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EPIDEMIOLOGICAL AND MICROBIOLOGICAL ASPECTS OF HEALTHCARE-ASSOCIATED INFECTIONS IN UKRAINE DURING THE 2009–2019 PERIOD

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ABSTRACT

INTRODUCTION. Healthcare-associated infections (HCAIs) are a global health problem, and the problem of HCAIs in Ukraine remains poorly understood because of problems with the registration system.

OBJECTIVE. To analyze the official data of the number of registered HCAIs in Ukraine for the period 2009-2019, compare them with the available data in scientific publications.

MATERIAL AND METHODS. Statistical analysis of information from the “Laboratory Centers of the Ministry of Health of Ukraine” kindly provided by the State Institution “Public Health Center of the Ministry of Health of Ukraine”.

RESULTS. In 2019, 2,611 cases of HCAIs were registered, the lowest annual number of registered HCAIs in the last twelve years. The maximum number of HCAIs in 2011 was 7,448. An average of 5,089±756 cases of HCAIs has been registered annually. By age structure, the average for 2009-2019 was 78.0±5.8 % for adults and 22.0 % for children (0-17 y.o.). In 2019 13.8% of registered potential HCAIs agents were identified as MDR, and 80.0-87.0% belongs to the group of 12-17, the most common pathogens.

CONCLUSIONS. The estimated minimum number of HCAIs in Ukraine was expected to be about 1 million per year. Official statistics on registered cases of HCAIs in Ukraine do not reflect reality, so the registration system and investigation of HCAIs in Ukraine needs to be reformed.

Key words: *healthcare-associated infections, HCAIs, nosocomial infections, statistical analysis, pathogens*

INTRODUCTION

Healthcare-associated infections (HCAIs, HAIs) are a global health problem. For bacterial infections, it is infections that occur while receiving health care, developed in a hospital or other health care facility that first appear 48 hours or more after hospital admission, or within 30 days after having received health care, provided that at the time of hospitalization, patients were not in the incubation period (1,2).

According to Ukrainian law, HCAIs - diseases that occur in a patient during a stay in the health care institution or in another institution that provides medical care. Infectious diseases that available or in the incubation period at the time of hospitalization or at the beginning of treatment do not belong to HCAIs. HCAIs include infectious diseases acquired in the health care institution but clinically manifested after

finishing treatment, in the case of a reliably proven connection with the treatment or diagnostic measures. A separate group of HCAIs are infectious diseases among health care workers acquired directly during the performance of professional duties.

In high-income countries, approximately 30% of patients in intensive care units (ICU) are affected by at least one HCAI, from 3.5% to 12.0% of hospitalized patients have HCAIs (the EU average is 7.1%). In low- and middle-income countries, HCAIs vary between 5.7% and 19.1%; the frequency of ICU-acquired infection is at least 2-3 fold higher than in high-income countries, and it can reach 88.9% of hospitalized patients (2). Of all HCAIs, the device-associated infection is up to 13 times higher than in other types of HCAIs. Newborns are at higher risk of acquiring HCAIs in developing countries, with infection rates to 20 times higher than in high-income countries.

The economic consequences of HCAs are significant and estimated at approximately €7 billion per year in Europe, including direct costs only and reflecting 16 million extra days of hospital stay, and at about US\$ 6.5 billion in the USA. It costs about \$ 4,888 to treat 1 case of catheter-associated circulatory infection and \$ 2,255 to treat 1 case of ventilator-associated pneumonia in the United States.

The problem of HCAs in Ukraine remains poorly understood. There are clinical, laboratory and epidemiological criteria of HCAI diagnosis based on the order of the Ministry of Health of Ukraine of 12/28/2015 № 905, which is based on WHO criteria. In Ukraine, local hospital epidemiologists and regular medical doctors may register HCAI cases and have to report to the local public health centre, which has to initiate the creation of a commission of HCAI case inquiry for investigation with possible sanctions for the healthcare unit. In our opinion, there is still a tendency in Ukrainian medical circles to keep silent and do not register cases of HCAs due to the possible sanctions mechanism, which punishes a doctor and a hospital for each case of HCAs rather than constructively investigates it.

OBJECTIVE

Therefore, the work aims to analyze the official data of the number of registered HCAs in Ukraine for the period 2009-2019, compare them with the available

data on cases of HCAs in scientific publications and predict the dynamics of HCAs.

METHODS

Statistical information from the «Reports on individual infections and parasitic diseases» of the regional «Laboratory Centers of the Ministry of Health of Ukraine», as well as summary statistics in Ukraine on HCAs, including the distribution of nosologies and pathogens, for the last 11 years of observations (2009-2019 years). All data was kindly provided by the State Institution «Public Health Center of the Ministry of Health of Ukraine» for a scientific purpose. Statistical analysis of the data was carried out with the help of Microsoft Excel 2019.

RESULTS

According to the Ministry of Health's official reports, the total number of registered cases of HCAs in Ukraine (absolute numbers) for 2009-2019 is shown in Figure 1 and tends to decrease. In 2019, 2,611 cases of HCAs were registered, the lowest annual number of registered HCAs in the last 10 years. The maximum number of HCAs in 2011 was 7,448. An average of $5,089 \pm 756$ cases of HCAs has been registered annually.

Comparing the change in the total number of HCAs compared to the previous year (Figure 1), there

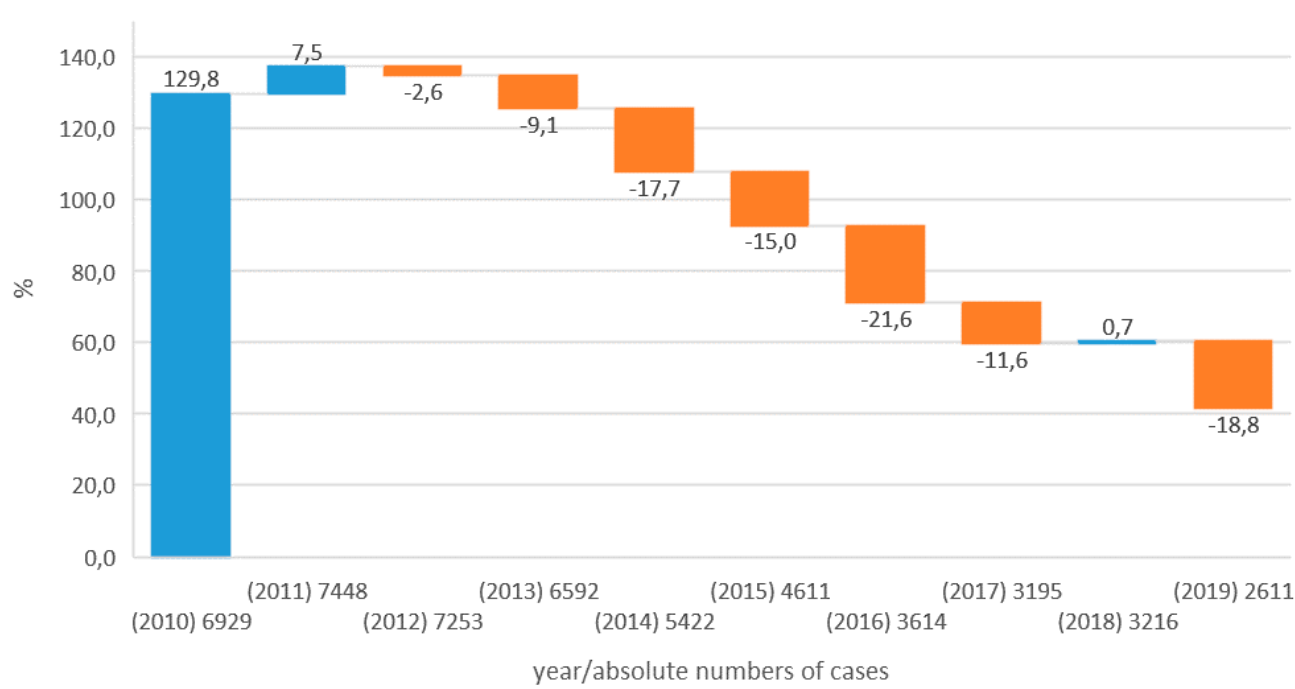


Figure 1. Trends in the total number of registered HCAs in Ukraine for the period 2009-2019 (%) compared to the previous year. Blue colour – increasing number of cases; orange colour – decreasing number of cases.

was a significant increase of 129.8% in 2010 compared to 2009 and 7.5% in 2011 compared to 2010. Further developments show a gradual annual decrease in reported HCAIs cases, averaging 12.0 % annually in 2011-2019. Thus, the total registered number of HCAIs in 2019 decreased by 64.9% compared to 2011.

By age structure, the average for 2009-2019 was 78.0 ± 5.8 % for adults (Figure 2) and 22.0 % for children (0-17). An increase of 33.6 % was registered among children in 2009, compared to 27.8 % in 2019. The decrease was 15.7% in 2015.

In the structure of the HCAIs for children, the majority (66.8 %) of children were newborns, and it was 14.7 % of all registered HCAIs in 2009 – 2019.

Concerning the types of HCAIs, in Ukraine, HCAIs cases are classified by nosological characteristics according to ICD-10 classification and grouped according to the organs' systems. The infectious process originated in 18 groups (Table 1).

The largest number was «Infections resulting from surgical and therapeutic interventions», with an average of 25.9 % of the total number of HCAIs, «Infections during pregnancy, childbirth and the post-natal period» accounted for 13.4 %, and «Infections of certain conditions occurring in the perinatal period» for 12.0 % (Figure 3). On average, all other HCAIs groups accounted for less than 10 % of the total average HCAIs, for example, “Skin and subcutaneous

fibre infections” 9.5 %, respiratory infections 8.3%, and 7.9 % of urinary tract infections.

Concerning the geographical distribution of HCAIs in Ukraine, 77.2 % of all cases of HCAIs in the period 2009-2019 were in the Odessa region, with 82.9 % of the total number of HCAIs in Ukraine in 2019 (Figure 4). Second in the rank comes Donetsk region 4.9%, the third place is taken by Kyiv and Kyiv region, totalling 3.6%.

DISCUSSION

According to WHO data, it is possible to predict the real level of HCAIs in Ukraine (2). Ukraine is classified as a low-income country and a middle-income country (3), with a corresponding HCAIs of 5.7% to 19.1%. In ICU, the estimated HCAIs frequency is 4.4% to 88.9% (average 42.7 per 1.000 patient-days), with device-associated (mainly central catheters and ventilators) occurring 19 times more frequently than in high-income countries. Neonatal HCAIs are 3 to 20 times more common than in high-income countries, accounting for 4.0 % to 56.0 % of neonatal deaths.

The minimum estimated level of HCAIs in Ukraine should be between 800,000 and 1.5 million cases annually (Table 2). Still, the actual number of reported cases does not exceed 8,000 per year, which shows that the system of epidemiological surveillance in Ukraine is inadequate.

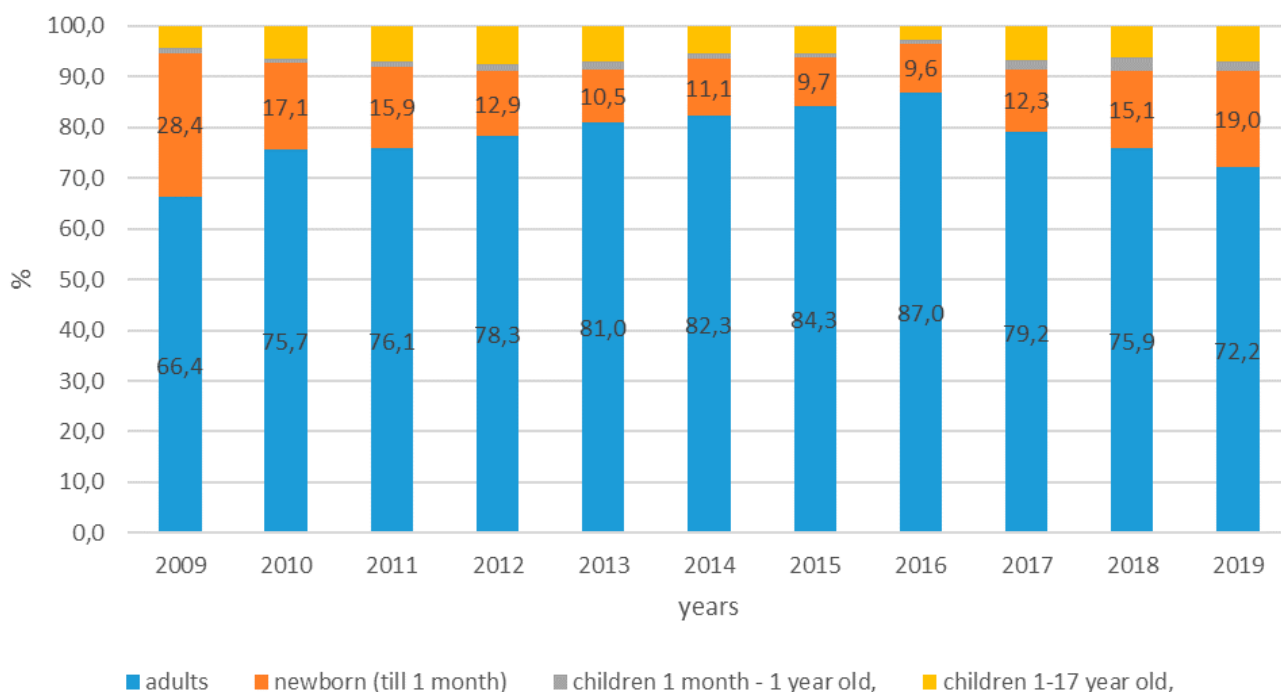


Figure 2. The age structure of registered cases of HCAIs in Ukraine for 2009 - 2019.

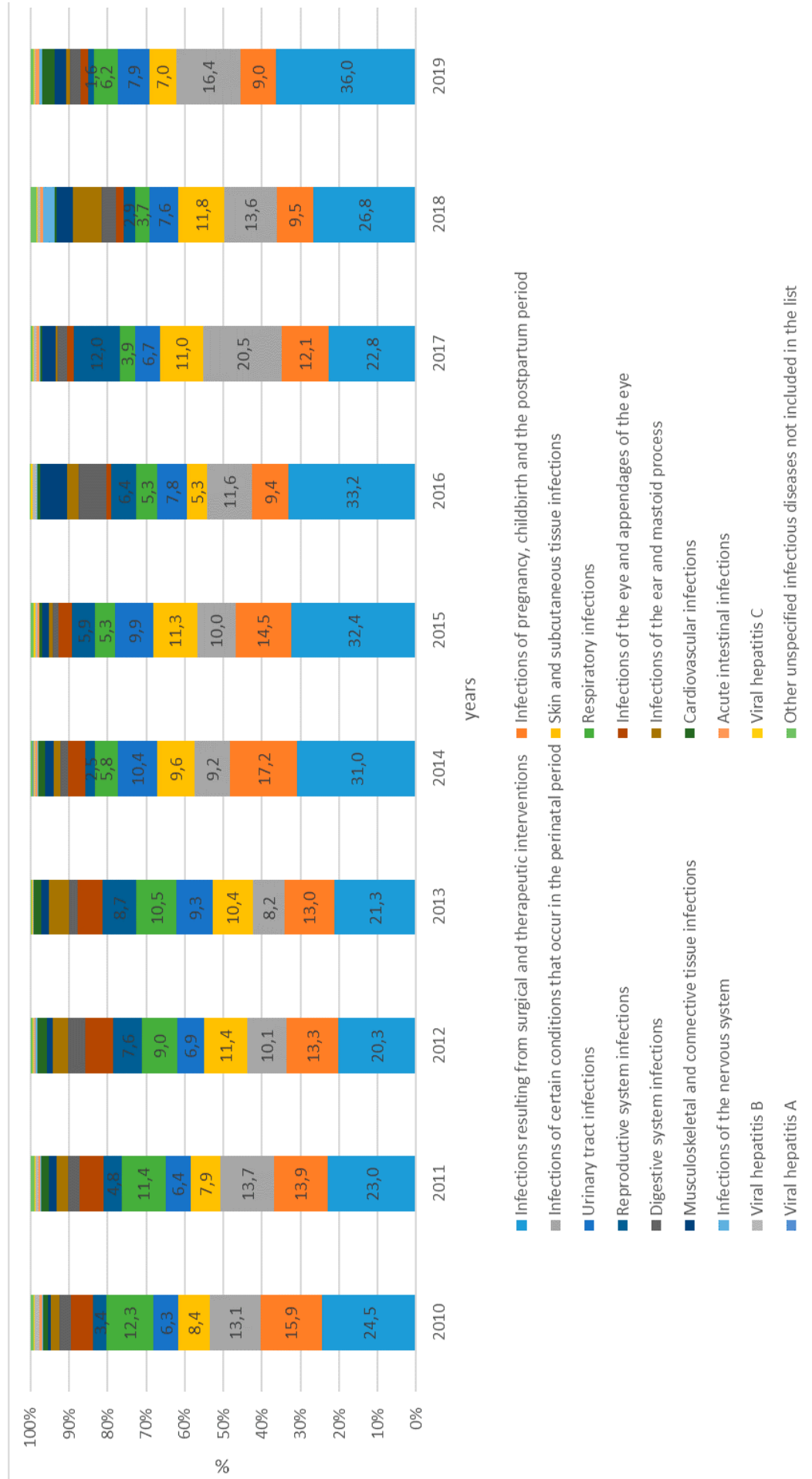


Figure 3. The nosological structure of HCAs in Ukraine in the period 2009-2019 shows data as a percentage of total HCAs in the current year.

Table 1. The number of registered cases of HCAs in Ukraine (absolute numbers) for the period 2009-1019, according to the localization of the infectious process (data from the Public Health Centre of Ukraine)

Name of diseases	ICD-10 code	2019*	2018	2017	2016	2015	2014	2013	2012	2011	2010
HCAs, total number:		2611	3216	3195	3614	4611	5422	6592	7253	7448	6929
including: Infections of the nervous system	G 00.1-G00.3, G00.8, G00.9, G01, G02.1, G02.8, G04, G05.0, G05.2, G06.0- G07	21	100	12	8	5	12	5	24	23	17
Infections of the eyes and appendages	H01.8, H05.0, H15.0, H15.1, H16.1 -H16.3, H20, H30, H44, H59	46	67	54	49	165	240	429	523	458	390
Infections of the ear and papilla	H60.0, H61.0, H66.0, H68.0, H70.0, H70.2, H70.8, H73.0, H81.2, H83.0, H95.8, H95.9	24	238	18	107	52	103	339	275	213	147
Infections of the cardiovascular system	I30.1, I33.0, I40.0, I77, I80.0- I80.2, I80.8, K75.1	86	15	9	25	32	86	133	188	149	77
Respiratory infections	J01-J06, J12-J16, J18, J20-J21, J85, J86	162	120	124	193	243	317	690	656	850	850
Digestive infections	K04- K06, K 10-K14, K29, K57, K61, K63, K65, K75, K81.0, K82, K83, K85	75	116	75	263	63	105	148	325	228	218
Skin and subcutaneous tissue infections	L02.0-L02.8, L03, L94.8, L98.6	182	380	352	191	522	523	684	827	590	579
Musculoskeletal and connective tissue infections	M46, M49, M50, M65, M71, M86	74	135	116	248	76	121	133	113	142	57
Urinary tract infections	N10-N12, N13.6, N15.1, N30, N34.0, N39.0	206	246	214	281	458	563	612	501	478	435
Reproductive system infections	N41.2, N45, N49, N61, N70, N71, N73, N75.1, N76	41	93	383	232	271	137	571	550	354	239
Infections of pregnancy, childbirth and the postpartum period	O 08.0, O23, O26.4, O75.2-3, O85, O86, O88.3, O91, O98	236	304	385	339	668	930	858	968	1035	1099
Infections of certain conditions that occur in the perinatal period	Separate A 00-B 99, P00.2, P23, P35-P39, P58.8	427	436	654	420	460	501	540	734	1024	907
Infections resulting from surgical and therapeutic interventions	T 79.3, T80.2, T81.4, T84.5- T84.7, T85.7, T87.4, T88.0	940	862	728	1200	1494	1683	1401	1470	1716	1698
Acute intestinal infections	A.00-A09	21	25	23	6	26	34	5	24	41	65
Viral hepatitis A	B15						9		3	1	1
Viral hepatitis B	B16	11	21	20	30	22	16	8	25	54	79
Viral hepatitis C	B17.1	6	6	8	19	21	10	11	11	13	19
Other unspecified infectious diseases not included in the list	B99	18	52	20	3	33	32	25	36	79	52

*The total of 2019 (2,611 cases) includes 35 unclassified cases.



Figure 4. Distribution of the average number of reported cases (absolute numbers) of HCAIs in Ukraine, by region, 2009 – 2019

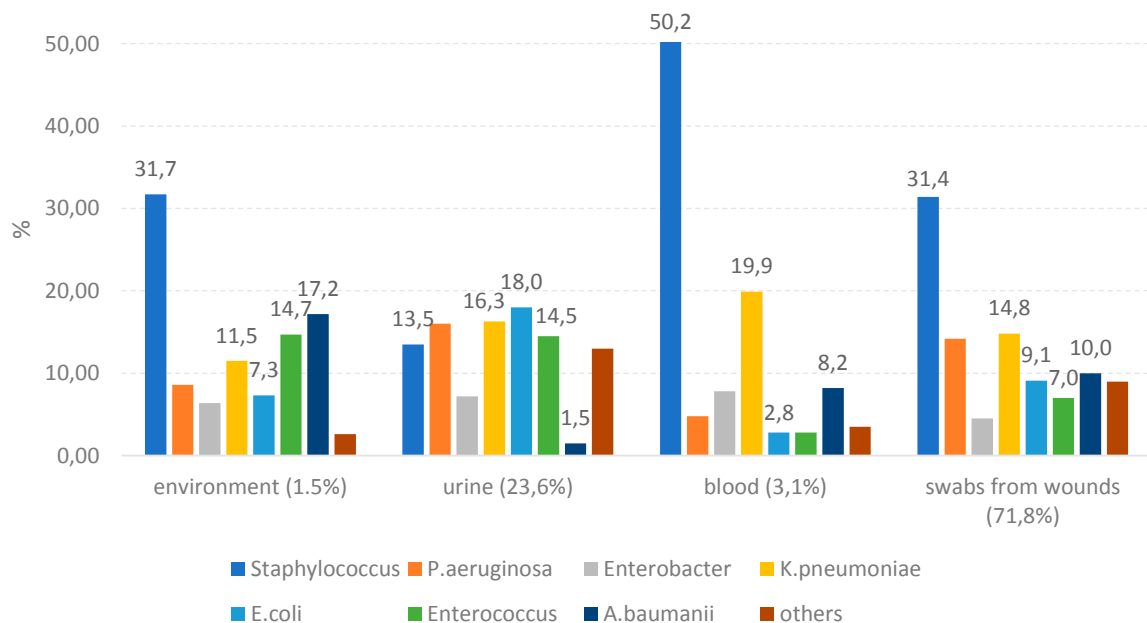


Figure 5. Species spectrum of MDR microorganisms isolated in 2019 in Ukraine

Table 2. The ratio of hospitalizations in healthcare facilities to the number of HCAs in Ukraine (Public Health Centre of Ukraine)

	2010	2015	2016	2017
Number of hospitalized patients, million people	10 500 000	8 600 000	8 600 000	8 300 000
Number of registered cases of HCAs, persons	6929	4611	3619	3195
Specific weight, %	0.07	0.05	0.04	0.04
The average percentage of HCAs in hospitalized patients according to the WHO, %	5-10% - developed countries up to 40% - in developing countries			
The minimum estimated number of HCAs in Ukraine, persons	1 050 000	860 000	860 000	830 000

If we compare Ukraine with neighbouring countries, for example, Poland and Romania as high-income economies according to World Bank classification (3), in Poland, HCAs rate is 24–45% of ICU patients (4) treatment duration and mortality. The aim of the study was to determine the prevalence and microbiological profile of HAIs in patients hospitalized in an ICU over a span of 10 years. The active surveillance method was used to detect HAIs in adult patients who spent over 48 h in a general ICU ward located in southern Poland between 2007 and 2016. The study was conducted in compliance with the methodology recommended by the Healthcare-associated Infections Surveillance Network (HAI-Net), and some meta-analyses in Poland showed that HCAs affected 30% of patients (5). As in Ukraine, HCAs represent a much-underestimated pathology in Romania. Official data show rates are only 0.078%–0.25% (6,7) can lead to a state of disability that reduces quality of life. Often, HAI are one of the factors that lead to death. The purpose of this study was to analyze the cases of HAI identified in public hospitals at the county level, through case report sheets, as they are reported according to the Romanian legislation. Methods: We performed a cross sectional study design based on the case law of the data reported to the Mures Public Health Directorate, by all the public hospitals belonging to this county. We tracked hospital-acquired infections reported for 2017–2018, respectively, a number of 1024 cases, which implies a prevalence rate of 0.44%, 1024/228,782 cases discharged from these hospitals during the studied period. Results: The most frequent HAIs were reported by the intensive care units (48.4% of hospitalized patients, and some single reports show 2,6% (8).

We understand that each country has its own HCAs registration system, and the data comparing two countries requires a deep understanding of HCAs registration system. But we want to highlight that in Ukraine, there are problems with fixation and registration phases, and the HCAs diagnostic criteria in Ukraine relevant to the Europe Union CDC` criteria

in our opinion, medical staff have enough knowledge for HCAs diagnostic and registration.

There are very few publications on HCAs cases in the regions of Ukraine. Available clinical cases of HCAs cases are more likely to allow for an in-hospital infection source, avoiding publication of evidence to support this. However, according to some authors (9) and account for substantial morbidity and mortality. Aim: To obtain the first estimates of the current prevalence of HAIs and antimicrobial resistance in acute care hospitals in Kyiv, Ukraine. Methods: Prospective surveillance was conducted from January 2014 to December 2016 in five acute care hospitals in Kyiv. Definitions of HAIs were adapted from the Centers for Disease Control and Prevention's National Healthcare Safety Network. Findings: Among 53,884 patients, 3753 (7%, 3573 patients from 5 emergency hospitals were identified in Kyiv between 2014 and 2016, with infectious disease pathogens retrospectively assessed as typical agents for HCAs. During the same period (2014-2016), 119 cases of HCAs were officially registered in Kyiv. According to official data, another publication (5) records 1912 patients with surgical HCAs in 3 hospitals in Kyiv for the period 2011-2013. The number of all registered HCAs for the same period is 304.

Another example is discovering 50 patients with HCAs in 3 hospitals for several months, whereas in Lviv and Lviv region in 2018, only 17 cases of HCAs were registered (10). In the city of Dnipro, 3178 patients were identified in a hospital during 2011 - 2014, with microorganisms strains described as HCAs (11). Still, during the same period, 541 cases of HCAs were officially registered throughout the Dnipro region. This confirms the colossal underestimation and inconsistency of official data with the real situation of the HCAs. The actual number of HCAs in Ukraine cannot be found in any report at any level, then national or individual hospital report (12).

According to the American Medical Association, if the occurrence of microbial seeding is analyzed according to the localization of the pathological process, in 2016, respiratory tract material (63.5 %), abdomen

(19.6 %), and blood (15.1 %) showed the highest levels of seeding. Catheter-associated infections account for 4.7 %. The trend is mainly the same for all regions of the world. Only in Eastern Europe (including Ukraine) and Latin America was the number of positive samples from urinary studies higher than from blood tests.

While the majority of HCAs cases worldwide are urinary tract infections (up to 40.0 %) and respiratory tract infections (30.0 %), the majority of reported cases of HCAs in Ukraine are infections due to surgical or therapeutic interventions (up to 36.0 per cent) (figure 3), and urinary tract infections account for up to 10.0 % of the total, not in relation to the statistical results of other countries.

There are extremely little official data about microbiological features of HCAs in Ukraine. Only very few papers about etiological structures and antibiotic sensitivity available.

According to the specific profile of HCAs agents, the main HCAs agents in the world are 12-17 microorganisms, which make up 80.0% - 87.0% of all *S. aureus*, *Enterococcus* species (e.g., *faecalis*, *faecium*), *E. coli*, coagulase-negative *Staphylococci*, *Candida* species (e.g., *albicans*, *glabrata*), *K. pneumoniae* and *Klebsiella oxytoca*, *P. aeruginosa*, *A. baumannii*, *Enterobacter*, *Proteus* spp., nitric oxide synthase yeast, *Bacteroides* spp. and other pathogens (1). A general trend in the distribution of HCAs factors by seed frequency is the predominance of more gram-negative microorganisms (62.2%), with *Pseudomonas* spp dominating the gram-positive (46.8%) with the predominance of *Staphylococcus aureus* in all geographical regions of the world, except North America, where gram-positive microorganisms are more likely to be detected by a small margin. Data from a small number of publications of HCAs in Ukraine (9,13) and account for substantial morbidity and mortality. Aim: To obtain the first estimates of the current prevalence of HAIs and antimicrobial resistance in acute care hospitals in Kyiv, Ukraine. Methods: Prospective surveillance was conducted from January 2014 to December 2016 in five acute care hospitals in Kyiv. Definitions of HAIs were adapted from the Centers for Disease Control and Prevention's National Healthcare Safety Network. Findings: Among 53,884 patients, 3753 (7% show a correlation between the species profile of the pathogens and the worldwide trend: prevalence of gram-negative microbiota (43.9-57.6%) with the dominance of *Pseudomonas* spp and *Enterobacteria* over gram-positive (35.9-37.2%) with the predominance of *Staphylococcus aureus*. According to individual studies, the prevalence of MRSA (methicillin-resistant *Staphylococcus aureus*) among other strains of *Staphylococcus aureus* in Ukraine in 2017 was 37.4%, which is not significantly

different from the majority in neighbouring countries of Ukraine (more than 50% in Romania, 15% in Poland, 25-50% in Belarus) (14) methicillin-resistant *Staphylococcus aureus* (MRSA).

Among these pathogens, 16.0% to 20.0% are multidrug resistance (MDR), but antimicrobial resistance (AMR) varies depending on the type of pathogen and the geographical region; for example, among Gram-negative agent device-associated, the MDR level is 40.0%. In Ukraine, for example, in the period 2014 - 2016, according to some authors (13), 26.3% of the pathogens of surgical interventions were resistant to 4 or more classes of antibiotics with different AMR profile (41.0% to lincosamides, 40.4% to tetracyclines, 27.8% to macrolides, 35.4% to chloramphenicol, 34.5% to beta-lactams, 31.5% to aminoglycosides, 24.2% to fluoroquinolones, 21.2% to glycopeptides, 11.3% to oxazolidinones) which is broadly consistent with the AMR profile in the region.

There is no unified antibiotic sensitivity registration system for HCAs in Ukraine. Generally, the EUCAST methodology was integrated in 2019, and no more than 20% of laboratories have WHONET or another software. According to incomplete data, in 2019, the laboratories of health care facilities conducted 1.4 million microbiological investigations, 94 thousand cultures of microorganisms were isolated (7.1%), of which 13.8% were identified as MDR (15).

Data on the etiological structure of HCAs pathogens are not recorded in the official reports of the Ministry of Health, but are reflected in separate scientific publications (9,16,17) and account for substantial morbidity and mortality. Aim: To obtain the first estimates of the current prevalence of HAIs and antimicrobial resistance in acute care hospitals in Kyiv, Ukraine. Methods: Prospective surveillance was conducted from January 2014 to December 2016 in five acute care hospitals in Kyiv. Definitions of HAIs were adapted from the Centers for Disease Control and Prevention's National Healthcare Safety Network. Findings: Among 53,884 patients, 3753 (7% show that typical HCAs pathogens in Ukraine correspond to typical pathogens found in other countries; the MRSA remains the lead agent ESBL (extended-spectrum beta-lactamase), CPE (carbapenemase-producing Enterobacteria), VRE (vancomycin-resistant Enterococci). 13.0-20.0% of HCAs cases are caused by rare agents, such as *Raoultella* spp (18). *Aeromonas* spp. *Pragia* spp. *Vibrio* spp (19). and others remain unexplored because their identification requires additional laboratory costs and skills.

According to the results of the study of AMR mechanisms among enterobacteria- HCAs agents, the most common type of multiple resistance is beta-lactamases ESBL (47.8%), carbapenemases were

found in 34.3% of the strains. Identifying strains with mixed phenotypes with different substrate specificities indicates an active inter-static and inter-species exchange of mobile genetic elements, encoding beta-lactamases, and poses significant risks due to resistance to a wide range of antibiotics (20).

HCAIs are characterized by a plurality of mechanisms and routes of transmission, among which it is common to distinguish: 1) natural (contact, airborne, faecal-oral); 2) artificial (artificial) - due to invasive diagnostic and therapeutic procedures. It should also be noted that in Ukraine, the most common are infections after surgical and therapeutic interventions (e.g. post-injection complications).

We didn't find official data (15) about sources of HCAIs in Ukraine, but according to the AMR screening in 2019 year, just 1.5% of MDR strains were isolated from the hospital's environment (Figure 5).

The hospital infection IPC (infection prevention and control) team is the cornerstone of HCAIs control and prevention. In the EU, the hospital IPC team leader is a medical doctor (MD) with a specialization in medical microbiology (clinical microbiologist) (21). Clinical microbiologists can diagnose patients, and prescribe medicines, including independently diagnose HCAIs and change antibiotic therapy. Clinical microbiologists were added to the list of medical specialists in Russia in 2019. Unfortunately, there are no clinical (medical) microbiologists in Ukraine, and there is no such specialization. There are epidemiologists in the hospitals, but they can't diagnose patients separately and diagnose HCAIs without current MD. In this case, the hospital administration is not interested in diagnosing HCAIs, because it leads to sanctions and fines from the Sanitary and Epidemiological Service (SES) - an obsolete rudiment of the Soviet Union. This service had been counselled in 2017 but was working during some part of the observation period, and the position of chair of SES was restored in 2020 to overcome the Covid-19 pandemic, but we believe that the restoration of the SES chairman position indicates the current government has taken a course to restore the SES, which was ineffective for the HCAIs IPC. Instead, the SES function in the EU is performed by the IPC team in the hospitals and Public Health Centers.

CONCLUSIONS

Official statistics of HCAIs in Ukraine do not reflect reality. The estimated minimum number of HCAIs in Ukraine should be about 1 million cases per year instead of 7 thousand. The main reason for HCAIs underestimating are problems with surveillance system during the primary (diagnosis and registration)

phase. IPC and AMR monitoring systems should be reformed.

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Author Contributions:

Research concept and design – YK,
Collection and/or assembly of data – MP, IT, OH
Data analysis and interpretation – OB, LZ, RK
Writing the article – YK,
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Final approval of the article – OK
Translation – MP

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