of this study include its retrospective design and conduct at a 45.8% regional hospitals (11 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 mastitis. This investigation provides valuable data as a first study for national surveillance of postpartum mastitis and potential comparison with data from other countries.

## CONCLUSIONS

Mastitis in the breastfeeding women in Ukraine requires medical attention it is common, and a lot of cases are caused by pathogens resistant to antibiotics. The most infections occur after hospital discharge. Use of information collected from hospital and ambulatory records allows efficient identification of women who are very likely to have postpartum mastitis. Knowledge about local data of resistance may contribute to limiting resistance and may have a significant role in designing effective antimicrobial stewardship policies. Optimizing the management and empirical antimicrobial therapy may reduce the burden of mastitis, but prevention is the key element.

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**Conflict of interest:**

*The Authors declare no conflict of interest*

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