MENTORS IN ORTHOPEDICS

SEPTIC ARTHRITIS OF THE KNEE JOINT IN AZERBAIJAN: A 5-YEAR RETROSPECTIVE MICROBIOLOGICAL INVESTIGATION

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SUMMARY

Background: Musculoskeletal infections, particularly septic arthritis of the knee, present significant diagnostic and therapeutic challenges in orthopedic surgery. While the global burden is well-documented, there is a paucity of microbiological data regarding native joint infections in specific regions such as Azerbaijan, which complicates the selection of appropriate empiric antimicrobial therapy.

Objective: This study aims to characterize the microbiological profile, clinical presentation, and antibiotic susceptibility patterns of knee septic arthritis in a cohort of patients treated at a tertiary referral center in Baku, Azerbaijan.

Key Points: A retrospective analysis of 54 patients (mean age 43.8 years) treated between 2014 and 2019 was conducted. Etiological factors included intra-articular steroid injections in 25.9% of cases and prior surgery in 9.3%. Cultures were positive in 79.6% of patients, with polymicrobial infections identified in 72.1% of those with positive results. Staphylococcus aureus was the most prevalent isolate (29.1%), followed by Candida albicans (24.4%) and Staphylococcus epidermidis (16.3%). Patients with bone involvement (septic osteoarthritis) exclusively exhibited mixed microflora. Surgical intervention was associated with a higher incidence of polymicrobial infections (83.7%) compared to conservative management (16.3%). Antimicrobial testing revealed high susceptibility to carbapenems, while resistance to aminoglycosides and the presence of vancomycin-intermediate Staphylococci were noted.

Conclusion: Septic arthritis of the knee in this region is frequently polymicrobial and often associated with prior medical interventions. The high prevalence of mixed flora and specific resistance patterns necessitate comprehensive microbiological screening to guide targeted antibiotic therapy and improve clinical outcomes in complex joint infections.

KEYWORDS

Arthritis, Infectious; Knee Joint; Staphylococcal Infections; Anti-Bacterial Agents; Microbial Sensitivity Tests

INTRODUCTION

Musculoskeletal infection remains a major issue in orthopedics, posing complex diagnostic and therapeutical dilemmas and being associated with high economical and social costs [1-3]. In fact, musculoskeletal infection remains a major problem not only for traumatologist-orthopedists, but also for microbiologists [7-9], with a lack of universally accepted therapeutical approach, due to the relative scarcity of scientific evidence [3]. Among the many challenges of bone and joint infections, the relative frequency of antibiotic-resistant strains in different clinical conditions and in the various geographical areas remains largely unknown [1,4-6].

To fill the gap, in 2017 the World Association against Infection in Orthopedics and Trauma (WAIOT) was established in Vienna, with the mission to increase and disseminate the scientific knowledge on bone and joint infections worldwide. Among the various targets, a WAIOT task force decided to start investigations on the microbiology of large joints infections in some underreported geographical areas. In fact, septic arthrtitis of large joints is a serious condition, that, if not appropriately treated in a timely manner, may lead to severe and permanent joint damage, with loss of function and the need for complex joint reconstruction surgeries [10].

The knowledge of the most frequent pathogens causing joint infections in a given geographical region may then play a strategic role to choose the most appropriate empiric antibiotic treatment, while waiting for cultural examination results [11-15]. Given the scarce reports about the microbiology of native knee joint infections in Azerbaijan and surrounding countries [16], as a part of the larger investigation, we here report the data of a cohort of patients, affected by knee septic arthritis, admitted to a one orthopedic referral center in Baku, Azerbaijan over the last 5 years.

MATERIALS AND METHODS

This study was designed as a retrospective analysis of 54 patients (39 males, 15 females), affected by septic arthritis (SA) of the knee and treated at a one orthopaedic center in Baku, Azerbaijan, from 2014 to 2019. Thirthy-nine patients (72.2%) were male and 15 (27.8%) female. Mean age was 43.8±4.9 years (min. 5, max. 77). Seven patients (13%) were treated conservatively and 47 (87%) underwent surgical treatment. Etiology of septic arthritis are showed in Tab.1.

Etiology of septic knee arthritis	All septic arthritis %
After injury	19 (35.2)
Hematogenous	7 (12.9)
After intraarticular steroid injection	14 (5.9)
Postoperative	5 (9.3)
Other or unknown etiology	9 (16.7)

The high value of steroid septic arthritis associated with intra-articular injection of the steroid drugs - (25.9%) is noteworthy. Patients were classified according to the criteria described by J.H. Newman (1976) [17] (Tab.2) with some modifications, as follows:

1. Septic arthritis and steroid septic arthritis (SSA) without involvement in bone tissue:

- Group A: positive cultures isolated from synovial fluid or from material taken during surgery
- Group B: negative cultures, but purulent drainage of the knee joint
- Group C: negative cultures, but pronounced clinical signs of local inflammatory process, correlating with laboratory data);

2. Septic osteoarthritis and steroid septic OA (SSOA) with involvement of bone tissue according to radiological methods of examination:

- Group D: positive synovial fluid cultures or from material taken during surgery
- Group E: negative cultures, but pronounced clinical signs of local inflammatory process, correlating with laboratory data

Arthritis	All arthritis	All osteoarthritis	SSA	SSOA	SA	SOA
n=54	n=40	n=14	n=9	n=5	n=31	n=9
group A	31 (77.5%)		3 (33.3%)		28 (90.3%)	
group B	4 (10%)		2 (22.2%)		2 (6.5%)	
group C	5 (12.5%)		4 (44.5%)		1 (3.2%)	
group D		12 (85.7%)		3 (60%)		9 (100%)
group E		2 (14.3%)		2 (40%)		-
Total 54	40 (74%)	14 (26%)	9 (16,7%)	5 (9.2%)	31 (57.4%)	9 (16.7%),

Microbiological samples were obtained by joint aspiration and swabbing of wounds during surgery. The biological samples taken from patients were cultured in proper agar plates and broth media. In particular, the purulent samples collected by swabs and the aspirated synovial fluids were seeded in differential-selective medium, as blood agar plate, mannitol sal agar (MSA for diagnosis of staphylococcus), eosin methylene blue (EMB for diagnosis of enterobacteria), Saburoud agar for diagnosis of candida and ifomycetes. Mono and polymicrobial cultures were analyzed and compared with clinical symptoms and other biochemical tests such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Each microorganism was isolated and identified. Microbial characterization was conducted by biochemical and phenotypical microbiological methods to determine the species and gender of gram-negative and gram-positive isolates. Susceptibility of isolates to different antibiotics were tested following Kirby Bauer disc diffusion method [18] using Muller Hinton Agar against selected antibiotics. Most antibiograms included MICs to determine the most effective antibiotic that will result in effective treatment. After 16 to 18 hours of incubation, each plate was examined, the diameters of the zones of inhibition (as judged by the unaided eye) are measured, including the diameter of the disc. Zones are measured to the nearest whole millimeter, using sliding calipers or a ruler, which is held on the back of the inverted Petri plate. Inhibition zone size was interpreted using standard recommendation of Performance Standards for Antimicrobial Susceptibility Testing; Seventeenth Informational Supplement (January 2007, M100-S17 Vol. 27 No. 1 Replaces M100-S16 Vol. 26 No. 3)

Statistical data processing was performed using the computer program Statistica 12.5. The results are presented in the form M±SD , where M - is the arithmetic mean, SD - is the standard deviation and are calculated on an online calculator. All subjects gave their informed consent for inclusion before they participated in the study. The study was approved by the Azerbaijan Research Institute of Traumatology and Orthopedics Ethical Committee.

RESULTS

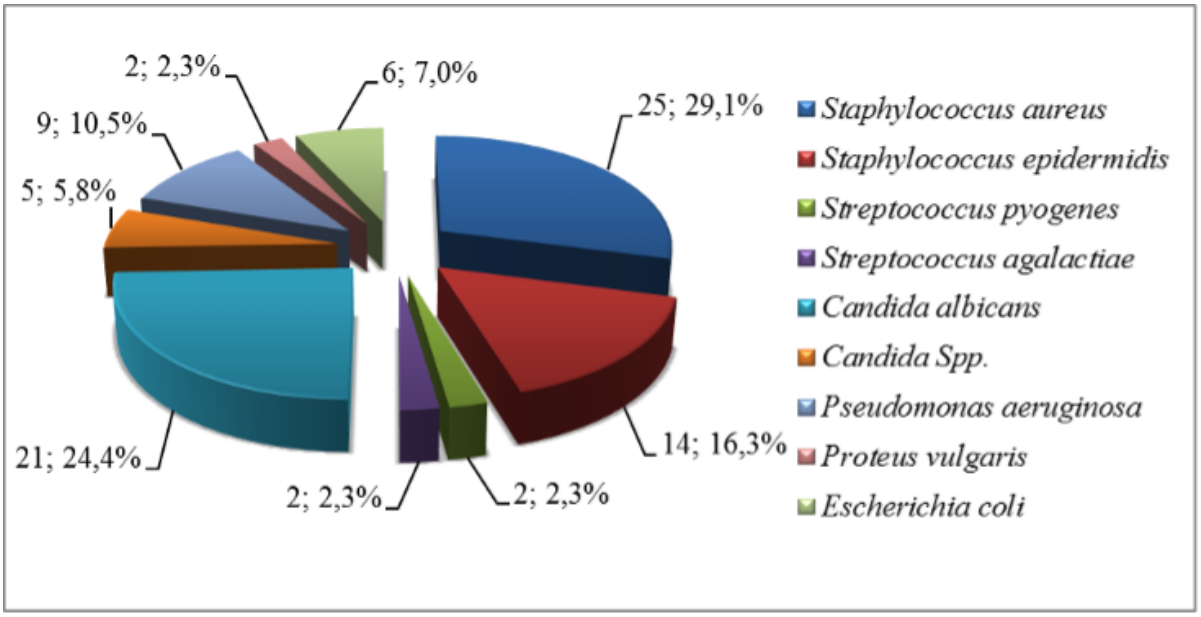
The etiologies of septic arthritis are shown in Tab. 1. Of note, 25.9% of the infections were subsequent to an intra-articular steroid injection and 9.3% were post-surgical. Thus, in 35.2% of patients, septic arthritis arose because of medical manipulations. According to the Newman criteria, 40 (74%) patients did not show radiographic signs of bone involvement; in particular, 31 (57.4%) were classified as Group A infections, 4 (7.4%) as Group B and 5 (9.2%) as Group C. Of the remaining patients, 12 (22.2%) were identified as Group D and 2 (3.7%) as Group E.

Etiology of septic knee arthritis	All septic arthritis %
After injury	19 (35.2)
Hematogenous	7 (12.9)
After intraarticular steroid injection	14 (5.9)
Postoperative	5 (9.3)
Other or unknown etiology	9 (16.7)

A positive culture was found in 43 cases (79.6%) and negative in 11 (20.4%) cases. Among positives cases, a single pathogen was detected in 12 (27.9%) patients, 2 pathogens were isolated in 17 patients (39.5%), and 3 pathogens were isolated in 14 patients (32.6%). Overall, 86 strains were isolated in 43 patients. The most common single isolated pathogen was Staphylococcus aureus, while the less often retrieved was Streptococcus pyogenes. If we take all cases of mixed microflora as 100% then mixed florae consisted of two microorganisms was found in 17 (54.8%) of patients, while infections with three microorganisms was found in 14 cases (45.2%). Most common associated microorganisms in two and three polymcrobial isolates were Staphylococcus aureus, Candida albicans and Staphylococcus epidermidis, Candida albicans, Escherichia coli respectively (Tab 3).

Microbial results (n=43 patients)	Number (%)
Mixed-culture (2 microrganisms)	
Staphylococcus aureus, Candida albicans	6 (19.3)
Staphylococcus aureus, Pseudomonas aeruginosa	3 (9.7)
Staphylococcus epidermidis, Candida albicans	3 (9.7)
Staphylococcus epidermidis, Candida spp.	2 (6.5)
Staphylococcus aureus, Streptococcus pyogenes	1 (3.2)
Staphylococcus aureus, Candida spp.	1 (3.2)
Staphylococcus epidermidis, Pseudomonas aeruginosa	1 (3.2)
Representativeness error (M±SD)	2.4±1.8
Mixed-culture (3 microorganisms)	
Staphylococcus epidermidis, Candida albicans, Escherichia coli	5 (16.1)
Staphylococcus aureus, Staphylococcus epidermidis, Candida albicans	2 (6.5)
Staphylococcus aureus, Streptococcus agalactiae, Candida spp.	2 (6.5)
Staphylococcus aureus, Candida albicans, Proteus vulgaris	2 (6.5)
Staphylococcus aureus, Pseudomonas aeruginosa, Candida albicans	1 (3.2)
Staphylococcus aureus, Candida albicans, Escherichia coli	1 (3.2)
Staphylococcus epidermidis, Pseudomonas aeruginosa, Candida albicans	1 (3.2)
Representativeness error (M±SD)	2.0±1.4
Representativeness error (M±SD) (all mix-culture)	2.2±1.6

Considering the overall relative frequency of the isolated microorganisms, facultative anaerobe Gram-positive cocci were: Staphylococcus aureus (29.1%), Staphylococcus epidermidis (16.3%), Streptococcus pyogenes (2.3%), Streptococcus agalactiae (2.3%); facultative anaerobe Gram-negative bacilli were: Escherichia coli (7%), Proteus vulgaris (2.3%); anaerobe nonfermentive Gram-negative bacillus as Pseudomonas aeruginosa (10.5%); endosymbiotic fungi as Candida spp. (5.8%), Candida albicans (24.4%) (Diag. 1).



Diag. 1: Relative frequency of isolated microorganisms (n=86).

The overall incidence of mixed florae was 72.1% interestingly, the incidence of patients affected by the infection due to a mixed flora was 16.3% (7/43) in patients treated conservatively and 83.7% in those treated surgically.

In reviewing the results for each group, it is clear that in patients with SOA, the results were 100% positive and found only in mixed florae form. In patients with SA (n = 31), treated conservatively (7/31) negative microflora was not obtained. In patients treated operatively (24/31), negative culture responses were found in 3 (12.5%) cases. (Tab. 4).

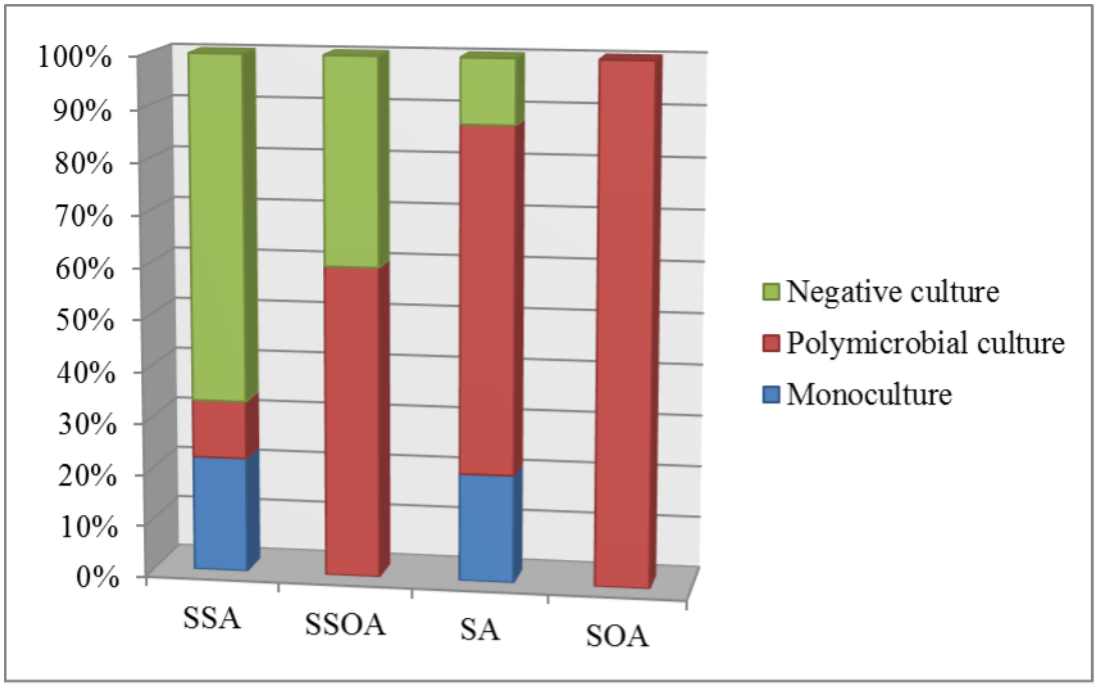
Clinical groups	Number of patient	Results of microbiological examinations					
		Patients treated by conservative method (n=7)			Patients who underwent surgical treatment (n=47)		
		Monoculture	Polymicrobial culture	Negativecul-ture	Monoculture	Polymicrobial culture	Negative culture
		Quantity (%)	Quantity (%)	Quantity (%)	Quantity (%)	Quantity (%)	Quantity (%)
SSA	9	-	-	-	2 (22.2)	1 (11.1)	6 (66.7)
SSOA	5	-	-	-	-	3 (60)	2 (40)
SA	31	5 (71.4)	2 (28.6)	-	5 (20.8)	16 (66.7)	3 (12.5)
SOA	9	-	-	-	-	9 (100)	-
Representativeness error (M±SD)					3.5±2.1	7.3±6.8	3.7±2.1

Patients treated conservatively showed most often a single pathogen (5/7; 71.4%), compared to those treated surgically, in which a single microorganism was found in only 5/47 cases (10.7%), while the remaining showed a mixed flora (29/47; 61.7%) or a negative culture (11/47; 23.4%). The frequency of incidence of microorganisms is related to the duration and phase of the disease. (Tab. 5).

Septic arthritis			
Phase	**Microorganisms**	**Phase**	**Microorganisms**
Acute	Staphylococcus aureus Streptococcus pyogenes Streptococcus agalactiae Pseudomonas aeruginosa Escherichia coli	**Chronic**	Staphylococcus aureus Staphylococcus epidermidis Streptococcus agalactiae Pseudomonas aeruginosa Candida albicans Candida S01pp. Proteus vulgaris Escherichia coli
Steroid Septic arthritis			
Acute (time after injec-tion of steroids < 2 weeks)	Staphylococcus aureus Staphylococcus epidermidis Pseudomonas aeruginosa	**Chronic** (time after injec-tion of steroids > 2 weeks)	Staphylococcus aureus Staphylococcus epidermidis Pseudomonas aeruginosa Candida albicans Proteus vulgaris

In patients with SSA in the acute phase (up to 2 weeks from the moment of injection), the number of isolated strains of microorganisms was significantly less than in patients in the acute phase of normal SA. In patients with the chronic phase of SSA, 5 strains of microorganisms were isolated, which is significantly less than in patients with SA - 8 strains.

Interesting data were obtained by correlating the data of positive microbiological tests depending on the type of pathology and etiology of the knee arthritis. In 40% of the patients with SSOA and in 66.7% of the patients with SSA the cultures were negative. Is it possible to interpret the inflammatory process as aseptic in this group of patients? We cannot answer this question yet (Diag.2).



Diag. 2: Results of bacteriological examinations on groups.

By reviewing the results of patients with SOA and SSOA, it is noticeable that suppurative microorganisms occurred only in mixed infections. This occurred in 100% of patients with SOA and in 60% of SSOA patients. In 40% of patients with SOA the cultures were negatives.

ANTIMICROBIAL SUSCEPTIBILITY

The study of the obtained strains of microorganisms for their sensitivity to antibiotics in patients with SSA showed a very high sensitivity to Carbapenems and very low sensitivity to aminoglycosides (Tab. 6).

Microorganisms			Staphylococcus aureus (n=3)			Staphylococcus epidermidis (n=4)			Pseudomonas aeruginosa (n=2)		
Antibiotics			R	S	I	R	S	I	R	S	I
Penicillins	Ampicillin		3			2		1	2		
		%	100			50		25	100		
	Bactamed		1		2	1	1	2	2		
		%	33		67	25	25	50	100		
Cephalosporins	Cefazolin			1	2		1	3	1		1
		%		33	67		25	75	50		50
	Ceftriaxone			2	1		2	1			2
		%		67	33		50	25			100
	Cefotaxime			2	1		2	2	1		1
		%		67	33		50	50	50		50
	Cefepime			1	2		1	3			2
		%		33	67		25	75			100
Carbapenems	Meropenem			3			4			2	
		%		100			100			100	
	İmipenem			3			4			2	
		%		100			100			100	
Macrolides	Erythromycin		3			4			2		
		%	100			100			100		
Aminoglycosides	Gentamicin				3	1		3	1		1
		%			100	25		75	50		50
	Streptomycin				3	2		2	2		
		%			100	50		50	100		
	Amikacin			1	2		1	3			2
		%		33	67		25	75			50
Quinolones (Fluoroquinolones)	Ciprofloxacin			1	2		1	2			2
		%		33	67		25	50			100
	Ofloxacin			2	1		1	3		1	1
		%		67	33		25	75		50	50
	Levofloxacin			3			2	2		1	1
		%		100			50	50		50	50
Glycopeptides	Vancomycin			1	2		1	2	1		1
		%		33	67		25	50	50		50

Also microorganisms obtained in patients with SA showed a high sensitivity to Carbapenems. (Tab. 7).

Microorganisms			Staphylococcus aureus (n=22)			Staphylococcus epidermidis (n=10)			Pseudomonas aeruginosa (n=7)			Escherichia coli (n=6)		
Antibiotics			R	S	I	R	S	I	R	S	I	R	S	I
Penicillins	Ampicillin		12		2	4		2	7			6		
		%	55		9	40		20	100			100		
	Bactamed		7	6	8	2	2	6	6		1	3		1
		%	32	27	36	20	20	60	86		14	50		17
Cephalosporins	Cefazolin		4	6	12	2	3	4	5		2			6
		%	18	27	55	20	30	40	72		28			100
	Ceftriaxone		1	12	9		6	4	1	1	5		6	
		%	5	54	41		60	40	14	14	72		100	
	Cefotaxime		1	13	8	1	4	5	5	1	1		5	1
		%	5	59	36	10	40	50	72	14	14		83	17
	Cefepime		2	7	13	2	3	5	2	1	4		5	1
		%	9	32	59	20	30	50	28	14	58		83	17
Carbapenems	Meropenem			20	2		9	1		7			4	2
		%		91	9		90	10		100			67	33
	İmipenem			19	3		8	2		6	1		4	2
		%		86	14		80	20		86	14		67	33
Macrolides	Erythromycin		17		3	9		1	6			6		
		%	77		14	90		10	86			100		
Aminoglycosides	Gentamicin		3	4	15	3	3	4	4		1		3	3
		%	14	18	68	30	30	40	58		14		50	50
	Streptomycin		4	1	16	3	1	6	5		1			5
		%	18	5	77	30	10	60	72		14			83
	Amikacin		2	5	15	2	3	4	2	3	2		4	1
		%	9	23	68	20	30	40	28	44	28		67	17
Quinolones (Fluoroquinolones)	Ciprofloxacin		1	9	12	2	2	6	3	1	2		5	1
		%	5	41	54	20	20	60	44	14	28		83	17
	Ofloxacin		1	12	9	1	3	6	3	1	2		3	3
		%	5	54	41	10	30	60	44	14	28		50	50
	Levofloxacin			13	9		4	6	1	4	1		6	
		%		59	41		40	60	14	58	14		100	
Glycopeptides	Vancomycin			5	13		1	9	5		2			5
		%		23	59		10	90	72		28			83

Regarding Quinolones, a similar sensitivity in both groups was observed. Interestingly, an increased rate of Staphylococci vancomycin intermediates in both groups were also observed. In some patients, various fungi such as Candida albicans and Candida spp. have been obtained in polymicrobial associations. However, their analyzes, in particular by types of fungi and their sensitivity to various antifungal drugs, did not reveal a significant difference between different groups of patients.

DISCUSSION

J.H. Newman, 1976 [17] proposed to diagnose septic arthritis according to several criteria. We have included in our research all cases of knee septic arthritis as well as the reasons of the disease. We then introduced the concept of septic osteoarthritis (SOA) with the involvement of cortical and subcortical bone tissue, which wasn't previously considered by J.H.Neumann. Upon receipt of a negative microbiological result (11/54, 20.4%), for the diagnosis of SA, we, unlike J.H. Neumann [17] and Chao-Ming Chen et al. 2013 [19], proposed to additionally use as a criterion the data of CRP, ESR and white blood cell count. Only 43 of 54 patients (79.6%) had a positive culture. Monomicrobial infection was observed in 12 patients (22.2%). Polymicrobial infection was observed in 31 patients (57.4%).

Gram-positive bacteria are the most common isolates in septic knee arthritis [4,5,10,19,20-25,21,26]. Despite the presence of various microorganisms, Staphylococcus aureus was in general the most frequent isolated strain. Also in SA patients, gram-positive bacteria played a major role, especially the Staphylococci (45.4%) and Staphylococcus aureus (mean, 29.1%; range, 19-68.9%) was the first. Our findings are in line with a publication, that Staphylococcus aureus represents the main responsible etiological agents in SA. Similar results were observed by many authors [4,10,22-25, 26] for Staphylococcus epidermidis (16.3% vs 12-40%) of literature data. The results of the present study concur with these reports; even in multi-pathogen knee infections, Staphylococcus aureus was in general the most common bacterial isolate.

Positive cultures were observed in the majority (90.3%) of the patients with septic knee arthritis without bone involvement, in line with previous reports by Camilo et al. (91.8%) [5], Chao-Ming et al. (85.9%) [19], and Zar et al. (73%) [21]. By reviewing the results of the patients with SOA and SSOA, it is noticeable that suppurative microorganisms occurred only in multi-pathogen infections. This occurred in all patients with SOA and in 60% of the patients with SSOA (percentages are given for each group). In 40% of the patients with SSOA and in 66.7% of the patients with SSA the cultures were negative (Diag.2). We have not yet been able to interpret these results. We hope that further research will help answer to this question.

There are conflicting reports with respect to the incidence of septic knee arthritis after intra-articular steroid injections [19,27]. Chao-Ming Chen et al. [19], reported that the results of the treatment of SSA did not differ from the results of the treatment of SA with non-steroidal etiology. The authors made these conclusions on a small number of patients. On the other hand Choudhry M.N. et al. [27], reported that the administration of steroid drugs to the joint highly increases sugar in few hours in diabetic patients. According to our data, the difference in microbiological parameters between SA and SSA was expressed only in a higher percentage of negative tests in patients with SSA. Thus, it becomes obvious that it is necessary to continue the study of the effect of steroid drugs on the occurrence of SA, on the microflora and treatment results in more patients.

The ability of Staphylococcus aureus to create pyogenic arthritis as monomicrobial agent is already noted in the literature. This is in contrast with our study, which reports S.epidermidis as the main aetiological agent in monomicrobial infections. Similar results were observed in the early complications after arthroplasty [26,28]. As gram-negatives Pseudomonas aeruginosa was present in mono and in polimicrobial infections. Similar results were obtained in literature [29,30]

Regarding the sensitivity of the 86 isolated strains from all patients, it should be noted that the gram-positive microorganisms were resistant to several antibiotics. These results are confirmed by many studies [31,32,33]. The results of our studies show that polymicrobial microflora is very common in patients with SA. The frequency of polymicrobial microflora especially increases in patients with SOA. In patients with SSA, negative microbiological tests are very common. These features should be taken into account when prescribing antibiotic therapy in patients with knee SA.

CONCLUSION

The results of the bacteriological examinations prove that SA of the knee joint is clinically severe. Besides this, conducting the microbiological analysis in these patients considered a part of the comprehensive examination. Thus, clinicians, prior to receiving the results of microbiological data, may include antibiotics in complex treatment, based on the data obtained.

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