INTRODUCTION
Intra-abdominal infections (IAIs), encompassing a wide spectrum of pathological conditions from uncomplicated appendicitis to fecal peritonitis, are a common cause of morbidity and mortality worldwide [1-3].

A complete classification that includes the origin of source of infection, the anatomical extent of infection, the presumed pathogens involved and risk factors for major resistance patterns, and the patient’s clinical condition does not exist [4]. A simple and universally accepted classification divides IAIs into complicated and uncomplicated [5]. In the event of uncomplicated IAIs, the infection only involves a single organ and does not extend to the peritoneum. When the focus of infection is controlled by surgical excision, post-operative antibiotic therapy is not necessary [6, 7]. In the event of complicated IAIs, the infectious process proceeds beyond the organ into the peritoneum, causing either localized or diffuse peritonitis [4]. Early clinical diagnosis and appropriate antimicrobial therapy in critically ill patients are the cornerstones in the management of IAIs. An insufficient or otherwise inadequate antimicrobial regimen is one of the variables most strongly associated with unfavorable outcomes [9, 10].

In the past few decades, an increased prevalence of infections caused by antibiotic-resistant pathogens, including methicillin-resistant Staphylococcus aureus (MRSA) [11], vancomycin-resistant enterococci (VRE) [12], carbapenem-resistant Pseudomonas aeruginosa [13], extended-spectrum β-lactamase (ESBL)-producing Escherichia coli [14] and Klebsiella species, and multidrug-resistant Acinetobacter species, has been observed [15], especially in IAIs [3, 16]. Current guidelines recommend a wide range of antimicrobial regimens based on patient characteristics, expected involved pathogens and local resistance epidemiology [17]. In this setting, epidemiological surveys are of paramount importance to ensure adequacy of empirical antimicrobial treatment.

THE AIM
Aim of our work was to obtain the first national estimates of the current prevalence of IAIs and resistance of their causative agents to antibiotics in Ukrainian hospitals.
MATERIALS AND METHODS

STUDY POPULATION

Over a 24 month period (January 2014 to December 2015), this multicentre retrospective study was performed in 9 Ukrainian acute care hospitals that are similar in terms of medical equipment, laboratory facilities and number of surgeries performed. Adult patients undergoing surgery or interventional drainage for IAI with positive microbiological culture (intra-abdominal samples from surgery or interventional drainage procedures) and identification of microorganisms were included in the database.

ETHICS

According to Ukrainian law, as this retrospective study did not modify the laboratory or clinical practices of the physicians, no informed consent and no approval of an Ethics Committee were required.

DATA COLLECTION

In each centre, the microbiologist identified as the centre coordinator and the attending physician collected the data in an electronic case report form. Case identification was triggered by the microbiologist after a positive peritoneal culture. After verification, microbiological and clinical data were recorded on the case report form.

DEFINITIONS

IAIs were classified as community-acquired or nosocomial infections. Nosocomial IAI was defined as an infection absent upon admission that became evident 48 h or more after admission in patients hospitalized for a reason other than IAI [18]. Only patients with post-operative infections were considered as nosocomial cases.

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MICROBIOLOGICAL SAMPLING

The intraoperative specimens of abdominal fluid were collected during laparotomy in sterile containers using all aseptic precautions. The identification and antimicrobial susceptibility of the cultures were determined, using auto-mated microbiology analyzer Vitek 2 Compact (BioMerieux, France). Some antimicrobial susceptibility test used Kirby — Bauer antibiotic testing. Interpretative criteria were those suggested by the CLSI [19].

STATISTICAL ANALYSIS

The analysis of statistical data was performed using Microsoft Excel for Windows. Results are expressed as median (range), mean± standard deviation for continuous variables and the number with the corresponding percentage for qualitative variables. The primary endpoint was the epidemiology of the microorganisms isolated in intra-abdominal samples and their resistance to antibiotics. Statistical significance was defined as P < 0.05.

RESULTS

PATIENT AND DISEASE CHARACTERISTICS

Over the studied period, 1986 patients (52.8% female, 61±20 years, range 19–87 years) with microbiologically proven IAI were included, with a mean of 14.8 patients per centre (range 2–36 patients). Among these patients,
1404 community-acquired (70.7%) and 582 nosocomial (29.3%) infections were observed, yielding a total of 4879 intraperitoneal specimens. Type and location of peritonitis differed in nosocomial and community-acquired cases (table I). Death during hospitalization was reported in 57 (4.1%) community-acquired cases and 45 (7.7%) nosocomial cases.

**Microbiological Results**

Positive blood cultures were reported in 78 community-acquired (6.1%) and 48 nosocomial (8.7%) patients in the peri-operative period. The number of peritoneal microorganisms per sample was ≥3 in 33.7% and 54.4% of cases, respectively, for community-acquired and nosocomial infections (P < 0.001). A total of 4879 microorganisms were cultured. The distribution of the microorganisms differed according to the nosocomial or community origin of the infection (table II) but not according to their location (data not shown). In nosocomial patients, increased proportions of aerobic bacteria were observed (P < 0.05) with increased proportions of *Enterococcus faecalis* (32.6% vs. 18.9% in community-acquired patients; P < 0.05) and *Pseudomonas aeruginosa* strains (12.8% vs. 4.9% in community-acquired patients; P < 0.01). Conversely, decreased proportions of *Escherichia coli* (51.9% vs. 71.3% in community-acquired patients, P < 0.001) and streptococci strains were observed in nosocomial patients (30.5% vs. 50.0% in community-acquired patients, P < 0.01). 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.

**Antibacterial Resistance**

Among the antimicrobial agents tested, the carbapenems (imipenem and ertapenem) and amikacin were the most consistently active in vitro against *Enterobacteriaceae* in both community-acquired and nosocomial infections (table III). Against *P. aeruginosa*, amikacin, imipenem, ceftazidime and ciprofloxacin were the most active agents in community-acquired infections, while imipenem, ceftepime and amikacin were the most active agents in nosocomial IAI cases (table III). No MRSA or VRE strains were cultured. When taking into account the global activity

Table II. Microorganisms isolated from peritoneal fluid in IAI

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Community-acquired infections</th>
<th>Nosocomial infections</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aerobes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>2226 (70.9%)</td>
<td>1321 (75.9%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>1338 (42.6%)</td>
<td>751 (43.1%)</td>
<td>NS</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>954 (71.3%)</td>
<td>390 (51.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>Enterobacter</em> spp.</td>
<td>90 (6.7%)</td>
<td>78 (10.4%)</td>
<td>NS</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>168 (12.6%)</td>
<td>138 (18.4%)</td>
<td>NS</td>
</tr>
<tr>
<td><em>Pseudomonas</em> aeruginosa</td>
<td>54 (4.0%)</td>
<td>42 (5.6%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Gram-positive cocci</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>888 (28.3%)</td>
<td>570 (32.7%)</td>
<td>NS</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>168 (18.9%)</td>
<td>186 (32.6%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><em>Enterococcus</em> (other)</td>
<td>96 (10.8%)</td>
<td>48 (8.4%)</td>
<td>NS</td>
</tr>
<tr>
<td><em>Streptococcus</em> spp.</td>
<td>78 (8.8%)</td>
<td>78 (13.7%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Anaerobes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Anaerobes</em> spp.</td>
<td>798 (25.4%)</td>
<td>342 (20%)</td>
<td>NS</td>
</tr>
<tr>
<td><em>Bacteroides</em> spp.</td>
<td>240 (30.1%)</td>
<td>102 (29.8%)</td>
<td>NS</td>
</tr>
<tr>
<td><em>Clostridium</em> spp.</td>
<td>444 (55.6%)</td>
<td>180 (52.6%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Fungi</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>114 (3.6%)</td>
<td>78 (4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Other</td>
<td>30 (26.3%)</td>
<td>30 (38.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3138 (100.0)</td>
<td>1741 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Note: NS, not statistically significant.
against the Gram-positive bacteria, vancomycin and teicoplanin were the most consistently active in vitro in both community-acquired and nosocomial infections, due to the strains of *E. faecium* (table IV).

**DISCUSSION**

To our knowledge, this is the first IAI surveillance multicenter study in Ukraine, which describes incidence of community-acquired and nosocomial IAI. This epidemiological multicenter retrospective study, performed over a short period of time (2014-2015), investigated the microbiological findings in a mixed group of patients with community-acquired and nosocomial IAIs. We assume that this descriptive study reflects ‘real-life’ conditions. The principal results are a higher diversity of microorganisms isolated in nosocomial infections and decreased susceptibility among these strains.

Several epidemiological studies addressing susceptibility testing in the course of IAIs published over recent years at an international level [2, 20-22] or a single centre level have made important contributions to the description of enteric microorganisms. In the studies by Paterson et al. [20] and Baquero et al. [22], *E. coli* peritoneal isolates were -50% community-acquired and 50% hospital-acquired (isolated >48 h after hospitalization). However, from the perspective of clinicians in the field, these results are either too broad [20-22] or too restrictive [23, 24] to be useful in clinical practice. Each type of study has its own deficiencies and strengths. Larger studies may show regional or even global trends that may not be apparent in smaller studies [2, 20-22]. Single centre studies have their own value by demonstrating local resistance patterns [23, 24]. Our study provides data situated between the two.

Our results confirm the difference in clinical and microbiological features between community-acquired and nosocomial peritonitis already observed in the rare comparative data available in the literature [23, 25]. The disease data referring to the source of infection, organs involved or type or source of peritonitis do not substantially differ from the data in the literature for either community-acquired or nosocomial infections [23-26].

The bacterial spectrum observed in patients with community-acquired peritonitis matches the previous reports well, with *E. coli*, *Streptococcus* spp. and *Bacteroides fragilis* group as the most frequently isolated microorganisms [23, 26]. ESBL-producing *E. coli* collected from IAIs may not be very prevalent in Europe or the USA, but have been reported with a relatively high prevalence in Latin America (16%) and Asia (25%) [22]. However, this feature was not observed in the present study conducted during the same period (2014-2015), for either community-acquired or nosocomial IAIs. This discrepancy between urinary tract and peritoneal samples has been previously described in Spain with 92% of ESBL-producing *E. coli* isolated from urine cultures and 1% from peritoneal fluid [27]. The low rate of ESBL strains and the low severity of the cases could explain the frequent prescription of amoxicillin/clavulanic acid in monotherapy in community-acquired peritonitis as reported previously [26]. Such an empirical policy should be revised and the antibiotic spectrum broadened.

Overall, enterococci accounted for more than 10% of the isolates in community-acquired infections, a higher

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**Table III. Antibiotic susceptibilities (% susceptible) of aerobic Gram-negative bacteria isolated from patients with community-acquired (CA) and nosocomial (N) IAIs**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th><em>Escherichia coli</em>&lt;br&gt;(n=1344)</th>
<th><em>Klebsiella</em> spp.&lt;br&gt;(n=168)</th>
<th><em>Enterobacter</em> spp.&lt;br&gt;(n=306)</th>
<th><em>Proteus mirabilis</em>&lt;br&gt;(n=96)</th>
<th><em>P. aeruginosa</em>&lt;br&gt;(n=162)</th>
<th><em>Acinetobacter</em> spp.&lt;br&gt;(n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CA</td>
<td>N</td>
<td>CA</td>
<td>N</td>
<td>CA</td>
<td>N</td>
</tr>
<tr>
<td>AMX</td>
<td>65.2</td>
<td>45.8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AMC</td>
<td>78.1</td>
<td>58.2</td>
<td>85.2</td>
<td>80.2</td>
<td>39.8</td>
<td>33.2</td>
</tr>
<tr>
<td>TIC</td>
<td>69.9</td>
<td>48.2</td>
<td>0</td>
<td>0</td>
<td>92.7</td>
<td>64.1</td>
</tr>
<tr>
<td>TZP</td>
<td>97.3</td>
<td>86.1</td>
<td>100</td>
<td>92.3</td>
<td>96.5</td>
<td>64.2</td>
</tr>
<tr>
<td>IPM</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>EPM</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>CTX</td>
<td>99.1</td>
<td>90.2</td>
<td>100</td>
<td>98.8</td>
<td>96</td>
<td>61</td>
</tr>
<tr>
<td>CAZ</td>
<td>99.4</td>
<td>88.7</td>
<td>100</td>
<td>94.5</td>
<td>96</td>
<td>64</td>
</tr>
<tr>
<td>FEP</td>
<td>99.3</td>
<td>96.1</td>
<td>100</td>
<td>96.7</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>GEN</td>
<td>98.5</td>
<td>88.7</td>
<td>100</td>
<td>99.2</td>
<td>100</td>
<td>91</td>
</tr>
<tr>
<td>AMK</td>
<td>99</td>
<td>88.5</td>
<td>100</td>
<td>88.6</td>
<td>100</td>
<td>91</td>
</tr>
<tr>
<td>CIP</td>
<td>94.8</td>
<td>87.2</td>
<td>100</td>
<td>98.1</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>LVX</td>
<td>100</td>
<td>67.3</td>
<td>100</td>
<td>96.7</td>
<td>100</td>
<td>67</td>
</tr>
</tbody>
</table>

Notes: AMX, amoxicillin; AMC, amoxicillin/clavulanic acid; TIC, ticarcillin; TZP, piperacillin/tazobactam; IPM, imipenem; EPM, ertapenem; CTX, cefotaxime; CAZ, ceftazidime; FEP, cefepime; GEN, gentamicin; AMK, amikacin; CIP, ciprofloxacin; LVX, levofloxacin.
The mortality rate reported in our study was in the range of 14.4% in community-acquired peritonitis and 28% in nosocomial peritonitis. In a recent study, focused on ICU patients, reported 24% of patients with nosocomial peritonitis. With community-acquired peritonitis died of complications versus 39% of patients with nosocomial peritonitis. In a recent study, focused on ICU patients, reported 24% mortality in community-acquired peritonitis and 28% in nosocomial infection [23-25]. However, the enterococcal proportions in nosocomial cases appear to be low when compared with other studies in nosocomial infections [28]. The low incidence of VRE in Ukraine was confirmed by its absence during this survey.

The susceptibility of anaerobic organisms towards usual treatments remains good. However, the poor susceptibility of bacteroides against clindamycin should be stressed. This drug is no longer recommended for empirical treatment of community-acquired peritonitis because of its low efficacy. On the other hand, the efficacy of carbapenems remains remarkable both in community-acquired and nosocomial infections. These features raise the issue of routine identification and susceptibility testing of anaerobes in peritoneal samples. Susceptibility testing is the only way to report the prevalence of resistance and to detect trends over time.

The mortality rate reported in our study was in the range of those reported in the literature for community-acquired infections but appeared low for post-operative nosocomial infections. In the Roehrborn et al.[23] study, 9% of patients with community-acquired peritonitis died of complications versus 39% of patients with nosocomial peritonitis. In a recent study, focused on ICU patients, reported 24% mortality in community-acquired peritonitis and 28% in nosocomial infection [25].

LIMITATIONS IN THE OUR STUDY
Retrospective studies have their own limitations. This is the case in the current investigation as a limited number of centres participated in the survey. Results from these centres may not necessarily always be relevant to other Ukrainian hospitals. The lack of centralized microbiological analysis of the strains in a reference laboratory, which would have allowed complete susceptibility data availability, has to be mentioned. However, all microbiological laboratories follow the same guidelines issued by the Ministry of Health of Ukraine, decreasing the heterogeneity. As this was an retrospective study, the treatment response was not monitored, which is a weakness in a study of a polymicrobial infection where the isolated microorganisms are not all responsible for the host response. As a consequence, our results should be considered cautiously.

CONCLUSIONS
The significant risk factors defined should be addressed preoperatively to decrease the risk for nosocomial infections. Early detection and treatment is essential to minimize complications of IAIs. Antibiotics application tactics should be determined in accordance with the local data of resistance to them in each surgical in-patient institution. Taking into account the constant changes and significant differences of the resistance levels observed in various hospitals and regions, the constant monitoring of antibiotic resistance to antimicrobials in every in-patient medical institution is required and on the base of the local obtained results to elaborate the hospital record sheets.

REFERENCES


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Authors’ contributions:
According to the order of the Authorship.

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

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