Effective measures to combat healthcare-associated infections are directly dependent on a thorough study of the prerequisites for their occurrence.

**The purpose of the study** is to analyze healthcare-associated infections in the Ruse region of Bulgaria by medical facilities and the impact of the COVID-19 pandemic on them for 2014-2021.

**Materials and methods:** The study covers the registration of patients who were served and registered healthcare-associated infections sorted by year in all medical facilities (9 units) in the district. The data was collected from the system for epidemiological surveillance of hospitals, and the analysis of the country and Ruse region and the analysis of the Ruse Regional Health Inspectorate. Documentary, statistical, and graphic methods are used.

**Results and discussion:** The data show that the number of patients served in the district in 2014-2021 increased (71,501 people in 2014), with small fluctuations in 2017, among which it fell to the initial level of 71,014 for 2021. There are data on the influence of the population structure and the workload of medical facilities. One of the hospitals - University Multiprofile Hospital for Active Treatment “Kanev” JSC, Ruse accounts for almost half of the patients admitted for treatment. Reported cases of healthcare-associated infections in the region by year show holding at one level, with no sharp fluctuations until 2019. A link has been established between the increasing incidence of COVID-19 and registered healthcare-associated infections in 2020 and 2021.

The COVID-19 pandemic affected both healthcare-associated infections prevalence and pathogen profiles.

**Conclusions:** In the initial period from 2014 to 2016, surgical site infections - 49.38% (2014), 33.00% (2015), and 18.35% (2016) were leading in the structure of the healthcare-associated infections, followed by respiratory infections 17.93%. (2014), urinary tract infections 13.32 % (2015), 17.23 % (2016). In the years of the pandemic, -2020 leading were lower respiratory tract infections at 27.93% and Pneumonia associated with intubation at 25.74% in 2021.

**Keywords:** healthcare-associated infections, registration, retrospective analysis, COVID-19, pathogens,

**INTRODUCTION:**

In the conditions of modern medical practice, during the extraordinary global pandemic of COVID-19, the problems of epidemiological surveillance of healthcare-associated infections in medical facilities-hospitals were put to the test. Under pressure with limited resources, insufficient numbers of health professionals, and fear of restructuring related to the opening of new facilities, patient and staff safety itself proved to be an indicator of the quality of treatment and prevention activities and assessment of infection control related to medical assistance. Effective measures to combat them are directly dependent on a thorough study of the prerequisites for their occurrence.

Large hospital complexes with a special ecology: overcrowding - high density of people with reduced immune protection, closed environment (hospital rooms, diagnostic and therapeutic procedures, with special medical equipment), create an artificial mechanism for the transmission of pathogens and contribute to the formation of hospital strains of microorganisms, with high virulence, invasiveness and polyresistance. The related tasks are so significant and complex that they cannot be solved only with administrative measures and means [1, 2, 3, 4]. Research work, expanding and deepening the epidemiological knowledge of doctors and service personnel, is an urgent task for healthcare specialists.

**MATERIALS AND METHODS:**

The purpose of the study is to analyze healthcare-associated infections in the Ruse region by medical facilities and the impact of the COVID-19 pandemic on them for the period 2014-2021. In fulfillment of the purpose of the study covers the registration of served and registered patients with in-hospital infections by year in all medical facilities (9 units) in the district. The data were collected from the system for epidemiological supervision and annual analyzes of the medical facilities for hospital care in the territory of the Ruse region, inquiries, analyses, pathogen profiles and microbiological studies in the Regional Health Inspectorate-Ruse. Data of the National Health Insurance Fund and Ministry of Health-Sofia, electronic reference - form “3” – 05, which is sent every three months. Documentary, statistical, and graphic methods are used. Results were processed with SPSS v. 20.0 using variance,
comparative and correlation analysis. We accept p<0.05 as the level of significance.

RESULTS AND DISCUSSION:
Limiting the occurrence, spread, morbidity and mortality of infectious diseases by implementing effective epidemiological surveillance is a priority in the state health policy. Regional Health Inspectorate - Ruse is part of the system of regional health inspections, which operates on the territory of the Ruse region. Epidemiological monitoring includes analysis of the patients served, the registered intra-hospital infections, the clinical and etiological characteristics, the antibiotics used in the medical facilities and their medical prevention facilities for hospital care. Development and implementation of complex programs for the prevention and control of healthcare-associated infections, according to Ordinance No. 3 of May 8, 2013, on the approval of a medical standard for the prevention and control of healthcare-associated infections. In Ruse, the planning, development and implementation of health promotion policy are taken into account. Surveillance of infectious diseases and effective state health control to limit the incidence of healthcare-related infections is carried out by 9 medical facilities. For the analyzed period, the priority task was, dealing with the COVID-19 pandemic.

In figure 1, we show the medical facilities in the Ruse region.

Fig. 1. Medical facilities in the Ruse region

The analysis of the data from the register in the medical facilities in the Ruse region shows that for the period 2014-2021, a total of 606,999 patients were hospitalized, and 5,188 cases of health-care-associated infections were reported. The established average incidence is 8.856 per 1000 patients.

We analyze the registered indicators for the number of hospitalized patients and the number of reported healthcare-associated infections over the years for the observed period, compared to those for the country.

For the whole period, more than half of the patients from the Ruse district were hospitalized in two university structures - University Multiprofile Hospital for Active Treatment “Kanev” JSC Ruse (31.8%) (Fig.2) and Ruse and University Multiprofile Hospital for Active Treatment “Medica” JSC Ruse (22.34%).

Epidemiological surveillance includes the analysis of served patients and registered health-care-associated infections, the clinical and etiological characteristics, antibiotics used in medical facilities and the prevention of these infections.

We are looking at the patients who went through treatment over a period of eight years in the Ruse region (Fig. 2). The patients who were served in the district during the period 2014-2021 are on the rise (71,501 people in 2014), there are small fluctuations in 2017 and 2018 (80,169 people in 2019), after which the number falls to the initial level of 71,411 during 2020 and 2021. One of the hospitals, the University Multiprofile Hospital for Active Treatment “Kanev” JSC Ruse, forms almost half of the admissions (Fig. 2).
Fig. 2. Patients who were served (number) in Multiprofile Hospital for Active Treatment “Kanev” JSC Ruse and Ruse region for 2014-2021

The rest of the medical structures have a more limited scope, which has remained and decreased in recent years.

Registered cases of healthcare-associated infections (n=5188) total in the district by year show retention at one level, without sharp fluctuations until 2019, when a decrease is observed (n=503) cases (n=391). In 2020, at the beginning of the pandemic, the registered healthcare-associated infections increased to n=623 in 2020 and n=1111 in 2021 (Fig. 3).

It was found that there is no statistically significant difference concerning the registered healthcare-associated infections up to 2020 and then to p<0.05.

The morbidity rate of infections related to healthcare for the district is formed mainly 71.43% by the University Multiprofile Hospital for Active Treatment “Kanev” JSC (3706 in a total of 5188).

Fig. 3. Number of registered healthcare-associated infections in the Ruse region and in Multiprofile Hospital for Active Treatment “Kanev” JSC during 2014-2021

This hospital, like many other university structures in the country, has intensive care units, equipment and possibilities for emergency interventions, with more severe forecasts for patients and teams provided to deal with created emergency situations when a significant part of the accepted emergency cases have tested positive for COVID-19 [5].

The comparative data on the relative share of health infections in the Ruse region and the country show that it has an uneven course and small fluctuations, comparable to that for the country, except for 2021, when it was exceeded.

In figure 4, we show the relative share of healthcare-associated infections in the district and the two university structures in the regional University Multiprofile Hospital for Active Treatment “Kanev” JSC, Ruse region and “University Multiprofile Hospital for Active Treatment “Medicala” Ltd, Ruse compared to the average values for the country, Bulgaria.
Fig. 4 Relative share of healthcare-associated infections in Bulgaria, in the Ruse region, University Multiprofile Hospital for Active Treatment “Kanev” JSC  University Multiprofile Hospital for Active Treatment “Medica “ Ltd, Ruse and Bulgaria, for 2016-2021

The incidence of healthcare-related infections on average for the region for 2014-2021 is 0.86 per 1,000 treated patients, compared to 0.79 for the country for the same period.

In University Multiprofile Hospital for Active Treatment, “Kanev” JSC is twice as high as 1.66. The relative share is more than twice as high as that of the district for the entire period, reaching 2.36% in 2021.

Hospital for Active Treatment “Kanev” JSC - 1.67% (2014 ), 1.54% (2017 ), 2.36% (2021).

A retrospective analysis of recorded healthcare-associated infections from medical facilities confirms that several of them were only in certain years with single cases. Multiprofile Hospital for Active Treatment “Yulia Vrevska” - Byala total (n=8) healthcare-associated infections -2018, 2019, 2020. Byala State Psychiatric Hospital Total (n- 13) healthcare-associated infections for four years -2014, 2015, 2016, 2020. The registration of the Ruse Mental Health Centre is better, with a total of (n-134) healthcare-associated infections reported in all years, with an increased absolute number from (n-19) in 2014 to (n-49) in 2921. A total of (n-87) healthcare-associated infections were reported in the Ruse Comprehensive oncology center for the period from (n-3) in 2014, (n-13) in 2015 to (n-19) for 2020 and (n-7) in 2021. A specialized hospital for active treatment of pneumo-phthisiatric diseases, “Dr D. Gramatikov” Ltd, has not reported any cases, and in “Medica Cor”, only one case was reported in 2014 and 2015.

The created organization of work at Multiprofile Hospital for Active Treatment JSC Ruse contributed to the correct registration and reduction of healthcare-associated infections due to the extraordinary emergency anti-epidemic measures that were introduced in the first year of the pandemic in 2020 (separation of flows, separation and flow of activities, including disinfection and service personnel). Due to the large capacity and high-tech equipment, an influx of patients with COVID-19 has been received. This affected both the prevalence of healthcare-associated infections and the pathogen profiles and organ localization of agents.

In 2021, in the structure of clinical localization, the group “Pneumonia associated with intubation” is the leading group - there are 285 cases (25.65%) and 73 cases 11.72% for 2020

The analysis of the clinical localization of healthcare-associated infections shows that in the initial period from 2014 to 2016, surgical site infections 49.38% (2014), 33.00% (2015), 18.35% (2016) took the leading place, followed by respiratory 17.93% (2014) and urinary tract infections 13.32% (2015), 17.23% (2016).

Lower respiratory tract infections 9.74% (2015), 11.42% (2016), and pneumonias associated with intubation, 8.15% (2015) and 14.23% (2016) have a smaller relative share. In 2019, they increased by a share of 27.03% and pneumonias by 10.13%, and surgical site infections remained until the end of 2021 within the limits of 19.48% (2019), 15.89% (2020) 17.73% (2021) - Table1.

Surgical site infections are decreasing due to limited planned operations and out-of-room protocols and measures for COVID-19. There is an improvement in infection control on the one hand, but the high workload and frequent complications and prolonged hospital stay, combined with gaps in the application of individual protective equipment and disinfection, facilitated the transmission of nosocomial strains, including in sectors with limited planned hospitalization [5].
The leading pathogens of lower respiratory tract infections in most years are *Acinetobacter baumannii* 34.43% (2016), 19.11% (2019), and 24.14% (2020). Resistant to antibiotics, they easily colonize hospitals - 25.49% (2019), mainly from the intensive care units with a therapeutic focus on Multiprofile Hospital for Active Treatment “Kanev” JSC Ruse - 100%.

In the group “Pneumonia associated with intubation” in 2021 there are 285 cases (25.65%) and 73 cases 11.72% for (2020) with the leading role of gram-negative flora - *Acinetobacter baumannii* - 17.90%, *Klebsiella pneumoniae* - 9.12%, *Pseudomonas aeruginosa* – 7.37% and *Candida albicans* – 15.79%. In the COVID-19 department of Multiprofile Hospital for Active Treatment “Medica” Ltd., Ruse, there are 167 cases registered (58.59%) as well as in the “Anesthesiology and Intensive Care” department - 65 cases (22.80%). The trend is significantly expressed in intensive care units and consistent with the more severe prognoses of patients there. The widespread use of antibiotics has led to increased detection of fungi and highly resistant bacteria in healthcare-associated clinical samples, also reported by other authors [6, 7].

With the introduction of urgent epidemic measures for COVID-19 in medical facilities, the care of infected patients has improved and contributed to the registration and reduction of healthcare-associated infections. In overburdened hospitals/wards, the fear of the new infectious threat leads to irregular registration of healthcare-associated infections. The slow readjustment of part of medical specialists to the seriousness of these infections, as well as the gaps in the hygiene regime in the medical facilities, lead to an increase in the incidence of healthcare-associated infections and the occurrence of epidemic outbreaks [8, 9]. Our analysis shows that, despite the incomplete registration of the infections at the beginning of the COVID-19 pandemic, in 2021, the expected number of exceeds the usual incidence. The widespread and often uncontrolled use of antibiotics, characteristic of the pandemic period, superimposes on the main disease an atypical course of the infection, creates new problems and leads to an increase in a hospital stays. Departments with the highest number of patients on antimicrobial therapy did not register or report too few healthcare-associated infections.

**CONCLUSIONS:**
- Our analysis showed that the patients who underwent treatment for 2014-2021 in the Ruse region increased from 71 501 people in 2014 to 80 169 people in 2019, and in the years of COVID-19, they again reached the initial levels – 71 114 people in 2020 and 71 014 people in 2021.
- Despite the incomplete registration of healthcare-associated infections at the beginning of the COVID-19 pandemic, (n= 626) patients were registered in 2020 and (n= 1111) cases in 2021, which exceeds the usual morbidity.
- Morbidity of healthcare-associated infections is formed mainly by the University Multiprofile Hospital for Active Treatment “Kanev” JSC, Ruse (71.43%), twice as high as that in the district for the entire period.
- In the initial period from 2014 to 2016, surgical site infections (49.38% 2014), 33.00% (2015), 18.35% (2016), followed by respiratory infections 17.93%. (2014) and urinary tract infections at 13.32 % (2015) and 17.23 % (2016), and in the years of the pandemic in 2020 leading are lower respiratory tract infections at 27.93% and Pneumonia associated with intubation at 25.74% in 2021.
- The COVID-19 pandemic has affected both the prevalence of healthcare-associated infections and pathogen profiles. Lower respiratory tract infections and pneumonias (2020 and 2021) are leading in COVID-wards with colonized gram-negative flora – *A. baumannii* - 17.90%, *K. pneumoniae* - 9.12%, *P. aeruginosa* - 7.37% and *C. albicans* - 15.79 %.

Collaborative efforts of hospital management, professional cooperation more effective interaction with hospital epidemiologists, hospital microbiologists, clinical pharmacologists and all staff are needed to improve healthcare-associated infections surveillance and control.
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