

A TEN-YEAR RETROSPECTIVE ANALYSIS OF RISK FACTORS AND COMORBIDITIES PREVALENCE IN A GROUP OF SEPTIC ARTHRITIS PATIENTS

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SUMMARY

Objectives: The aim of this study was the evaluation of a group of patients treated at the Department of Orthopaedics and Traumatology of Locomotory Apparatus at Luis Pasteur University Hospital in Košice for septic arthritis in relation to risk factors and chronic diseases and its microbial aetiological profile.

Methods: We conducted a retrospective study of patients including all episodes of septic arthritis from March 2013 to August 2022. The occurrence of chronic diseases, risk factors and its microbiological profile were investigated.

Results: A total of 141 patients were included: 92 (65%) males and 49 (35%) females, the mean age of patients was 58.1 years. A continued decrease in cases was recorded during the period of COVID-19 pandemic and the post-pandemic years. The largest group of our cohort represented septic arthritis of the knee (87 cases, 61.7%), followed by hip and shoulder arthritis – 17 (12.1%) and 14 (9.9%) cases, respectively. Gram positive aetiological flora represented 87.5% of all pathogens isolated and antibiotics were administered to 46 (32.6%) patients before microbiological culture samples were obtained. The dominant chronic disease was diabetes mellitus with 42 (29.8%) cases and degenerative joint disease affecting the joint was verified in 86 (61%) patients. Dental foci in 28 (19.9%) cases and skin infections in 17 (12.1%) cases were the most numerous groups of risk factors with predominant distribution for cases without previous intervention in the affected joint leading to infection.

Conclusion: The distribution of joint involvement and microbial agents was similar to other literature without affecting negative culture results by prior administration of antibiotics. Representation of chronic diseases and risk factors was comparable to the work of other authors. Notable was the continued decline in total number of cases in post-pandemic years of COVID-19 pandemic. What was interesting was the number of confirmed cases of distant focal infection distributed mainly in the group of patients without a history of any previous intervention on the joint before the infection. There is a lack of literature on distant silent infection as a risk factor.

Key words: septic arthritis, chronic diseases, risk factors, distant focal infection

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INTRODUCTION

Septic arthritis is inflammation of the joint secondary to an infectious aetiology, usually bacterial, occasionally fungal, viral or mycobacterial. It is commonly monoarticular involving one large joint such as knee, hip or shoulder. Polyarticular septic arthritis involving multiple, usually smaller, joints may also occur. Despite the fact being an uncommon disease, septic arthritis is an orthopaedic emergency causing significant joint damage leading to increased morbidity and mortality. Early diagnosis and treatment are critical to maintain joint function. Long-term mortality in elderly patients with septic arthritis is increasing due to an increase in comorbid predisposing conditions (1).

Septic arthritis is an arthropathy caused by infection with microorganisms. It may occur during hematogenous spreading from a distant location in patients predisposed to septic arthritis,

or caused by open wounds, surgery, arthrocentesis (joint aspiration), and intra-articular injection (Table 1). Following preceding events include intravenous drug injections and behaviour associated with sexually transmitted diseases. Predisposing conditions encompass underlying rheumatoid arthritis or other connective tissue disorders and immunosuppression, diabetes mellitus or immunosuppressive therapy. Skin infections have been shown to increase the predisposition to joint infection of any individual with an underlying condition such as rheumatoid arthritis (2). Septic arthritis leads to sequelae such as joint structural changes and joint malfunction due to severe inflammatory reactions. On top of that, it can result in life-threatening condition with significant mortality rate of approximately 3–29% (3).

The increase of incidence in the last years is most likely related to the aging of the population which is consequently more susceptible to the occurrence of risk comorbidities and among other things, an increase in immunosuppressive conditions and

Table 1. Risk factors associated with bacterial arthritis

Pre-existing arthritis
Skin infection
Age (> 65 years)
Trauma, including intra-articular injections
Diabetes mellitus
Immunosuppression, e.g., infection with human immunodeficiency virus and immunosuppressive therapy
Intravenous drug abuse
Previous central venous catheterisation (sternoclavicular)
Geographical exposure (Lyme's disease, fungi)
Behaviour associated with sexually transmitted diseases

Source: Smith et al. (2)

an increased number of intra-articular interventions, mainly injections, punctures and operations. The data of incidence in the Slovak Republic are not available. The reported incidence of septic arthritis varies from 2–10 cases/100,000 individuals annually in the general population to 28–38 cases/100,000 individuals annually among patients with rheumatoid arthritis. In cases of joint interventions is the risk reported 1/25,000 injections, for simple arthrocentesis 1/20,000–50,000. An application of corticoids increases the rate of cases to 1/250–1,000 interventions, the same ratio applies for arthroscopic operations (2, 4).

Most commonly affected joint is the knee, followed by the hip, shoulder, wrist, and ankle. According to the literature, in 80–90% of cases is affected one joint, i.e. monoarthritis. Multiple joint involvement is reported in up to 10–20% of patients, particularly among those with rheumatoid arthritis. Joints of the hand are involved infrequently with bacterial arthritis, but commonly with viral arthritis. Infections of the sacroiliac and sternoclavicular joints have an association with parenteral drug abuse, sacroiliac and symphyseal joints arthritis may also be result of gynaecological procedures, while sternoclavicular joint septic arthritis can also be result of infected central lines with bacteria entering the joint from adjacent subclavian vein. The most common cause of infectious arthritis is *Staphylococcus aureus* (40–60%), followed by streptococci (20–30%), enterococci (10–20%), and gram-negative bacteria (10–20%). In 10–20% the causative agent cannot be detected. Acute septic bursitis is usually caused by *Staphylococcus aureus*, often after acute trauma. Common sites are the olecranon and pre-patellar bursa, from where the infection can spread to the adjacent joints (2, 4).

We do not have statistics evaluating the incidence of septic arthritis and consequently risk factors and chronic comorbidities prevalence in Slovakia. In our work we focused on the occurrence of the chronic comorbidities and risk-factors in our group of patients with septic arthritis.

MATERIALS AND METHODS

Our cohort is composed of patients treated for septic arthritis from 2013 to 2022 at the Department of Orthopaedics and Traumatology of Locomotory Apparatus at Luis Pasteur University Hospital in Košice. The documentation of patients found in the

hospital information system with a diagnosis of M00* (International Classification of Diseases 10th Revision) was retrospectively evaluated.

Statistical analysis was performed with the IBM SPSS (Statistical Package for the Social Science) statistics software, version 26. Relations between nominal variables was expressed with Cramer's V (ϕ_c). One-way ANOVA was used to test the differences between the means of more than 2 groups (F). The relation between two interval variables was obtained by the Pearson correlation (r_{xy}). The level of statistical significance was set at $p < 0.05$.

RESULTS

One hundred and sixty-six cases were identified with diagnosis of M00* treated at our Department from the March of 2013 to August of 2022; 25 patients were excluded in the light of wrong coding (prosthetic joint infections – not native joints, osteomyelitis, bursitis, and skin and soft tissue infections). Remaining 141 were statistically analysed; 92 (65%) patients were males, 49 (35%) females. The mean age of patients was 58.1 (± 19.6) years, with median and mode of 63 and 72 years, respectively, the range of age was 87 years. Patients under 19 years of age represented a group of 6 in our cohort. The youngest patient was 6-year-old child with septic arthritis of the knee after penetrating trauma. The oldest was 93-year-old woman with septic arthritis of the knee with accompanying skin infection – erysipelas. The average age of male and female patients was 56.5 (± 18.5) and 61.1 (± 21.3) years, respectively. The decrease in mean annual age of patients after it reached the peak in 2020, although statistically insignificant ($F = 0.6$, $p = 0.791$), was notable (Fig. 1), but following significant overall decline in the number of patients treated at our Department for septic arthritis.

The decline in annual number of cases after reaching the peak in 2019 can perhaps be explained by the onset of the first waves of COVID-19 pandemic. Figure 1 shows a continued decrease in the annual count of cases until the end of observation period in 2022.

Septic arthritis of the knee joint, represented by 87 (61.7%) cases, was the largest group of our cohort, followed by hip and shoulder arthritis – 17 (12.1%) and 14 (9.9%) cases, respectively. The incidence for other joints is shown in Table 2, and prevalence

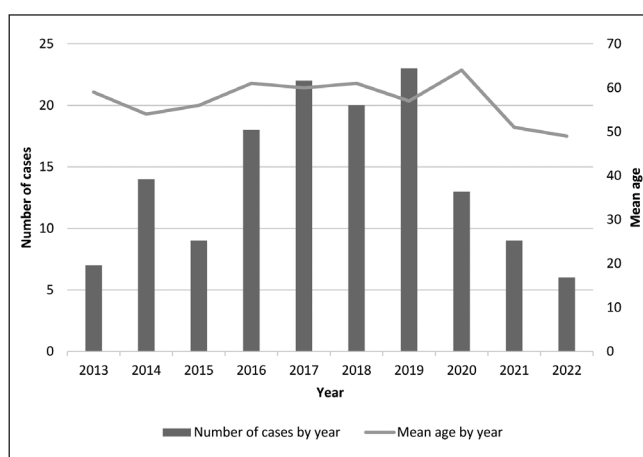


Fig. 1. Mean age of patients and number of cases.

of infectious agents in Table 3. It turns out that G+ (Gram plus) flora represents considerable number of cases accounting for 87.5% of all pathogens isolated. G- (Gram minus) flora was isolated in 6.3% and polymicrobial flora in 5.2% of all microorganisms. Mycobacterium tuberculosis was cultivated in only one case, representing 0.7% of all patients. It was 32-year-old female patient with persistent drug addiction, haemodialysis dependence and destructive arthritis of sacroiliac joint. In 45 (31.9%) cases the infectious agent was not proven. Antibiotics were administered to 46 (32.6%) patients prior to samples collection for microbiological cultivation. In our cohort it did not affect the negative result of microbiological culture ($\phi_c = 0.043$, $\chi^2 = 0.258$, $p = 0.611$). In the case of antibiotics administration, none of the group of microbial agents was cultured more often compared to the others ($\phi_c = 0.22$; $p = 0.603$). Bilateral septic arthritis was observed in 2 patients with diabetes mellitus and pre-existing knee arthritis, age over 65 years (68 and 83) and proven methicillin-sensitive *Staphylococcus aureus* (MSSA) causative microbial agent. First with a positive history of corticoid intra-articular injection and the second with administration of antibiotics before collection of samples for microbiological cultivation.

The dominant chronic disease (comorbidity) was diabetes mellitus in 42 (29.8%) cases, followed by chronic kidney disease in 19 (13.4%) cases (of which 4 in haemodialysis), rheumatic and oncologic diseases – both with 18 (12.8%) cases, chronic venous disease – 15 (10.6%) patients, peripheral artery disease – 9 (6.4%) patients, psychiatric disorders – 6 (4.3%) cases, and drug/alcohol

addiction – 6 (4.3%) individuals. Patients with poor social situation presented 3 (2.1%) cases, patients with anticoagulants and antiaggregant drugs were identified in 14 (9.9%) cases. Degenerative disease affecting the joint before the infection was verified in 86 patients, representing 61% of all, although this data was missing in 18 individuals. The incidence of degenerative joint diseases increased in direct proportion to the increasing age of patients ($\phi_c = 0.86$, $p = 0.007$). Patients with sacroiliac and sternoclavicular joint arthritis showed more frequent use of alcohol and drugs compared to other patients ($\phi_c = 0.64$, $p < 0.001$). Alcohol abuse and drug addiction were also more frequent at a younger age ($\phi_c = 0.89$, $p < 0.001$). The group consists of 6 cases, all under 35 years of age. The age distribution for each group of arthritis is shown in Figure 2, with statistically significant variability in means ($F = 3.07$, $p = 0.002$). In Figure 3 is displayed inhomogeneity in the average age of patients between groups without and with 1–3 comorbidities ($F = 6.65$, $p < 0.001$). Table 4 shows the representation of the counts of patients in groups with different numbers of comorbidities. The largest group of 51 (36.2%) patients had only one documented comorbidity in terms of a high-risk chronic disease, followed by the group without comorbidities with 48 (34%) patients. The rest, 42 (29.8%) cases are divided between groups with 2–4 comorbidities with a decreasing trend

Table 2. Incidence of septic arthritis for individual joints (N = 141)

	Frequency	%
Knee	87	61.7
Hip	17	12.1
Shoulder	14	9.9
Small joints of the hand	5	3.5
Talocrural joint	4	2.8
Small joints of the foot	4	2.8
Midfoot joints	3	2.1
Sacroiliac joint	3	2.1
Wrist	2	1.4
Elbow	1	0.7
Sternoclavicular joint	1	0.7

Table 3. Prevalence of infectious agents (N = 141)

	Frequency	%
Methicillin-sensitive <i>Staphylococcus aureus</i>	56	39.7
Methicillin-resistant <i>Staphylococcus aureus</i>	7	5
Coagulase-negative staphylococci	9	6.4
Streptococci	12	8.5
G- flora	6	4.3
Polymicrobial	5	3.5
Mycobacterium tuberculosis	1	0.7
Without isolation of infectious agent	45	31.9

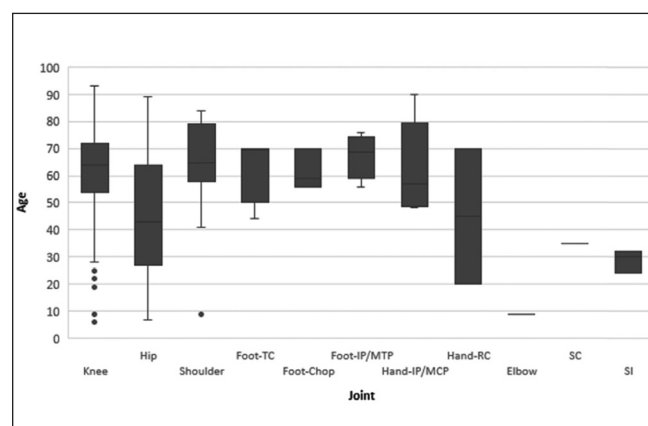


Fig. 2. Age distribution of patients according to localisation of arthritis.

Foot-TC – talocrural joint; foot-IP/MTP – small joints of the foot; hand-IP/MCP – small joints of the hand; hand RC – wrist; SC – sternoclavicular joint; SI – sacroiliac joint

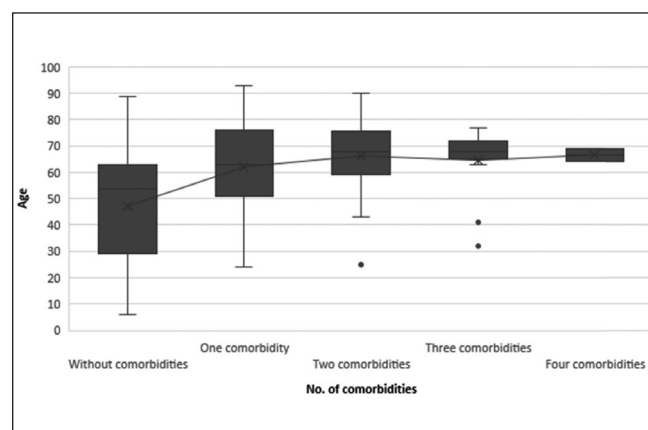


Fig. 3. Age distribution of patients according to number of comorbidities.

in the size of the groups. The age of the patients shows only weak correlation to increasing number of comorbidities ($r_{xy}=0.34$, $p<0.001$). The lethal outcome was in our cohort recorded in 2 (1.4%) cases. The first with septic arthritis of the shoulder joint in a 66-year-old female and the second with septic arthritis of the knee joint in a 91-year-old female, both with only one comorbidity, diabetes mellitus.

Information on the infectious focus was available in 80 (56.7%) patients. Focal infection was excluded in 20 (14.2%) cases, dental foci represent the most numerous group with 28 (19.9%) cases, followed by 17 (12.1%) cases of skin infections, the rest of focal infections displayed in Table 5 accounts for total of 15 (10.6%) cases. In 61 (43.3%) patients, the information was not mentioned

in the documentation. Table 5 shows symmetrical distribution of certain focal infections among the joints treated for septic arthritis at our Department, statistically insignificant ($\phi_c=0.25$, $p=0.987$). On the other hand, in Table 6 crosstabulation displayed predominant distribution of focal infection in the row without previous intervention, accounting for 49 of all 60 focal infections ($\phi_c=0.37$, $p=0.008$).

The average body mass index (BMI) in our group of patients was 27.6, with median and mode value 26.9 and 25.4, respectively. Correlation between increasing age and BMI was not demonstrated ($r_{xy}=0.23$, $p=0.17$), nor was there an association between BMI and increasing number of comorbidities ($r_{xy}=-0.06$, $p=0.55$).

Table 4. Number of comorbidities (N = 141)

	Frequency	%
Without comorbidities	48	34
One comorbidity	51	36.2
Two comorbidities	25	17.7
Three comorbidities	15	10.6
Four comorbidities	2	1.4

DISCUSSION

Septic arthritis is an orthopaedic emergency with necessity of prompt diagnosis and treatment. Early diagnosis, urgent and adequate surgical treatment and optimal antibiotic therapy are preconditions for successful outcome, i.e. preservation of joint function (1, 4).

The average age of patients in septic arthritis cohort treated at our Department in 2013–2022 was 58.1 years. Smith et al. (2)

Table 5. Distribution of focal infections for specific joints (N = 80)

	Excluded focus of infection	Dental foci	ENT focus of infection	Urological focus of infection	Skin infection	Recent infection	Other MS infection	Medical device or intervention related infections
Knee	11	16	2	1	13	5	2	1
Hip	5	5	1	0	1	0	0	0
Shoulder	1	3	0	0	1	1	0	2
Talocrural joint	0	1	0	0	1	0	0	0
Midfoot joints	0	1	0	0	0	0	0	0
Small joints of the hand	2	0	0	0	0	0	0	0
Wrist	0	1	0	0	0	0	0	0
Elbow	0	0	0	0	1	0	0	0
Sacroiliac joint	1	1	0	0	0	0	0	0

ENT – ear, nose, and throat; MS – musculoskeletal

Table 6. Crosstabulation of focal infections versus previous interventions (N = 80)

	Excluded focus of infection	Dental foci	ENT focus of infection	Urological focus of infection	Skin infection	Recent infection	Other MS infection	Medical device or intervention related infections
Without intervention	12	21	3	1	17	4	1	2
Arthrocentesis	1	5	0	0	0	1	0	1
Corticoid injection	1	0	0	0	0	1	0	0
Viscosupplement injection	2	1	0	0	0	0	0	0
Unspecified injection	0	0	0	0	0	0	1	0
Surgery	2	1	0	0	0	0	0	0
Traumatic wound	2	0	0	0	0	0	0	0

ENT – ear, nose, and throat; MS – musculoskeletal

stated age over 65 years as one of the first three risk factors associated with septic arthritis, however, mean age lower than 65 years is reported by several authors (4, 5). Nissim et al. observed significantly older age in female patients compared to males in native-joint septic arthritis group (6). Male patients make up almost two thirds (65%) of our cohort. Beside advanced age and pre-existing joint disease has been male gender suggested in retrospective studies to correlate with infection risk (7).

Decrease of mean annual number of cases during 2020 and 2021 COVID-19 pandemic can perhaps be explained by decreased number of clinical outpatient visits. Wong and Cheung report the decrease by 29.4% per week during the first wave of pandemic (8). The continued decline until the end of the study period could probably be elucidated by improved sterile measures gained from the pandemic.

The distribution of septic arthritis according to individual joints with the knee joint being dominantly affected (61.7%), followed by hip (12.1%) and shoulder (9.9%), is observed similarly to other works (2, 4, 9). MSSA was the most common cultured infectious agent, represented by 39.7% of all cases, methicillin-resistant *Staphylococcus aureus* (MRSA) was proven in only 7 (5%) cases. Similar representation is also described by other authors, but with increased number of MRSA cases (5, 10). Overall, G+ flora was responsible for 87.5% of septic arthritis with a proven causative microorganism, but the culture negative group represents almost a third of the patients (31.9%). Antibiotics administration prior to culture samples collection did not affect in our group the negative culture yield. Van der Merwe et al. observed similar results in paediatric group treated for acute haematogenous osteoarticular infections. In their cohort of 131 patients, antibiotic administration before surgery does not decrease surgical culture yield. They suggested that paediatric patients presented with suspected osteoarticular infection should receive appropriate systemic antibiotics promptly, but after obtaining the blood cultures (11). Rare microbiological agents in our group are *Mycobacterium tuberculosis*, which caused destructive arthritis of the sacroiliac joint in a drug addicted 35-year-old female patient, and *Salmonella choleraesuis* haematogenous arthritis of the knee joint in a 74-year-old man. The mentioned microorganisms are mostly given in the literature as case reports (12, 13). Also worth mentioning is the case of a 9-year-old patient with streptococcal arthritis of the elbow as a complication following chickenpox, also reported in the literature as isolated case studies of 3–5 patients (14).

The representation of comorbidities and risk factors more or less follows the table described by Smith et al. (2) (Table 1). The degenerative changes of the affected joints are present in 61% patients. If the prevalence of diabetes mellitus in Slovakia in 2022 for the age group 55–59 years was 11,467.6 cases per 100,000 inhabitants (15), then diabetes mellitus is within its 29.8% almost three times more common and most frequent chronic comorbidity in our cohort. Skin infections are the second most common focal infection. Immunosuppression, represented in a certain way by groups of chronic kidney disease, rheumatic and oncological disease, was represented by 39% in our group. Trauma including intra-articular injections and surgery stands in our cohort for 32.6%. The mean age characterising our cohort was 58.1 years, which is slightly less then referred in the Smith et al. study (2).

The distant focus of infection was identified mainly in cases without previous intervention. The most numerous group was

dental foci (75%, 21 of 28 cases), present in patients without a history of intervention on the joint. In the literature is septic arthritis related to dental infections mentioned rather as subsequent complication after dental procedures. The total number of references is remarkably handful (16–18). All of the 17 identified skin infections representing infection focus were identified on joints without preceding iatrogenic intervention. Among 61 patients without history of preceding intervention (including trauma, intra-articular injections and surgery) and assessed for distant infection was septic focus excluded only in 19.7%. In the rest of 80.3% was identified. It is noteworthy that the literature dealing with the connection of septic arthritis with a distant silent infectious focus is small (19, 20). However, it is necessary to add that the information on the infectious focus was available only in 56.7%.

In our cohort, a correlation between BMI and septic arthritis was not demonstrated. Likewise, the literature almost does not discuss this risk factor for native joint septic arthritis. Although Radhamony et al. described a high BMI level as one of the predictors of failure of single arthroscopic washout for septic arthritis of the knee joint (21).

CONCLUSION

Septic arthritis belongs to those orthopaedic conditions that requires prompt and adequate diagnostic management and treatment to prevent loss of joint function and complications that can lead to patient death. In our almost 10-yr cohort study, we observe a distribution of joint and microbial agents similar to other studies and slightly younger age of our patients and lower MRSA culture results. The administration of antibiotics before obtaining microbial samples did not affect negative culture results. The representation of chronic diseases and risk factors was comparable to the studies of other authors. The continued decline in the total number of cases in post-pandemic years of the COVID-19 pandemic was notable. What was interesting was the number of confirmed cases of distant focal infection distributed mainly in the group of patients without a history of any previous intervention on the joint before the infection. There is a lack of literature references on distant silent infection as a risk factor.

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Conflicts of Interest

None declared

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