Clinical features and aetiology of septic arthritis in northern Israel

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Objective. To assess the clinical features and determine the pathogens responsible for septic arthritis in patients admitted to two community hospitals in the Haifa district in northern Israel over a 17-yr period.

Methods. A retrospective study of the hospital records of patients with septic arthritis admitted to Carmel Medical Center and Bnai Zion Medical Center in Haifa between 1987 and 2003.

Results. Of 150 cases identified by discharge summary diagnostic codes, only 110 patients met criteria for the case definition of septic arthritis, and these form the basis of this report. Their mean age was 37.2 yr. Of the patients, 10.4% were recent immigrants, most of them from the former Soviet Union and from Ethiopia. Primary joint disease was reported in 21.8% of the cases, osteoarthritis being most prevalent (8.1%). Of the infected joints, 8.1% were prosthetic. *Staphylococcus aureus* was the most common pathogen isolated, making up 40% of all positive cultures. Streptococcal and Gram-negative bacilli were both identified in 14%. Eight patients had tuberculous arthritis (9%). Another pathogen, unusual in developed countries, was *Brucella* species, which was identified in 11% of the cases. Two-thirds of the patients underwent surgical joint drainage while the rest were treated solely with antibiotics.

Conclusions. The present study highlights the importance of characterizing the profile of species causing septic arthritis in specific regions, taking into account ethnic, genetic and environmental factors. In our survey population, tuberculous arthritis is a growing problem, mainly due to recent immigration waves, and brucella is an endemic and common pathogen. It is important to keep a high level of suspicion for these latter two bacteria, as they require special and unique care.

Key words: Septic arthritis, Israel, Tuberculous arthritis.

Septic arthritis refers to all joint infections caused by pyogenic bacteria. It is not a common condition; the overall estimated incidence in Europe is reported as 2–6 cases per 100 000 population per year [1–2].

There is distinct variability in the causative organisms of septic arthritis in different parts of the world. In most European and North American reports the most common bacterial isolates in septic joints have been staphylococci and streptococci [1–6], with *Neisseria gonorrhoeae* particularly prevalent in North America.

Israel is an Eastern Mediterranean country with endemic pathogens characteristic of that region. Its population is very diverse, being composed of variety of ethnic groups. Recently, large immigrant waves, especially from the former Soviet Union and Ethiopia, have introduced previously uncommon pathogens, such as *Mycobacterium tuberculosis*, to the local scene [7]. All these factors may be expected to influence on the clinical features and causative organisms of septic arthritis in Israel. Currently there is little information regarding septic arthritis in Israel. The data available consist of only one small survey in children younger than 2 yr of age [8].

The present study was undertaken to determine the epidemiological, clinical and laboratory data were collected by detailed charge review, with information recorded on a standard form.

Case definition

The case definition criteria we used have been used by others in similar studies and were derived from those of Newman [9].

The essential features of this definition of septic arthritis are:

Group A, microbial pathogen identified in, or isolated from, synovial fluid or joint tissue; Group B, typical features of septic arthritis with pathogen isolated from the blood; and Group C, pus obtained from the joint, but joint culture sterile because of previous administration of antibiotics.

Methods

The study population was that of the greater Haifa region in northern Israel (population circa 400 000), which is served by three hospitals. The data were collected from two of the hospitals, serving approximately half of this population. The source of patients’ records was the medical archives of the two hospitals (Carmel Medical Center and Bnai-Zion Medical Center) for the period 1 January 1987 to 31 December 2003. Patients with discharge diagnosis coded by ICD-9 for pyogenic arthritis or infectious arthritis (711.0, 711.4, 711.6, 711.7, 711.9), tuberculous arthritis (015.0–015.9) and arthritis associated with brucellosis (023) were identified. The medical records were located and epidemiological, clinical and laboratory data were collected by detailed charge review, with information recorded on a standard form.
Inclusion criteria for tuberculous arthritis were adopted from Newman [9] so that patients identified fulfilled one of the following criteria: (i) identification of tubercle bacilli from affected joint (by direct microscopy or culture); (ii) evidence of caseating granuloma on biopsy from affected site when tubercle bacilli were not found; and (iii) isolation of tubercle bacilli from a non-skeletal focus and evidence of response of the joint infection to antituberculous therapy.

The diagnosis of brucella arthritis was established by signs and symptoms of arthritis (pain, tenderness, swelling, heat of the joint) or by imaging indicative of joint inflammation in the presence of an antibody titre greater than 1:160 in the tube agglutination test or by positive culture.

Medical chart review

Upon examination of patient records, pertinent details catalogued included: sex, patient age at presentation, demographic data (date of immigration, country of birth, ethnic origin), previous history of joint disease, history of recent trauma or instrumentation (including joint injections), underlying immunosuppression and comorbid conditions, presenting symptoms, the duration of symptoms before admission, antibiotic treatment at presentation, sites of extra-articular infection, fever during admission, white blood cell count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) at admission, analysis of synovial fluid (white blood cell count, Gram stain for bacteria), results of microbiological testing, details of medical and surgical treatments, length of hospital stay, complications and mortality attributable to acute septic arthritis.

Results

One hundred and fifty possible cases of septic arthritis were identified using the computerized ICD-9 system of the hospital archives. Of these, 110 episodes fulfilled the case criteria for septic arthritis and form the basis of this report. The 40 cases identified but not satisfying the criteria were excluded (sterile cultures without prior antibiotic treatment, lack of sufficient clinical data or no cultures were obtained). No statistically significant differences were found between the excluded cases and the study group with respect to age, sex, ethnicity, habitat and recent immigration. The numbers of cases fulfilling each of the required diagnostic criteria are shown in Table 1.

Demographic data

The sex ratio was approximately equal, with 51.8% male. The study population included adults and children, with the mean age of 37.2 yr, range of 9 days to 99 yr. Distribution by age is depicted in Fig. 1. Arabs accounted for 29.1%, similar to their relative representation in the local district population. Eleven patients (10.4%) were recent immigrants, most of them from the former Soviet Union (eight patients) and the rest being from Ethiopia.

Primary joint disease

Primary joint disease was detailed in 24 (21.8%) patients. The most prevalent was osteoarthritis (nine patients, 8.1%), while three patients (2.7%) had rheumatoid arthritis (RA), one patient had systemic lupus erythematosus (SLE) and two patients had unclassified inflammatory arthritis. One of the patients with RA had been recently treated with infliximab and the patient with SLE was under chronic treatment with steroids and azathioprine. The remaining nine patients, who underwent invasive joint procedures (intra-articular joint injection, four patients; prosthetic joint five patients), lack more detailed data on the nature of their joint disease.

Previous episodes of septic arthritis were documented in five patients (4.5%).

Comorbidities and potential risk factors for septic arthritis

Comorbidities were recorded in 41 patients: 13 patients (11.8%) had diabetes mellitus and chronic renal failure was diagnosed in seven patients (6.3%).

In Table 2 the sources of infection are itemized according to patient category. Forty-seven patients (42.7%) had no readily identifiable risk factor for septic arthritis.

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![Fig. 1. Age distribution of patients with septic arthritis.](image-url)

<p>| Table 1. Newman’s diagnostic criteria for septic arthritis met by study patients |
|---------------------------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Criteria fulfilled</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>Group A: Pathogen from joint</td>
</tr>
<tr>
<td>13</td>
<td>Group B: Pathogen from other source</td>
</tr>
<tr>
<td>15</td>
<td>Group C: Prior antibiotics</td>
</tr>
<tr>
<td>7</td>
<td>Positive titer of <em>Brucella</em></td>
</tr>
<tr>
<td>110</td>
<td>Total</td>
</tr>
</tbody>
</table>

<p>| Table 2. Potential risk factors for septic arthritis |
|---------------------------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distant site of infection</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4</td>
</tr>
<tr>
<td>Skin infection close to the joint</td>
<td>9</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1</td>
</tr>
<tr>
<td>Chronic osteomyelitis</td>
<td>3</td>
</tr>
<tr>
<td>Invasive procedure</td>
<td></td>
</tr>
<tr>
<td>Recent orthopaedic surgery</td>
<td>5</td>
</tr>
<tr>
<td>Recent arthroscopy</td>
<td>2</td>
</tr>
<tr>
<td>Recent intra-articular injection</td>
<td>10</td>
</tr>
<tr>
<td>Recent oesophagoscopy</td>
<td>1</td>
</tr>
<tr>
<td>Intravenous drug abuse</td>
<td>3</td>
</tr>
<tr>
<td>Prosthetic joint</td>
<td>9</td>
</tr>
<tr>
<td>Local trauma</td>
<td>13</td>
</tr>
</tbody>
</table>
 Symptoms, signs and investigation at presentation

The median length of time from onset of symptoms until admission was 5.9 days, 16 patients having symptoms for more than a month before admission. Of these, seven patients had tuberculous arthritis and four had an infected prosthetic joint. The most frequent presenting symptom was pain, reported by 66.4% of the patients. Fever at presentation, defined as an oral temperature above or equal to 38°C, was present in only 50.9% of the patients. New joint swelling was recorded in 58.2% of the patients at presentation. Leucocytosis, defined as blood leucocyte count above 11×10⁹/litre, was recorded in 35.4% of the patients. All patients with tuberculous arthritis had a normal body temperature and normal white blood cell counts at presentation. ESR (average 77.2 mm/h; normal for females <25 mm/h, for males <17 mm/h) and CRP (average CRP 168.5 mg/l; normal <5 mg/l) were constantly raised in 91.6 and 100% of the patients, respectively. The average white blood cell count in the synovial fluid was 92×10⁹/litre (range 7–260×10⁹/litre).

 Joints involved

Knees (41.8%) and hips (23.6%) were the joints most commonly affected. Of the infected joints, nine (8.1%) were prosthetic. There were five patients with polyarticular bacterial arthritis, one patient with bilateral knee infection, one with involvement of ankle and knee in the context of staphylococcal sepsis, another with involvement of hip and ankle, and the remaining with infective spondyloarthritis, one with TB and another with brucellosis.

 Joint bacterial pathogens

In 65 cases, positive synovial fluid culture alone was diagnostic, while in 12 cases both synovial fluid and blood culture were positive; in 11 cases blood culture alone was used to identify the responsible infective agent.

In 22 patients no bacteria were cultured in the blood or synovial fluid; of these patients, 15 had received antibiotics before admission and hence their cultures were obtained under antibiotic treatment. In the other seven culture-negative patients, bacteria were identified on direct microscopy of the synovial fluid. Also, three of these had received antibiotics prior to admission.

The diagnosis of culture-negative septic arthritis was established based on clinical features and response to antibiotics, synovial fluid characteristics (i.e. absence of crystals) and imaging, which served to rule out other common aetiologies of acute monoarthritis. Five of these patients presented with acute monoarthritis following a penetrating injury to the joint; one patient had a recent septic arthritis of the same joint and two patients had subcutaneous abscesses adjacent to the inflamed joint.

In the 110 cases surveyed, 15 species of bacteria were identified via cultures of synovial fluid or blood (Fig. 2). *Staphylococcus aureus* was the most common pathogen, found in 40% of all positive cultures. Streptococcal species were identified in 14%, as were Gram-negative bacilli. In five patients, more than one species was isolated.

Eight patients (9%) had tuberculous arthritis; their average age was 54.8 yr. Most of them were recent immigrants to Israel, four from the former Soviet Union and three from Ethiopia. Risk factors for TB reactivation were present in only one patient, who was suffering from SLE and was treated chronically with steroids and azathioprine.

All cases of spinal TB were diagnosed based on involvement of intervertebral joints, as demonstrated by computed tomography or magnetic resonance imaging and isolation of *M. tuberculosis*. None of the involved joints was aspirated with bacteria isolated from extra-articular sites, such as the peritoneum and lymph nodes.

None of these patients had fever during admission; 75% had elevated acute-phase reactants (CRP, ESR). Joints involved included the spine (three patients), knee (two patients), and hip, foot and elbow (one patient each). In only five out of the eight cases was *M. tuberculosis* identified directly from the infected joint. In the other cases of TB arthritis (all involving the spine), the diagnosis was made based on identification of the bacteria at a distant site: one patient in the peritoneum and two in an inguinal lymph node. No cases of atypical *Mycobacterium* were identified.

Eleven patients (11%) were diagnosed as suffering from brucella arthritis; one had positive synovial culture, two had positive blood culture and the rest were diagnosed on the basis of positive serological tests alone. All of them were infected with *Brucella melitensis*. Eight of the patients had close contact with livestock or had consumed unpasteurized dairy products as possible sources of their infection. Most of the affected patients were young (average age 14.7 yr). All of them lived in rural areas, nine of them were Arab. The affected joints were: spine, three patients; knee, three patients; hip, three patients; hand, one patient; and foot, one patient. Two patients had two joints involved. In only one case was synovial fluid aspirated. All of the patients were treated conservatively with antibiotics and none required surgical drainage.

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**Fig. 2.** Organisms causing septic arthritis.
**Treatment**

All of the patients were treated with antibiotics. The most frequently used antibiotics were cloxacillin (43 patients) and second-generation cephalosporin (34 patients). Sixty-five patients (60%) underwent an operative procedure, usually for the purpose of drainage, 12 of them more than once. The average time from admission to surgery was 5 days. The most frequent operation was arthroscopy and arthroscopic drainage (53 patients). The most frequent joint infections that were treated surgically were of the ankle (71%), knee (62%), shoulder (62%) and hip (61%).

**Complications**

The course of hospitalization of 14 patients was complicated: five patients were admitted to an intensive care unit; three patients were mechanically ventilated; four patients had acute renal failure or needed emergency dialysis; three suffered from significant postoperative wound infection; and one patient suffered an acute myocardial infarction. The average age of the patients with complications was 68 yr. Most of them had background chronic debilitating conditions (diabetes mellitus, four; chronic renal failure, two; heart disease, five). The most frequent bacteria isolated in this group were *S. aureus* (seven patients) and Gram-negative bacilli (three patients). Two patients died of sepsis.

**Discussion**

To our knowledge, this is the first large-scale study of septic arthritis in Israel. In this retrospective study of patients with septic arthritis we included only patients who fulfilled grades A, B and C of Newman’s criteria [9].

We identified 110 proven cases of septic arthritis. Forty patients were excluded as no pathogen was demonstrated by culture or smear and they did not fulfill the criteria, although their clinical picture and course of disease was otherwise consistent with that of septic arthritis. In consideration of the above, the likely true incidence rate of septic arthritis in our population may be higher than represented in our analysis. Review of a sample of the cases not included in our analysis did not reveal a pattern of systematic exclusion that might have biased the results (data not presented).

A further possible limitation of the present study is its inclusion of cases meeting Newman’s criterion C, which includes patients with sterile culture of pus obtained from an inflamed joint after prior antibiotic treatment. These patients may merely suffer from an idiopathic inflammatory or crystal-induced arthritis. Thus, overestimation of the number of septic arthritis cases may have resulted. The number of such patients in this survey is low.

There was a low prevalence of two generally described high-risk patient groups in our study population: oncology and intravenous drug abuse patients. The absence of the first group can be explained partially by the fact that these patients are centred in the third medical centre in our region, which was not included in the survey and acts as a referral centre for those conditions. Nevertheless, it should be noted that the prevalence of intravenous drug abuse is much lower in Israel than in Europe or North America.

The present data confirm the findings of past studies [10] supporting the central importance of obtaining synovial fluid cultures before administration of antibiotics. Here too, blood cultures contributed to diagnosis when synovial cultures were sterile. The data also confirm that over-reliance on other non-specific parameters, such as peripheral white blood cell count and body temperature, may be misleading. Acute-phase reactants such as ESR and CRP, however, were of assistance in the present study as more sensitive indicators of possible septic arthritis.

In the present survey, a considerable percentage of the joint infections followed an invasive procedure of the joint, such as intra-articular joint injection or arthroscopy. The reported incidence of post-injection septic arthritis is 1:3000–50000 [11–12]. A recent survey [11] that evaluated the precautionary measures used by physicians before intra-articular injection indicated that there is a trend towards minimal use of antiseptic techniques. Thus, greater adherence to the use of sterile techniques before invasive procedures involving the joint and well as careful reconsideration of these procedures in high-risk groups may reduce the incidence of these infections in our region.

There were no cases of gonococcal arthritis in our study. The reported prevalence in North American studies is typically one in five cases and it is the commonest cause of septic arthritis in young adults [13]. A high prevalence rate has also been reported from Australia [14], the numbers being lower in European studies [1–5, 15–17]. Probable reasons for this observation are the very low incidence of gonorrhoea in Israel and the characteristics of our survey population, with its low numbers of intravenous drug users and AIDS patients. Moreover, it has been suggested by Hook [18] that there is variability in the arthritogenic potential of Neisseria gonorrhoeae strains in various geographical areas.

Tuberculous arthritis is a growing problem in Western societies. There has been resurgence in TB worldwide, especially extra-pulmonary TB [19]. TB has re-emerged in Israel in the past 15 yr, mainly due to immigration from the former Soviet Union as well as from Ethiopia, where it is more prevalent [20]. While there is a trend towards more TB reported in other recent European studies [21–22], the percentage reported in our study is higher than reported from Europe. As in a previous Israeli report [23], most of the TB cases in our study, were found among recent immigrants, all of them HIV negative. Symptoms were present in all of these patients for more than a month before diagnosis was established. This delay may be explained by the indolent nature of the infection and the low level of suspicion for this infection in Western society.

Brucellosis is endemic in the Mediterranean basin. Incidence has been steadily increasing in Israel’s neighbouring countries in recent decades. The high incidence in Israel is centred mainly among Arabs who have close contact with governmentally supervised livestock and its products [24]. Brucella is rarely reported as a cause of septic arthritis in European studies [1–6]. In the present series, in only one instance was the diagnosis of brucella arthritis based on a positive synovial fluid culture; this was the only case in which synovial fluid was aspirated. From local experience it should be noted that the presenting local sign and symptoms in this condition are not as acute and phlogistic as in arthritis caused by ‘conventional’ bacteria. Specifically, none of these patients required surgical joint drainage, and, while assessment of the long-term outcome of these patients was not within the scope of this study, it is accepted generally to be quite good [25]. One possible reason for the somewhat different clinical features of brucella arthritis may be that some of the cases actually represent a reactive type of arthritis and not direct invasion by the pathogen [26].

**Conclusions**

The present study highlights the importance of characterizing the profile of species causing septic arthritis in specific regions, taking into account ethnic, genetic and environmental factors.

Israel, as a Mediterranean country, may be a representative of this region. Increased immigration from Eastern Europe and Africa has introduced previously uncommon pathogens to the local scene. Specific pathogens may be more prevalent among subgroups in a population such as recent immigrants or ethnic groups. Evaluation and treatment protocols need to be modified in accordance with local patterns of septic arthritis.
### Key messages

- Synovial and blood cultures prior to use of antibiotics are essential.
- Fever and leucocytosis have low sensitivity for septic arthritis.
- With unresponsive chronic mono-arthritis, consider TB.
- When adjacent to endemic areas, consider brucellosis.

The authors have declared no conflicts of interest.

### References

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