

SURGICAL SITE INFECTIONS AFTER NEUROSURGICAL PROCEDURES IN UKRAINE: RESULTS OF A MULTICENTER STUDY (2018-2020)

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ABSTRACT

The aim: To obtain the first estimates the incidence of surgical site infection in patients undergoing neurosurgical procedures and antimicrobial resistance of responsible pathogens, and determine their impact on inpatient mortality in Ukraine.

Materials and methods: We performed a multicenter prospective study was patient-based data of SSIs were according to CDC/NHSN methodology. This study included patients undergoing a neurosurgical procedure in 11 tertiary care hospitals from different regions of Ukraine from January 1st, 2018 to December 31st, 2020.

Results: A total of 1697 neurosurgical procedures associated with a 90-day SSI were identified (19.4% of 8741 procedures). Of these, 69.5% SSI were identified after craniotomy and 30.5% after ventricular shunt. The Meningitis or ventriculitis (20.9%) were found to be the most common underlying condition among these patients followed by Intracranial infection (18.7%), and Osteomyelitis (14.6%) congenital malformation. Over a 90-day surveillance period, 387 died (4.4%). Fifty seven percent of deaths in SSI patients were attributable to infection. Meningitis or ventriculitis and Intracranial infection were associated with a higher mortality. Craniotomy was associated with a higher mortality more frequently than did Ventricular shunt. *Escherichia coli* were most commonly reported, accounting for 26.3% of all organisms, followed by *Staphylococcus aureus*, *Enterobacter* spp., *Pseudomonas aeruginosa*, *Enterococcus* spp., and *Klebsiella pneumoniae*. Meticillin resistance was found in 33.7% of *S. aureus* isolates, and vancomycin resistance was found in 12.7% of enterococci.

Conclusions: The incidence of SSI and mortality after neurosurgical procedures in Ukraine is high. This is due to increase emergence of antimicrobial-resistant pathogens and risk factors in neurosurgery patients.

KEY WORDS: Neurosurgery, Surgical Site Infection, mortality, antimicrobial resistance, Ukraine

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INTRODUCTION

Surgical site infection (SSI) is considered the most common health care-associated infection (HAI) [1-3]. A multicenter study conducted in Ukraine in 2019 found an SSI rate of 60% among the HAIs evaluated [2]. SSIs increase both mortality and morbidity rates. In USA SSI is the most costly HAI type with an estimated annual cost of \$3.3 billion, and is associated with nearly 1 million additional inpatient days annually [4,5]. Despite of advances have been made in infection control practices, including improved operating room ventilation, sterilization methods, barriers, surgical technique, and availability of antimicrobial prophylaxis, SSIs remain a substantial cause of morbidity, prolonged hospitalization, and death [6]

SSIs after neurosurgical procedures in Ukraine are among the most common HAIs [7]. SSIs in patients undergoing neurosurgical procedures represent a serious problem that requires immediate attention. According literature data, SSIs in neurosurgical patients are associated with longer

post-operative hospital stays, may necessitate additional surgical procedures, may require intensive care, and result in higher attributable morbidity and mortality [8-10]. SSIs after neurosurgical procedures are hence an important target for the surveillance of HAI.

In neurosurgery, increasing efforts have been employed to improve clinical outcomes including reducing mortality. However, there is a paucity of data demonstrating the impact that quality initiatives have on health-assessment metrics including risk of mortality [8,9]. Presently there is no reliable source for rating the quality of overall neurosurgical care, nor is there a good and complete source for understanding the quality of neurosurgical care in the Ukraine. Only few studies have evaluated the impact of SSIs after neurosurgical procedures and antimicrobial resistance that causes these infectious agents on inpatient mortality. Quality improvement of neurosurgical procedures and in perioperative care is of greatest interest to enhance patient safety. In neurosurgery, many health-assessment

metrics are also increasingly being emphasized for the aforementioned reasons. Mortality rates are one of the most frequently assessed quality measures, especially in complex surgical subspecialties such as neurosurgery, and much effort has gone into understanding and decreasing these rates [8]. Multiple studies have examined the role of antibiotic prophylaxis in relation to HAI after neurosurgical procedures, with recent studies demonstrating that antibiotic prophylaxis decreases the incidence of SSI. However, incidence rates of SSIs after neurosurgical procedures, inpatient mortality and antimicrobial resistance in Ukraine are currently unknown.

THE AIM

To obtain the first estimates the incidence of surgical site infection in patients undergoing neurosurgical procedures and antimicrobial resistance of responsible pathogens, and determine their impact on inpatient mortality in Ukraine.

MATERIALS AND METHODS

SETTING AND PARTICIPANTS

We performed a multicenter prospective study was patient-based data of SSIs were according to CDC/NHSN methodology. This study included adult patients undergoing a neurosurgical procedure in 11 tertiary care hospitals from different regions of Ukraine from January 1st, 2018 to December 31st, 2020. In these hospitals were 420 beds for neurosurgical patients. The hospitals are similar in terms of medical equipment, staff and were required to have at least one full-time infection-control professional and clinical microbiology laboratory. This study included hospitals that provided data for at least three years. In this study all patients were local residents. Patients who underwent elective or emergency neurosurgical procedures and survived at least 7 days after surgery were included in the study. Patients highly suspicious of central nervous infection prior to the neurosurgical procedure, patients who underwent reoperation, passed away within 48 hours after surgery, or did not have the incision site closed were excluded.

DEFINITION

Neurosurgery procedure-acquired SSI surveillance definitions were adapted from the 2017 CDC/NHSN definitions [11, 12]. In accordance with these criteria, SSIs were classified depending on the degree of infection as follows: superficial incisional, deep incisional, and organ/space. Because no clear distinction exists between superficial and deep incisional infection in brain surgery, we included skin or subcutaneous tissue in the definition of superficial incisional infection, and fascia/muscle layers and aponeurosis/skull bone in that of deep incisional infection. Infections occurring at more than one site in the same patient were reported as two separate infection episodes. Cerebrospinal fluid leak was defined as any leak of the fluid that surrounds

the brain and spinal cord and escapes from the cavities within the brain or central canal in the spinal cord [13], and was reported to be associated with the development of meningitis [14].

We used the current procedural terminology (CPT), as defined by the American Medical Association (AMA). The neurosurgical procedures performed were stratified by type of operation conforming to ICD 10-PCS, according to the SSI Protocol on the NHSN code. An NHSN operative procedure performed on a patient whose date of admission to the healthcare facility and the date of discharge are different calendar days. An NHSN Operative Procedure is a procedure that is included in the CPT NHSN operative procedure code mapping and takes place during an operation where at least one incision (including cranial Burr holes) is made through the skin or mucous membrane, or reoperation via an incision that was left open during a prior operative procedure, and takes place in an operating room or interventional radiology room, defined as a patient care area. Exclusions: Otherwise eligible procedures that are assigned an ASA score of 6 are not eligible for NHSN SSI surveillance.

DATA COLLECTION

For surveillance, surgical procedures were classified according to the NHSN-SSI code. Patients were monitored for 90 days after surgery; those discharged or transferred were monitored at outpatient clinics. We collected the data using structured NHSN procedure form. Data included were age, gender, elective or emergency surgery, NHSN procedure code, date of procedure, operation time, wound class (clean, clean-contaminated, contaminated, and dirty) [15], ASA score [16], emergency, trauma, scope, diabetes mellitus, closure technique, infection, and infecting microorganisms. This form is used for reporting data on each patient having one of the NHSN operative procedures selected for monitoring. Cases of SSIs after neurosurgical procedures that met standard case definitions were identified through active follow up during the hospital stay, on return to hospital, and during visits to ambulatory. Medical records were accessed in the Department of Neurosurgery where patients were admitted, while laboratory records were obtained from the Department of Medical Microbiology at the hospitals. The medical records and postoperative courses for all patients involved in neurosurgical procedures at our study were reviewed to determine the incidence of SSI, the identity of offending organisms, and the factors associated with infection. In each hospital data were collected by the by the one full-time infection-control professional (physician or nurse) visited the neurosurgery unit (ward/ICU) daily. At outpatient clinic data were collected by nurse practitioners who completed the NHSN-SSI surveillance training course at least once a year.

MICROBIOLOGICAL METHODS

Clinical samples (blood, pus, pus swabs, cerebrospinal fluid (CSF), catheter tips, wound aspirates and tissues) were collected by medical doctors in the neurosurgical unit as part

Table I. Incidence of SSI among 8741 neurosurgical patients after operative procedures and relative frequency of NHSN SSI types in Ukrainian hospitals (2018-2020)

NHSN SSI Types	Number of patients with SSI	SSI %	95% CI
All	1697	100	
Meningitis or ventriculitis	355	20,9	19,9 – 21,9
Intracranial infection	317	18,7	17,7 – 19,7
Osteomyelitis	248	14,6	13,7 – 15,5
Superficial Incisional Secondary	183	10,8	10,1 – 11,6
Sinusitis	142	8,4	7,7 – 9,1
Spinal abscess/infection	129	7,6	6,9 – 8,2
Deep Incisional Secondary	118	7,0	6,4 – 7,6
Superficial Incisional Primary	104	6,1	5,5 – 6,7
Deep Incisional Primary	101	6,0	5,4 – 6,6

*NHSN. SSIs – Surgical Site Infections; CI – confidence interval;

of routine patient management and submitted to the department of medical microbiology at the hospitals for analysis.

Microbial isolates were identified using standard microbiological techniques. Antimicrobial susceptibility testing of the isolated organism was done by Kirby Bauer disc diffusion method as per Clinical and Laboratory Standards Institute (CLSI) guidelines 2015 [17]. In this study strains in the intermediate range were classified as resistant for data analysis.

ETHICS

The Shupyk National Healthcare University of Ukraine Ethics Committee approved this study. Written informed consent was obtained from all individual participants. To protect the privacy of the patients, the study excluded sensitive patient identifiers. All participants' data were anonymised prior to the analysis.

STATISTICAL ANALYSIS

Statistical analysis of the collected material employed IBM SPSS (SPSS—Statistical Package for the Social Sciences) software, STATISTICS 24, Armonk, NY, USA, and Microsoft Excel, Microsoft Office, 2016, Redmond, WA, USA. Statistical analysis was carried out with the use of basic statistical parameters, i.e., mean, standard deviation, 95% confidence intervals for the mean, and median. Chi-square tests or Fisher exact tests were used to compare categorical and continuous variables, respectively. The level of significance was set at $p < 0.05$.

RESULTS

INCIDENCE OF SSI

Of the 8741 neurosurgical patients undergoing operative procedures (craniotomy and ventricular shunt) during the study period, 1697 developed an SSI during the first 3 months with an overall incidence of SSI of 19.4%. Of the 1697 SSIs identified, 1191 (70.9%) were organ-space infections, 287 (16.9%) were superficial incisional infections, and 219 (12.9%) were deep

incisional infections. In the present study, 1179 (69.5%) SSI were identified after Craniotomy and 518 (30.5%) after Ventricular shunt. The Meningitis or ventriculitis (20.9%) were found to be the most common underlying condition among these patients followed by Intracranial infection (18.7%), and Osteomyelitis (14.6%) congenital malformation. The distribution of SSI among neurosurgical patients after operative procedures and relative frequency of NHSN SSI types is showed in Table I.

The overall incidence rate of SSI was higher in female than in male (20.3% vs 18.8%) and increased with age. Patient demographics, incidence of SSI, risk factors for SSIs in neurosurgical patients with, and without SSIs at Ukrainian hospitals are displayed in Table II. Main risk factors for SSI were age, duration of operative procedure, comorbidity index, wound class and physical status class. Neurosurgical patients with SSI had significantly longer hospital stay. In this study multivariate analysis showed that factors found significant in univariate analysis frequently occur together.

MORTALITY PATIENTS WITH SSI

Of the 8741 neurosurgical patients included over a 90-day surveillance period, 387 died (4.4%). Mortality increased with age for both men and women. In present study a high Charlson comorbidity index also gave increased mortality. SSI for neurosurgical patients was a significant predictor of mortality, independently of NNIS risk index and other survival predictors. Fifty seven (137/236) percent of deaths in SSI patients were attributable to infection. Meningitis or ventriculitis and Intracranial infection were associated with a higher mortality and required re-operation more frequently than did Osteomyelitis and Sinusitis. Mortality varied according to the surgical procedure. Craniotomy was associated with a higher mortality more frequently than did Ventricular shunt.

CAUSATIVE AGENTS AND ANTIMICROBIAL RESISTANCE

In this study, 2128 specimens were isolated from 1697 neurosurgical patients with SSIs (Table III). Overall, Gram-neg-

Table II. Patient demographics and risk factors for surgical site infections (SSIs) in neurosurgical patients with and without SSIs at Ukrainian hospitals (2018-2020)

Characteristics	All patients		SSI				P value	Incidence of SSI 95% CI
	n	%	No		Yes			
			n	%	n	%		
All	8741	100	7044	80,6	1697	19,4	0,031	19,0 – 19,8
Gender							0,051	
Male	4653	53,2	3785	81,3	868	18,8		18,2 – 18,8
Female	4088	46,8	3259	79,7	829	20,3		19,7 – 20,9
Age (years)							0,001	
16 – 20	279	3,2	257	92,1	22	7,9		6,3 – 9,5
21 – 25	317	3,6	276	87,1	41	12,9		11,1 – 14,7
26 – 30	542	6,2	493	91,0	49	9,0		7,8 – 10,2
31 – 40	647	7,4	558	86,2	89	13,8		12,4 – 15,2
41–50	1286	14,7	1159	90,1	127	9,9		9,1 – 10,7
51 – 60	1367	15,6	1170	85,6	197	14,4		13,5 – 15,3
61 – 70	2164	24,8	1669	77,1	495	22,9		22,0 – 23,8
71 – 80	1384	15,8	990	71,5	394	28,5		27,3 – 29,7
≥81	755	8,6	472	62,5	283	37,5		35,7 – 39,3
Admission type							0,052	
Emergency or Urgent	2988	34,2	2114	70,7	874	29,3		28,4 – 30,1
Elective	5753	65,8	4930	85,7	823	14,3		13,8 – 14,8
McCabe score							0,001	
Non-fatal	5556	62,8	5081	91,5	475	8,5		8,1 – 8,9
Ultimately fatal	1502	10,0	849	56,5	653	43,5		42,2 – 44,8
Rapidly fatal	706	8,1	285	40,4	421	59,6		57,7 – 61,4
Missing	977	11,2	829	84,9	148	15,1		13,9 – 16,1
ASA Physical Status class							0,023	
1	116	1,3	104	89,7	12	10,3		5,9 – 12,1
2	632	7,2	574	90,8	58	9,2		8,1 – 10,3
3	3671	42,0	3159	86,1	512	13,9		13,3 – 14,5
4	2673	30,6	2106	78,8	567	21,2		20,4 – 22,0
5	1649	18,9	1101	66,8	548	33,2		32,0 – 34,4
Duration of operative procedure (hrs)							0,034	
≤4	3528	40,4	2817	79,8	711	12,4		11,8 – 12,9
>4	5213	59,6	4227	81,1	986	32,6		31,9 – 33,2
Wound class							0,047	
Clean	4317	49,4	3636	84,2	681	15,8		15,2 – 16,4
Clean-Contaminated	2671	30,6	2320	86,9	351	13,1		12,4 – 13,7
Contaminated	1637	18,7	1026	62,7	611	37,3		36,1 – 38,5
Dirty/Infected	116	1,3	62	53,4	54	46,6		44,9 – 48,2
Charlson comorbidity index							0,0012	
0	1789	20,5	1702	95,1	87	4,9		4,4 – 5,4
1	1939	22,2	1783	92,0	156	8,0		7,4 – 8,6
2	1543	17,7	1376	89,2	167	10,8		10,0 – 11,6
3	1286	14,7	985	76,6	301	23,4		22,2 – 24,6
4	1197	13,7	732	61,2	465	38,8		37,4 – 40,2
>4	987	11,3	466	47,2	521	52,8		51,2 – 54,4
Diabetes Mellitus							0,051	
Yes	1528	17,5	1140	74,6	388	25,4		24,3 – 26,5
No	7213	82,5	5904	81,9	1309	18,1		17,6 – 18,6
Trauma							0,059	
Yes	1211	13,9	930	76,8	281	23,2		22,0 – 24,4
No	7530	86,1	6114	81,2	1416	18,8		18,3 – 19,3

SSIs – Surgical Site Infections; CI – confidence interval; ASA – American Society of Anesthesiologists'

ative bacteria predominated. *Escherichia coli* were most commonly reported, accounting for 26.3% of all organisms, followed by *Staphylococcus aureus* (15.9%), *Enterobacter* spp.

(13,1%), *Pseudomonas aeruginosa* (11.7%), *Enterococcus* spp (7.3%), *Klebsiella pneumoniae* (7,1%), CoNS (5,2%), *Acinetobacter* spp.(4,7%), and *Serratia* spp. (3.1%) (Table III).

Table III. Microorganisms (n =2128) causing Surgical Site Infections (SSIs) in neurosurgical patients in Ukrainian hospitals (2018-2020)

Microorganisms	All isolates	
	n	%
<i>Gram-positive cocci</i>	630	29,6
<i>Staphylococcus aureus</i>	339	15,9
CoNS	111	5,2
<i>Streptococcus spp.</i>	24	1,1
<i>Enterococcus spp.</i>	156	7,3
<i>Gram-negative bacilli</i>	1444	67,9
<i>Escherichia coli</i>	560	26,3
<i>Enterobacter spp.</i>	279	13,1
<i>Citrobacter spp.</i>	26	1,2
<i>Klebsiella pneumoniae</i>	152	7,1
<i>Serratia spp.</i>	67	3,1
<i>Pseudomonas aeruginosa</i>	243	11,7
<i>Acinetobacter spp.</i>	100	4,7
Other	17	0,8
Fungi	54	2,5
<i>Candida albicans</i>	45	2,1
Other	9	0,4
Total no. of isolates	2128	100,0

CoNS – Coagulase negative staphylococci

Antimicrobial susceptibility testing data were available on the day of the survey for all of micro-organisms reported as causing SSIs in neurosurgical patients. In this study, meticillin resistance was found in 33.7% of *S. aureus* isolates, and vancomycin resistance was found in 12.7% of enterococci. Resistance to third-generation cephalosporins was detected in 37.3% of all Enterobacteriaceae, and was most common among *K. pneumoniae* (46.2%) and *E. coli* (35.3%). Carbapenem resistance was found in 11.3% of Enterobacteriaceae, and in 32.9% and 68.1% of *P. aeruginosa* and *Acinetobacter spp.* isolates, respectively.

DISCUSSION

We performed the first a multicenter prospective study was patient-based surveillance data of SSIs after neurosurgical procedures were according to CDC/NHSN methodology in Ukraine. A total of 1697 neurosurgical procedures associated with a 90-day SSI were identified (19.4% of 8741 procedures). Of these, 69.5% SSI were identified after craniotomy and 30.5% after ventricular shunt. The Meningitis or ventriculitis (20.9%) were found to be the most common underlying condition among these patients followed by Intracranial infection (18.7%), and Osteomyelitis (14.6%) congenital malformation. Over a 90-day surveillance period, 387 died (4.4%). Fifty seven percent of deaths in SSI patients were attributable to infection. Meningitis or ventriculitis and Intracranial infection were associated with a higher mortality. Craniotomy was associated with a higher

mortality more frequently than did Ventricular shunt. *E. coli* were most commonly reported, accounting for 26.3% of all organisms, isolated from neurosurgical patients with SSIs, followed by *S. aureus*, *Enterobacter spp.*, *P. aeruginosa*, *Enterococcus spp.*, and *K. pneumoniae*. Meticillin resistance was found in 33.7% of *S. aureus* isolates, and vancomycin resistance was found in 12.7% of enterococci. Our study showed that the significant impact of SSI on mortality and morbidity in neurosurgical patients is an additional reason to reinforce compliance of surgical staff with preventive measures and hygiene practices.

The overall SSI rate after neurosurgical procedures in our study was 19.4%. This percentage is higher than those reported in previous studies [18, 19]. The high rate of SSI after neurosurgical procedures found in the current study could be partly explained by the use of different definitions and a stricter and longer patient follow-up than in previous research.

According to literature, SSI after craniotomy (SSI-CRAN) is a serious complication, risk factors for its development have not been well defined [20]. In our study, main risk factors for SSI were age, duration of operative procedure, comorbidity index, wound class and physical status class. Multivariate analysis showed that factors found significant in univariate analysis frequently occur together.

To the best of our knowledge, this is the first multicenter prospective study evaluating SSI after neurosurgical procedures aetiologies according to surgical site in Ukraine. In previous studies reported that the most frequently isolated microorganisms were Gram-positive cocci, as seen in many previous studies [21-23].

STUDY LIMITATIONS

The strengths of the present study lie in the application of CDC/NHSN methodology for surveillance. A limitation of the study is that it only include 11 (45.8%) from 24 regional hospitals in Ukraine.

CONCLUSIONS

Surgical Site infections are a cause for mortality and morbidity among patients after neurosurgical procedures. The incidence of SSI and mortality after neurosurgical procedures in Ukraine is high. This is due to increase emergence of antimicrobial-resistant pathogens and risk factors in neurosurgery patients. The results of our study and literature data show that early identification and modification of prognostic patient factors in neurosurgery patients in the preoperative setting play an important role in mitigating the risk of adverse outcomes after surgery procedures. Routinely collected surveillance data are of great value as a basis for studying the consequences of SSS.

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Conflict of interest:

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