



STUDY OF TRENDS IN THE ETIOLOGICAL STRUCTURE OF NOSOCOMIAL INFECTIONS BEFORE AND DURING THE COVID-19 PANDEMIC IN THE RUSE REGION FOR 2017-2021

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ABSTRACT

The most important and very difficult thing is to establish the cause (etiology) for the occurrence of nosocomial infections in medical facilities in the country and the world.

Objective: To study the frequency and structure of nosocomial infections before and during the Covid-19 pandemic in the Ruse region for 2017-2021.

Materials and methods: A retrospective analysis of the data on the registered nosocomial infections for a period of five years (2017 - 2021), reports, analyses, and laboratory studies of Regional Health Inspectorate Ruse, from national governmental studies, normative documents and literature are applied.

Results: The analysis of the data from the etiological diagnosis of nosocomial infections in the Ruse region is from 9 medical facilities included in the national electronic system for the control of nosocomial infections (NIs). The etiological structure of NIs in the Ruse region is represented by 39 microbial species. The relative share of the untested varies from 10.59% in 2017 to 15.75% in 2021. For the etiologically unproven, it is from 2.39% for 2019 to 1.68% for 2021, with a decreasing trend.

Conclusions: The analysis of the isolated microbial species by group shows that for the entire period, the proportion of gram-negative flora was 62% of the isolates (2017), followed by 23.02% of gram-positive microorganisms (2017), and the relative proportion of fungi and viruses was ~ 3 %.

Keywords: etiology, nosocomial infections, structure, laboratory diagnostics,

The mass nature of medical care, the widespread use of antibiotics, changes in the demographic structure of the population, the nature of pathogens, and the body's immune reactivity are leading factors in the emergence, development and spread of HAI. The most important and very difficult is the establishment of the cause of the occurrence of the disease. The medical science that studies the causes of the occurrence of diseases is etiology (from Greek: αιτια - “cause” and λογος - “science”). The reasons (risk factors) for the spread of NI are studied. More important of them are: the presence of concomitant diseases, dependence on the pre-morbid state of the patient, many different microbial agents, very high drug resistance and wrong therapeutic approach [1, 2].

OBJECTIVE:

To study the frequency and structure of nosocomial infections in the Ruse region for 2017-2021.

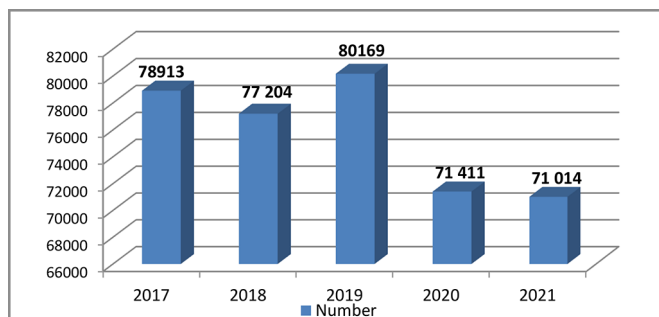
MATERIALS AND METHODS:

A retrospective analysis of the data on the registered nosocomial infections for a period of five years (2017 - 2021), the procedures for the registration of nosocomial infections on the territory of the district with 9 medical facilities per report in Ruse, access to public information (State educational requirements) was applied), reports, analyzes and laboratory analyzes of Regional Health Inspectorate Ruse. Documentary method and comparative analysis are supplemented with statistical processing and presented in graphical and tabular form.

The analysis of the data from the etiological decoding of nosocomial infections in the Ruse region is from 9 medical facilities included in the national electronic information system for the control of nosocomial infections (according to Ordinance No. 3 of May 8, 2013, for the approval of medical standards on prevention and control of nosocomial infections).

For the period 2017-2021, a total of 378,711 patients were hospitalized in the Ruse region, and the data by year show an uneven trend from 78,913 (2017) people, 80,169 (2019) people, to 71,014 (2021) people, probably influenced by the covid19 pandemic (Fig. 1).

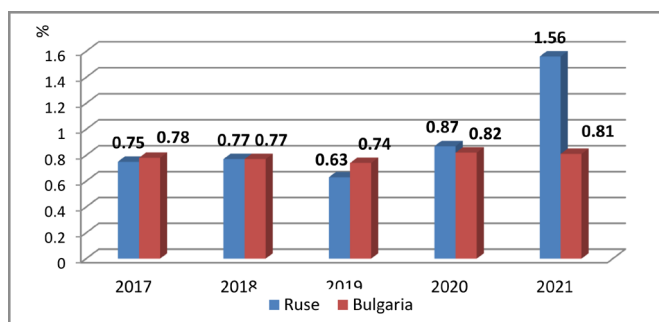
Fig. 1. Number of hospitalized patients in medical facilities in the Ruse region for 2017-2021



The incidence of nosocomial infections in the Ruse region for 2017-2021 is shown per 1,000 transferred patients, comparing it with the average values for Bulgaria. With a total of 3,426 registered nosocomial infections, the indicator is 0.90 per 1,000 transferred patients for this period (Fig. 2).

The relative share of nosocomial infections, compared with that for the country, shows that the trends are on the rise in the district and without sharp fluctuations by those for Bulgaria. The sharp jump to 1.56% in 2021 in Ruse is related to the Covid-19 pandemic, reduced number of sick patients, but many severe cases and double registered NI.

Fig. 2. Relative share of nosocomial infections in Ruse region and Bulgaria for 2017-2021



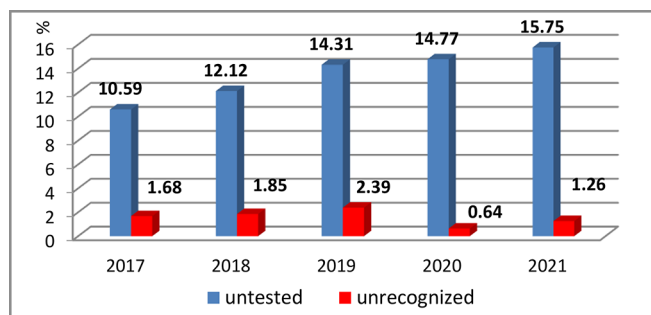
We analyze the microbiological laboratory tests, which specify an etiological diagnosis, the most accurate and pointing to the correct therapy. For the five-year period, 187 types of microbial pathogens were diagnosed, from the beginning of 2017, from 35 types, 2018-33 types, 2019- 36 types, 2020-38 types, reaching 39 types in 2021.

Table. 2. Most frequently isolated 24 types of nosocomial infections microbial agents in the Ruse region for 2017-2021

Year	2017	2018	2019	2020	2021
Etiological pathogen (%)					
<i>Acinetobacter baumannii</i>	17,65	9,93	11,14	11,08	11,25
<i>Klebsiella pneumoniae</i>	11,26	9,93	10,34	9,63	9,9
<i>Pseudomonas aeruginosa</i>	7,39	10,94	9,94	14,45	9,36
CNS		12,63	11,53	11,08	8,28

The relative share of the untested NIs is with a rising trend and an unrecognized descending trend (Fig. 3). The decrease leads to better therapeutic choices. These data are important for assessing the compliance and the ability of healthcare facilities to adequately deal with the NI problem.

Fig. 3. Relative share of the untested and unrecognized cases in the structure of the nosocomial infections in the Ruse region for 2017-2021



The presented microbial species are considered according to their characteristics: bacteria (gram-positive and gram-negative), viruses, fungi, anaerobes (Tab. 1). Knowing their characteristics and antimicrobial resistance is part of microbiological research and helps treatment.

Table. 1. Isolated microbial species: bacteria (By Gram), viruses, fungi, anaerobes in the Ruse Rusegion for 2017-2021

Year / %	2017	2018	2019	2020	2021
Bacteria – Gr.(-)	61,68	60,25	72	61,47	56,88
Bacteria – Gr. (+)	23,02	25,25	28	11,8	0
Fungi	3,52	3,03	0,4	4,65	8,55
Viruses	3,03	0,51	0,8	3,96	0
Anaerobes	0,17	0	0	0	0

The predominance Gram-negative bacteria is unfavorable. They have less sensitivity to antibiotics, which is an important problem in the control of NIs.

The relative share of the isolated types of microbial agents from the diagnosed NIs by year for a five-year period is presented in tabular form. We show the most important 24 types (Tab. 2).

<i>Serratia marcescens</i>		3,54	2,58	1,41	6,93
<i>Candida albicans</i>	2,52	1,85	1,99	4,03	5,58
SARS-Cov-2				0	3,96
<i>Acinetobacter</i>	0,84	1,18	2,39	0,64	3,69
<i>Enterococcus faecalis</i>	4,71	3,2	1,99	2,25	3,42
<i>Staphylococcus aureus</i>	8,05	5,72	3,78	4,17	2,61
<i>Enterobacter spp.</i>	0	0,67	2,19	1,12	2,61
<i>Escherichia coli</i>	4,03	5,89	5,57	3,37	2,43
<i>Candida spp.</i>	0,84	0,84	0,2	0,64	2,25
<i>Enterococcus spp.</i>	0,34	1,18	0,6	2,09	1
<i>Proteus mirabilis</i>	1,68	1,18	2,58	2,41	1,44
<i>Enterobacter cloacae</i>	1,51	1,18	1,59	1,28	1,17
<i>Enterobacter aerogenes</i>	0,84	2,02	0,6	0,64	1,08
<i>Candida krusei</i>	0,17	0,34		0	0,72
<i>Klebsiella oxytoca</i>	1,51	1,18	1,19	1,93	0,72
<i>Corynebacterium spp.</i>	2,02	1,01	0,8	4,65	0,63
<i>Pseudomonas spp.</i>	4,71	3,51	1,8	1,12	0,63
<i>Proteus vulgaris</i>	4,71	0,51	0,8	0,16	0,45
<i>Clostridium difficile</i>			0,2	0,8	0,45
<i>Citrobacter spp.</i>	4,71	1,01	1,59	1,12	0,36

The main causative agents that we found in the analysis for five years period in the Ruse region are representatives of the Gram-negative bacterial flora: *Acinetobacter*, *Pseudomonas*, *Enterobacter*, *Escherichia*, *Klebsiella*, etc. (Tab. 1, 2). In all years, the values are high, from 61.68% in 2017 and 72% in 2019, with a drop to 56.88% in 2021. This has also been described in studies showing that these infections develop in a compromised environment, in immunocompromised patients with acute or chronic disease whose upper respiratory tract is colonized with Gram-negative microorganisms. This creates a real possibility for NI during respiratory resuscitation [3].

Gram-positive flora: (*Clostridium*, *Corynebacterium*, *Staphylococci* and *Streptococci*, etc.) are represented with a much smaller share, up to 11.08% for 2020 as well as a decrease at the end of the period to 0.17% for 2021.

Another group of infectious agents are viruses, presented by *influenza*, *rotaviruses* and *SARS-Cov-2*. Diagnosed viruses in the study were recorded over 4 years with a range of 3.52% to 3.96% (Tab. 2). These pathogens also carry a risk for the development of nosocomial infections, which in recent years have been extensively studied throughout the world [4].

Three groups of *Candida* occupy one of the leading positions in the ranking of causative agents isolated in the Ruse region: *Candida krusei*, *Candida albicans* and other *Candida spp.* (Table 1). The relative share has grown three times from 3.52% to 8.55% in these years. *Candida albicans* isolates grew to 5.58% in 2017 Invasive candidiasis in patients with COVID-19 also reflected their prevalence to 4.65% in 2020 and 8.55% in 2021. In the conditions of hospitalization, some drugs – antibiotics and

corticosteroids increase the risk of developing a fungal infection. Hyperglycemia promotes fungal growth. Patients hospitalized with COVID-19 were at risk for blood-related infections caused by *Candida* (candidemia), reported by our authors [3, 4].

With a smaller relative share, 1% in the structure of nosocomial infections are anaerobic bacteria, which are present in two of the five years. The apparatus for their diagnosis requires that they be placed in a transport nutrient medium (they do not use oxygen) that preserves the viability of the bacteria. This is not always observed during sampling, and this affects the etiological interpretation. Most anaerobic infections are associated with contamination of wounds by normal microflora of the mucous membrane of the oral cavity, pharynx or gastrointestinal tract.

The analysis of the isolated types of etiological causative agents by year shows that a group of causative agents *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Coagulase-negative staphylococci* (CNS), *Serratia marcescens*, *Candida albicans* is forming, which occupy the first three to five positions in the ranking, changing individual in years their places. In total, they form over 50% of NIs registered in the district's medical facilities. (Fig.4)

Our study shows the various etiological agents with their organ (clinical) localization distributed by year:

Acinetobacter baumannii. This pathogen predominates in all years with Lower Respiratory Tract Infections (LRTIs), Ventilator-associated pneumonia (VAP) and Blood Stream Infections (BSIs) (fig. 5).

Fig. 4. Relative share of microorganisms group with leading ranking positions in the structure of the nosocomial infections for 2017-2021 (* Incl.: *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, CNS, *Serratia marcescens* *Candida albicans*)

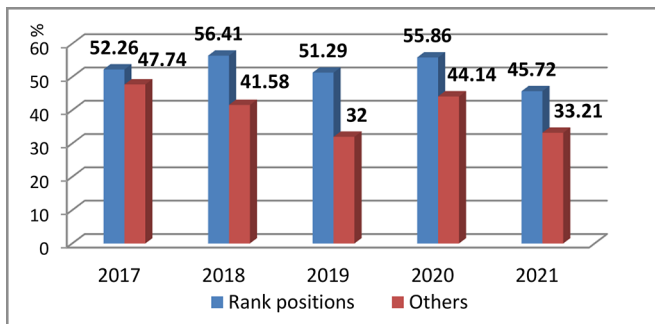
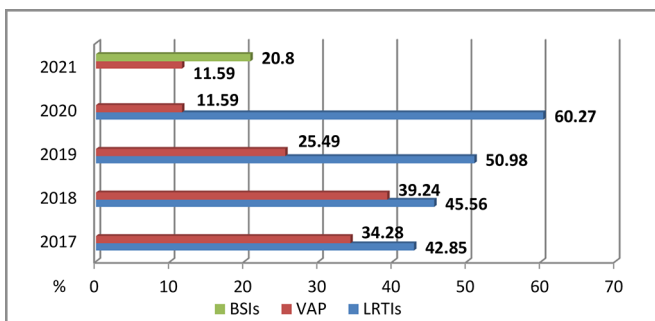
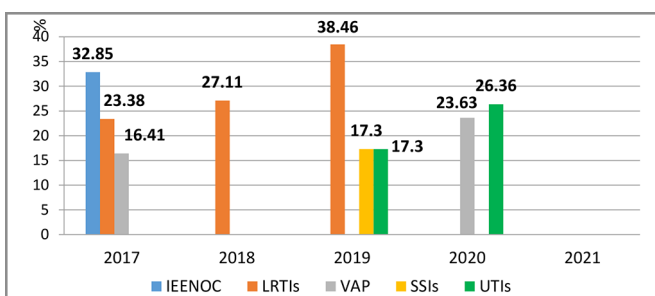


Fig. 5. Relative share of clinical localization for *Acinetobacter baumannii* in the Ruse region for 2017-2021.



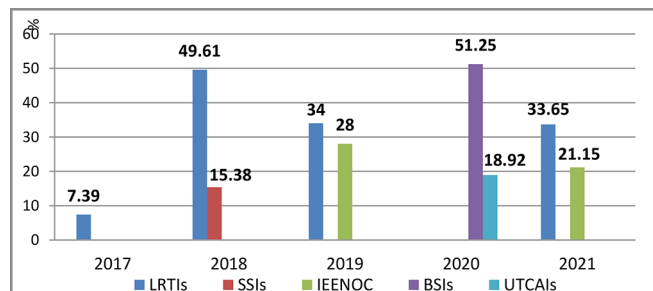
***Klebsiella pneumoniae*.** Five groups of organ infection localizations are available: 1. Infections of the eye, ear, nose and oro-pharyngeal cavity (IEENOC); 2. LRTIs; 3. VAP; 4. Surgical site infections (SSIs); 5. Urinary tract infections (UTIs) (Fig. 6)

Fig. 6. Relative share of clinical localization for *Klebsiella pneumoniae* in the Ruse region for 2017-2021.



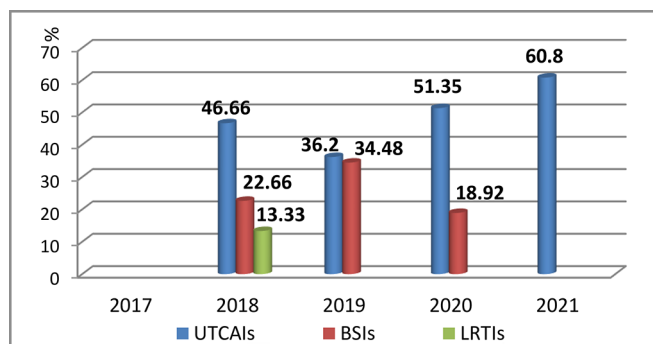
***Pseudomonas aeruginosa*.** There are 5 groups of organ localizations of NI: 1. VAP; 2. IEENOC; 3. LTRIs; 4. BSIs; urinary-tract catheter associated infections (UTCAIs).

Fig. 7. Clinical localizations of *Pseudomonas aeruginosa* in Ruse region for 2017-2021



CNS. Three organ localizations of NIs caused by CNS were registered during our investigation for the entire period. (Fig. 8)

Fig. 8. Relative share of clinical localizations of CNS NIs in the region for 2017-2021



The isolated *Escherichia coli* (2018, 2019), *Corynebacterium spp.* (2020), *Staphylococcus aureus* (2017, 2018) are only SSIs. *Serratia marcescens* is with one organ localization in 2021 – BSI.

The summary analysis of the etiological structure of healthcare associated infections is variable, determined not only by the profile of the department but also related to the mass use of antibiotics, sometimes incorrect. Most nosocomial infections arise from endogenous bacterial flora, although many critically ill patients eventually become colonized with resistant bacterial hospital strains. [5]. The Departments for the treatment of LRTIs and Pneumonia is a closed environment (hospital rooms, diagnostic offices, therapeutic offices) inhabited by pathogens - *Staphylococci*, *Pseudomonas* and others with a specific microbiological characteristic, with polyresistance, high virulence and invasiveness. They cause nosocomial epidemic outbreaks, which have been described [5].

In our studies, 37.88% of healthcare associated infections (HAIs) caused by CNS are laboratory-confirmed BSIs.

UTCAIs are very often superimposed on the main disease for which the patient is hospitalized, creating new problems and increasing his hospital stay. In 2021 this type infections occupied the fourth position in terms of frequency - 13.23 %. The most recorded cases of local infection are those related to central venous catheter (with negative result from blood culture) – 51.70%. The spread of HAIs can spoil surgical interventions of vital importance organs to increase postoperative mortality. The omissions in the sanitary-hygiene regime, improper disinfection in medical facilities, wrong methods of sterilization lead to spread of NI. The incorrect manipulation technics lead to injuries to the skin and mucous membranes, which are the entrance door for pathogens that cause NI [6].

The analysis of the etiological structure of HCIs for 2017-2021 in the Ruse region shows a decrease of unrecognized etiological agent from 2.39% for 2019 to 1.68% for 2021. Untested NIs cases maintain an upward trend. In comparison, the report of Y. Mitova and N. Ribarova (2009) on the dynamics of the etiological and clinical structure of nosocomial infections in Bulgaria during the period 1982-2008 shows that in our study, the indicators for untested infections (32.13%) are two or more times lower and for unrecognized infections (18.83%) ten times lower [7, 8]. The correct assessment and follow-up of colonization with microbial species in the wards, according to their profile, with priority to risk structures and regular training and internal control, contributed to this [6].

A leading place in the etiological structure of registered HAIs during the entire monitored period 2017-2021 in the Ruse region is occupied by *Acinetobacter baumannii* 17.65% (2017) and 11.25% (2021), *Klebsiella pneumoniae* 11.12% (2017), 9.93% (2018), *Pseudomonas aeruginosa* 10.94% (2018), 14.45% (2020), 9.36% (2021), CNS 12.63% (2018), 8.28% (2021).

Leading in the nosological structure according to their localization in organs and systems are LRTIs in four out of five years 2017, 2018, 2019, 2020 - n=696, followed by SSIs, occupying the second position in the five years n=611 and in third place are UTCAIs in 2018,2019 n=272, followed by pneumonia in 2019, 2020 – n=168 and BSIs in 2021 – n=160

CONCLUSIONS:

The etiological structure of nosocomial infections in the Ruse region is represented by 39 microbial species, with a share of the untested from 10.59% in 2017 reaching 15.75% in 2021, and the unrecognized from 2.39% in 2019 to 1.68% in 2021.

Gram-negative flora is a group with the largest relative share among the isolated microbial species - 62% (2017), followed by gram-positive 23.02% (2017) and a much smaller relative share of fungi, viruses up to 3%, and single anaerobes.

The clinical localization of the leading etiological agents is three organ localizations for *Acinetobacter baumannii*, five organ localizations for *Klebsiella pneumoniae*, and 5 organ localizations for *Pseudomonas aeruginosa*.

Analysis of healthcare-associated infections (HAIs) caused by the CNS in 2021 shows that 37.88% are laboratory-confirmed BSIs.

In the structure of the species of microorganisms in 2021, Gram (-) and fungi dominate due to the excessive antibiotic use in the Covid-19 period. The registration of BSIs caused by *Acinetobacter baumannii* and *Pseudomonas aeruginosa* is increasing due to the large number of blood manipulations. The relative share of LTRIs and VAP caused by *Acinetobacter baumannii* and *Klebsiella pneumoniae* in 2020-2021 is increasing, as described by other authors [3, 5].

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