Article

Epidemiological and microbiological aspects of health care-associated infections in Ukraine during the 2009–2019 period

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Abstract: Statistical data on officially registered cases of health care-associated infections (HCAIs) in Ukraine in the period 2009-2019 have been analysed. On average, 5089±756 cases of HCAIs were registered annually. Odessa region of Ukraine is the leading country in the number of reported cases. The majority of HCAIs cases involve surgical and therapeutic invasive interventions and perinatal HCAIs. On average, 78.0±5.8 % of HCAIs cases involved adults. 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 system of registration and investigation of HCAIs in Ukraine needs to be reformed.

Keywords: health care-associated infections, HCAIs, hospital acquired infections, nosocomial infections, statistical analysis

1. Introduction

Health care-associated infections (HCAIs) is a global health problem, it is an 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).

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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 varies 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). From all types of HCAIs, the device-associated infection are up to 13 times higher than in others 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 HCAIs are significant and estimated at approximately €7 billion per year in the 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 HCAIs in Ukraine remains poorly understood. There is still a tendency in Ukrainian medical circles to keep silent and do not register cases of HCAIs due to the sanctions mechanism, which punishes a doctor and a hospital for each case of HCAIs rather than constructively investigates it.

Therefore, the aim of the work is to analyze the official data of the number of registered HCAIs in Ukraine for the period 2019-2019, compare them with the available data on cases of HCAIs in scientific publications and predict the dynamics of HCAIs.

2. Materials and 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 HCAIs, including the distribution of nosologies and pathogens, for the last 10 years of observations (2009-2019 years), provided by the State Institution "Public Health Center of the Ministry of Health of Ukraine". Statistical analysis of the data was carried out with the help of Microsoft Excel 2019.

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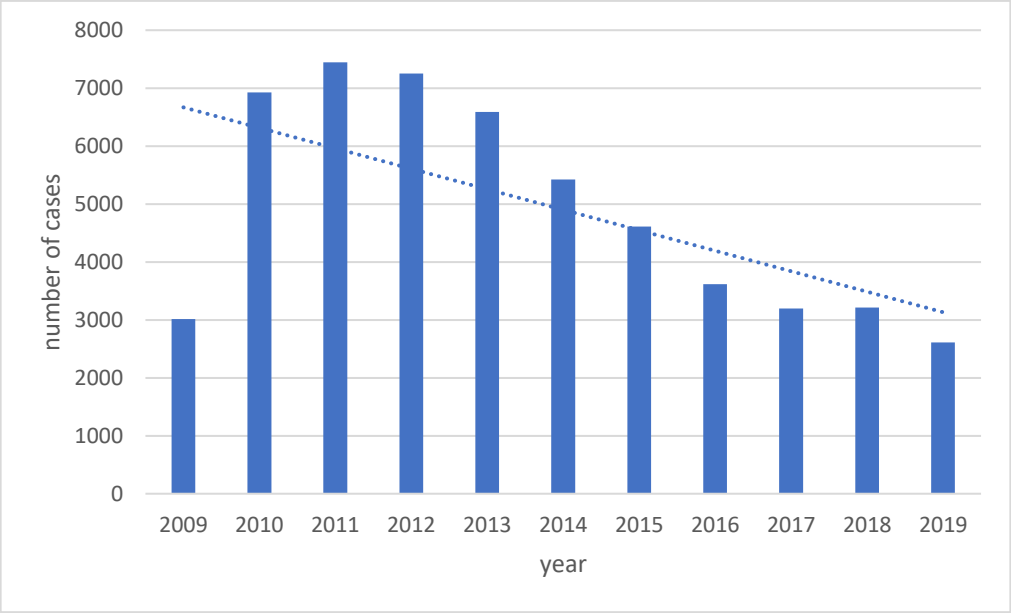
3. Results

According to the official reports registered by the Ministry of Health, the total number of registered cases of HCAIs in Ukraine (absolute numbers) for 2009-2019 is shown in Figure 1 and tends to decrease. In 2019, 2.611 cases of HCAIs were registered, the lowest annual number of registered HCAIs in the last 10 years. The maximum number of HCAIs in 2011 was 7.448. An average of 5.089±756 cases of HCAIs were registered annually.

Figure 1. The total number of registered cases HCAIs cases in Ukraine between 2009 and 2019 (absolute numbers) and the trend line.



Comparing the change in the total number of HCAIs compared to the previous year (Figure 2), there 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 the number of reported HCAIs cases, averaging 12.0 %annually in the period 2011-2019. Thus, the total registered number of HCAIs in 2019 decreased by 64.9% compared to 2011.

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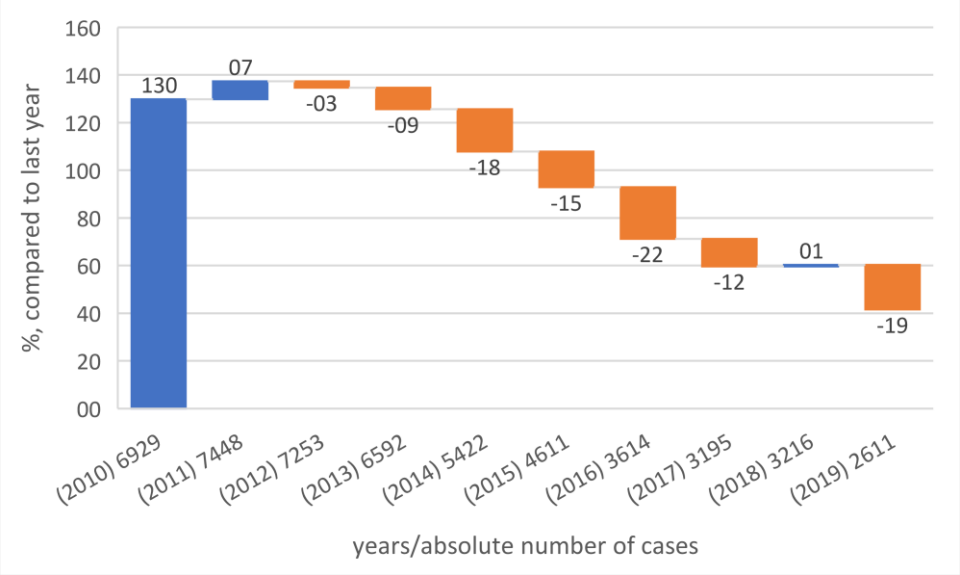
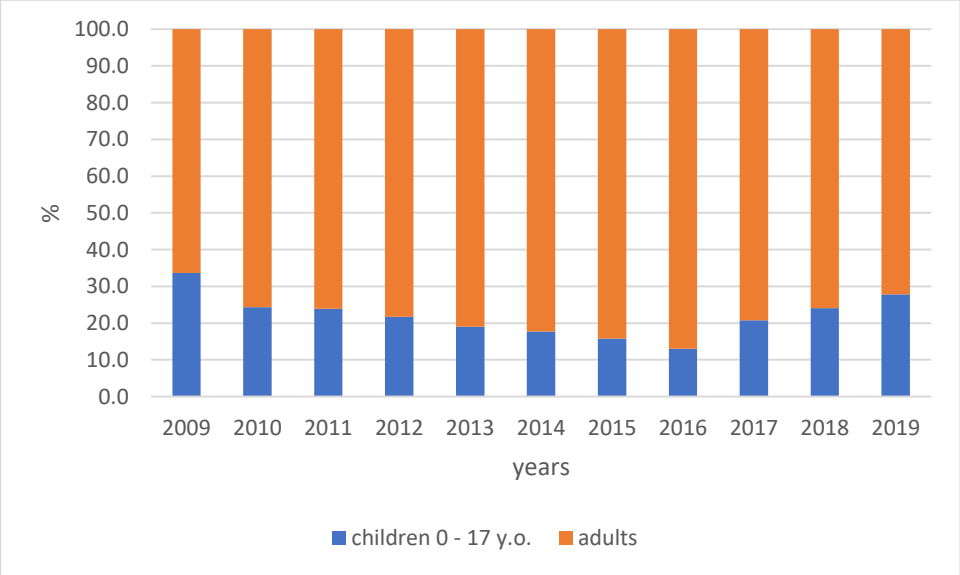
Figure 2. Trends in the total number of registered HCAIs in Ukraine for the period 2009 - 2019 (%) compared to the previous year. Blue collour – increasing number of cases; orange colour – decreasing number of cases.



By age structure, the average for 2009-2019 was 78.0 5.8 %for adults (Figure 3) 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 (Figure 3).

Figure 3. Age structure of registered cases of HCAIs in Ukraine for 2009 - 2019.



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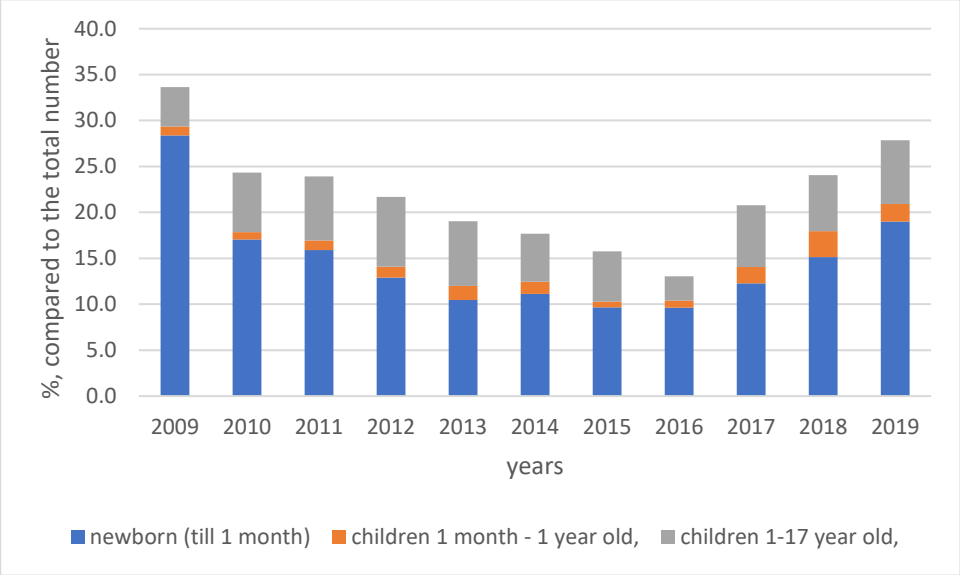
In the structure of the HCAIs, the majority (66.8 per cent) of children are born with HCAIs, with an average of 14.7 %of all registered HCAIs in 2009 - 2019 (Figure 4). The rate of HCAIs among newborns has increased slightly over the last three years.

Figure 4. The age structure of reported cases of HCAIs among children of different ages in Ukraine for the period 2009 - 2019.



With regard to the types of HCAIs, in Ukraine HCAIs cases are classified by nosological characteristic according to ICD-10 classification and grouped according to the systems of organs in which the infectious process originated into 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 5). On average, all other HCAIs groups accounted for less than 10 % of the total average HCAIs, for example, "Skin and subcutaneous fiber infections", 9.5 %, of respiratory infections 8.3%, and 7.9 %of urinary tract infections.

With regard to the geographical distribution of HCAIs in Ukraine, 77.2 %of all cases of HCAIs in the period 2009-2019 were in Odessa region, with 82.9 %of the total number of HCAIs in Ukraine in 2019 (Table 2, Figure 6, Figure 7). Second in the rank comes Donetsk region 4.9%, the third place is taken by Kyiv and Kyiv region with totalling amount 3.6%.

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Table 1. Number of registered cases of HCAIs 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**
HCAIs, 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,	24	238	18	107	52	103	339	275	213	147

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	H95.8, H95.9										
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,	206	246	214	281	458	563	612	501	478	435

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	N15.1, N30, N34.0, N39.0										
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	Окремі 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

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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 5. Nosological structure of HCAIs in Ukraine in the period 2009-2019, data as a percentage of total HCAIs in the current year.

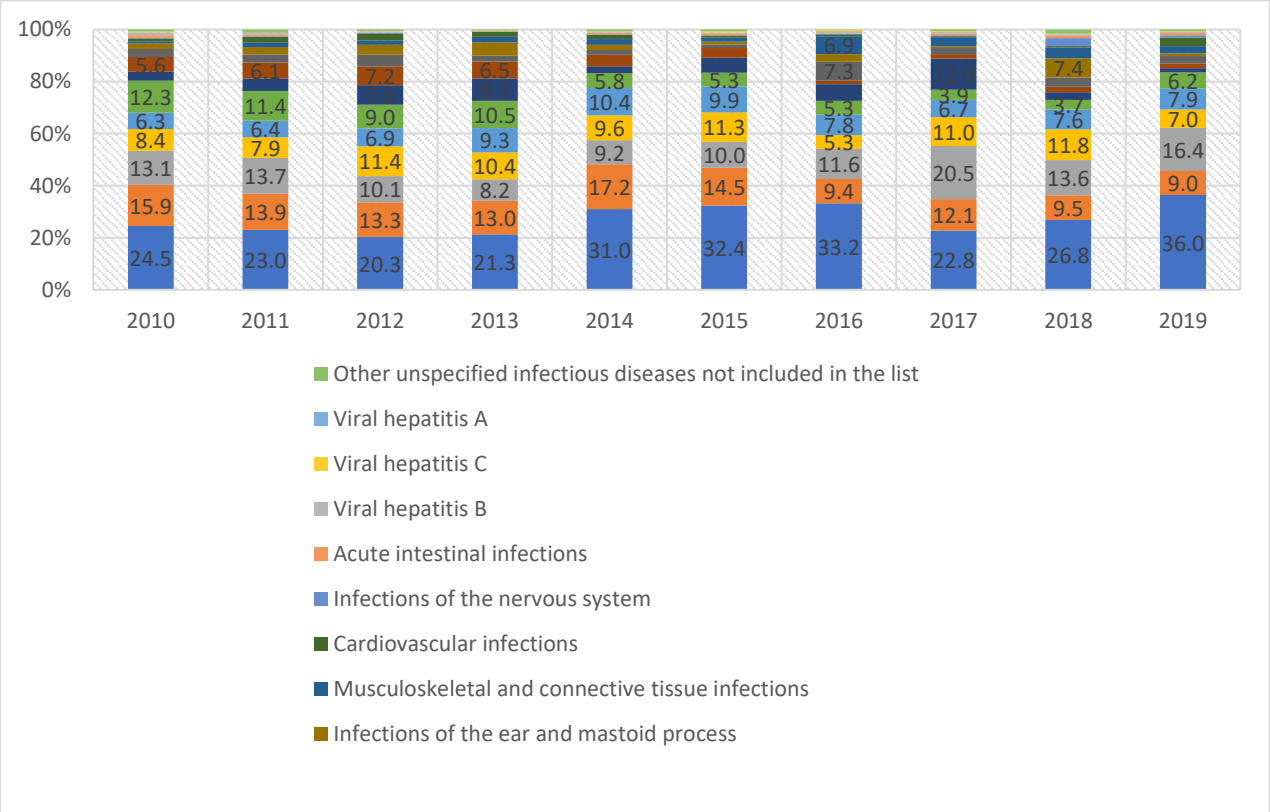

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Table 2. Geographical distribution of the number of registered cases of HCAIs in Ukraine by regions in 2009 - 2019 (data from the Public Health Centre of Ukraine).

Regions of Ukraine	**Total number of registered cases / year**									
	2019	**2018**	**2017**	**2016**	**2015**	**2014**	**2013**	**2012**	**2011**	**2010**
Crimea							39	65	71	84
Vinnytsia	35	30	33	62	69	60	50	73	91	100
Volyn	1	3	3	3	2	8		3	5	13
Dnipro	66	66	55	60	56	116	141	137	147	173
Donetsk	47	110	59	49	41	54	378	447	709	619
Zhytomyr	12	32	35	25	24	26	31	64	114	92
Zakarpattya		1			5		27	20	22	30
Zaporizhia	22	15	43	33	40	21	27	50	69	92
Ivano-Frankivsk	2	10	9	10	6	2	9	11	21	19
Kyiv`s region	36	37	66	50	94	150	137	251	203	84
Kropyvnytskyi	7	8	12	15	8	8	9	15	24	30
Luhansk	19	7	8	2	3	5	26	60	89	80
Lviv	4	17	14	23	26	22	16	36	51	80
Mykolayivska	25	14	23	17	38	49	41	43	70	77
Odessa	2165	2740	2683	3076	3868	4668	5386	5546	5076	4478
Poltava	42	25	28	26	26	22	26	36	58	59
Rivne	22	24		5	4	3	13	20	34	31
Sumy	20		3	7	10	9	8	10	12	25
Ternopil	3	2	5	3	8	8	12	10	13	19
Kharkiv	24	24	23	29	35	38	34	52	124	232
Kherson	28	16	22	14	21	24	14	27	20	21
Khmelnytsky	4	3	3	2	2	3	2	16	34	42
Cherkasy	5	10	10	10	12	23	26	76	103	97
Chernivtsi	8	8	36	57	150	36	34	98	120	95
Chernihiv	4	4	3	11	20	16	8	16	10	15
Kyiv city	10	10	19	25	43	51	93	66	145	238
Sevastopol city							5	5	13	4
UKRAINE	**2611**	**3216**	**3195**	**3614**	**4611**	**5422**	**6592**	**7253**	**7448**	**6929**

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Figure 6. Distribution of the average HCAIs level by region of Ukraine 2010 - 2019

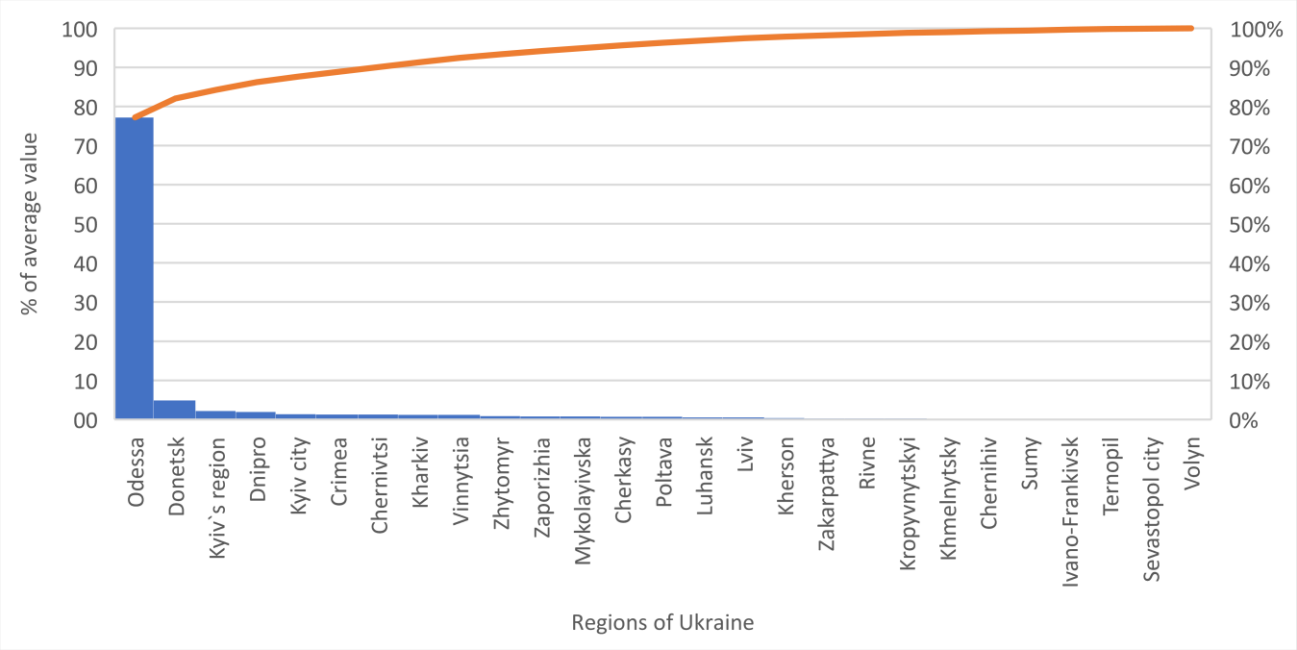

Figure 7. Distribution of the average number of reported cases of HCAIs in Ukraine, by region, 2009 – 2019

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4. 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 as 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 devayasiciovany (mainly central catheters and ventilators) occurring 19 times more frequently than in high-income countries. Neonatal HCAIs is 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 3), but 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.

There are very few publications on HCAIs cases in the regions of Ukraine. Available clinical cases of HCAIs cases are more likely to allow for an in-hospital source of infection, avoiding publication of evidence to support this. However, according to some authors (4), 3573 patients from 5 emergency hospitals were identified in Kyiv between 2014 and 2016, with infectious disease pathogens retrospectively assessed as typical agents for HCAIs. During the same period (2014-2016), 119 cases of HCAIs were officially registered in Kyiv (Table 2). Or other publication (5) that records 1912 patients with surgical HCAIs in 3 hospitals in Kyiv for the period 2011-2013, according to official data (Table 2) The number of all registered HCAIs for the same period is 304. Another example is the discovery of 50 patients with HCAIs in 3 hospitals for several months (6), whereas in Lviv and Lviv region in 2018 only 17 cases of HCAIs were registered. In the city of Dnipro, 3178 patients were identified in a hospital during 2011 - 2014, with microorganisms strains described as HCAIs (7), but during the same period 541 cases of HCAIs were officially registered throughout the Dnipro region. This once again confirms the colossal underestimation and inconsistency of official data with the real situation of the HCAIs, and the actual number of HCAIs in Ukraine cannot be found in any report at any level, then national or individual hospital report (8).

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Table 3. Ratio of hospitalizations in health-care facilities to the number of HCAIs in Ukraine (Public Health Centre of Ukraine).

	2010 p.	2015 p.	2016 p.	2017 p.
Number of hospitalized patients, million people	10 500 000	8 600 000	8 600 000	8 300 000
Number of registered cases of HCAIs, persons	6929	4611	3619	3195
Specific weight, %	0,07	0,05	0,04	0,04
The average percentage of HCAIs in hospitalized patients according to the WHO, %	5-10% - розвинені країни до 40% - в країнах що розвиваються			
The minimum estimated number of HCAIs in Ukraine, persons	1 050 000	860 000	860 000	830 000

According to the American Medical Association, if the occurrence of microbial seeding is analysed 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 HCAIs cases worldwide are urinary tract infections (up to 40.0 %) and respiratory tract infections (30.0 %), the majority of reported cases of HCAIs in Ukraine are infections due to surgical or therapeutic interventions (up to 36.0 per cent) (figure 5), and urinary tract infections account for up to 10.0 % of the total, not in relation to the statistical results of other countries.

According to the specific profile of HCAIs agents, the main HCAIs 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., NOS yeast, *Bacteroides* spp. and other pathogens (1). A general trend in the distribution of HCAIs factors by seed frequency is the predominance of more gram-negative micro-organisms (62.2%), with Pseudomonas spp dominating the gram-positive (46.8%) with predominance of *Staphylococcus aureus* in all geographical regions of the world, with the exception of North America,

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where gram-positive microorganisms are more likely to be detected by a small margin. Data from a small number of publications of HCAIs in Ukraine (4,9) show a correlation between the species profile of the pathogens and the worldwide trend: prevalence of gram-negative microbiota (43.9-57.6%) with dominance of *Pseudomonas* spp and *Enterobacteria* over gram-positive (35.9-37.2%) with predominance of *Staphylococcus aureus*. According to individual studies, the prevalence of MRSA among other strains of *Staphylococcus aureus* in Ukraine in 2017 was 37.4%, which is not significantly different from the prevalence in neighbouring countries of Ukraine (more than 50% in Romunia, 15% in Poland, 25-50% in Belarus) (10).

Among these pathogens, 16.0% to 20.0% are MRA, but antibiotic resistance varies depending on the type of pathogen and the geographical region, for example among Gram negative agent device-associated the MRA level is 40.0%. In Ukraine, for example, in the period 2014 - 2016, according to some authors (9), 26.3% of the pathogens of surgical interventions were resistant to 4 or more classes of antibiotics with different antibiotic resistance profile (41.0% to lincosamides, 40.4% to tetracyclines, 27.8% to macrolides, 35.4% to chloramphenicol, 34.5% to betal lactams, 31.5% to aminoglycosides, 24.2% to fluoroquinolones, 21.2% to glycopleptides, 11.3% to oxazolidons) which is broadly consistent with the antibiotic resistance profile in the region.

Data on the ethological structure of HCAIs pathogens are not recorded in the official reports of the Ministry of Health, but are reflected in separate scientific publications (4–6,11) show that typical HCAIs pathogens in Ukraine correspond to typical pathogens found in other countries, The MRSA remains the lead agency (methicillin-resistant Staphylococcus aureus) BPBL (strains of bacteria producing beta-lactamases of the extended spectrum), CPE (carbapenemase-producing Enterobacteria), VRE (vancomycin-resistant Enterococci). 13.0-20.0% of HCAIs cases caused by rare agents, such as *Raoultella* spp. *Aeromonas* spp. *Pragia* spp. *Vibrio* spp. and others remain unexplored, because their identification requires additional laboratory costs and skills.

According to the results of the study of antibiotic resistance mechanisms among enterobacteria- HCAIs agents, the most common type of multiple resistance is beta-lactamases ESβL (47.8%), carbapenemases were found in 34.3% of the strains. The identification of strains with mixed phenotypes with different substrate specificities indicates an active intermostatic and inter-species

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exchange of mobile genetic elements, encoding beta-lactamases and poses significant risks due to resistance to a wide range of antibiotics (12).

5. Conclusions

Infectious control, with continuous epidemiological surveillance, remains an important, if not the main, method of controlling HCAIs, which should be combined with the control of antimicrobial resistance of the main HCAIs agents. Official statistics on registered cases of HCAIs in Ukraine do not reflect reality. In the process of reform, the Ukrainian health-care system is being involved in international systems and structures for monitoring antibiotic resistance to the most pressing factors of infectious diseases and for monitoring the HCAIs. The success of such measures can be guaranteed only through the reliable registration of HCAIs cases in Ukraine, the results of microbiological diagnostics using modern methods and the standardization of results processing.

Author Contributions: Yulian Konechnyi - writing—original draft preparation, Marta Panas - writing—review and editing, Iryna Tymchuk - visualization, Roksolana Konechna - software, Olena Borysiuk - methodology, Iryna Hubytska - formal analysis, Lesya Zhurakhivska - investigation, Olena Korniychuk - project administration

All authors have read and agreed to the published version of the manuscript.

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