Paediatric bone and joint infections are more common in boys and toddlers: a national epidemiology study

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ABSTRACT

Aim: Little is known about bone and joint infections (BJIs) in children, despite the risk of growth disturbance. This study examined BJIs epidemiology using the French National Hospital Discharge Database (HD).

Methods: Any child <15 years hospitalized with an HD diagnosis of BJI, alone or in combination with sepsis or orthopaedic procedure, was included. The majority of BJIs (96%) were haematogenic infections. We conducted descriptive analyses to evaluate epidemiological and economic outcomes of paediatric haematogenic BJIs.

Results: There were 2592 paediatric patients with 2911 BJI hospitalizations and an overall incidence of 22 per 100 000. BJIs occurred more frequently in boys than girls (24 vs 19 per 100 000) and in toddlers. Septic arthritis (52%) and osteomyelitis (44%) were the most frequent infections, 16.6% of patients had a micro-organism coded (61% were Staphylococci) and 13% of had comorbidities. The mean hospital stay was 8.6 days, costing approximately €5200 per BJI stay.

Conclusion: This national study of paediatric BJIs in France showed a higher prevalence in toddlers and boys and demonstrated that the HD database can be used to study BJIs. However, the number of BJI cases was maybe overestimated by coding reactive arthritis as septic arthritis in the absence of bacterial evidence.

INTRODUCTION

Bone and joint infections (BJIs), including septic arthritis, osteomyelitis and spondylodiscitis, may be a significant cause of morbidity. These BJIs infections can occur throughout life and can be native or device associated, although the latter is rare in childhood. The overall incidence of paediatric bone and joint infection is not well estimated in Western countries (1,2), particularly in France, where only a few studies have been conducted.

Although they do not occur frequently, paediatric BJIs are an important public health issue because they require hospitalization and can potentially cause growth disturbance and sequelae, including severe motion limitation (2–6). BJIs constitute a diagnostic and therapeutic emergency in children due to the risk of growth disturbance (7–10). Due to the very rich vascularization of children’s bones, antibiotics can diffuse readily, reducing the risk of failure and chronicity (1,9).

The small numbers of studies that have estimated the incidence of BJIs have often been limited, as they have focused on one hospital or a hospital system in a specific area. In France, every single hospital discharge (HD) from a public or a private hospital must be registered with the French National Hospital Discharge Database (NHDD). The aim of this study was to describe the national epidemiology and clinical and financial outcomes of hospitalized paediatric BJI cases using the 2008 NHDD.

METHODS

A retrospective analysis of the 2008 NHDD was conducted, with an algorithm used to create a case definition for BJI (see Appendix S1 for supporting information). Children under 15 years of age were selected if they were discharged from hospital with a primary or secondary diagnosis of BJI, which appeared alone or in combination with either sepsis or a specific orthopaedic surgical procedure. The International
Classification of Diseases, Tenth Revision (ICD-10) codes for septic arthritis, osteomyelitis, spondylodiscitis and infectious complications of surgery were used. The orthopaedic procedure codes were selected from the French Common Classification of Medical Acts (FCCMA). Osteomyelitis and septic arthritis were distinguished based on the coding process of medical doctors.

The patient database was created by linking multiple hospitalizations to anonymized patient data, using a unique encrypted patient number. The great majority (96%) of hospitalizations to anonymized patient data, using a unique medical doctors.

The BJI case definition was validated in two steps using a convenience sample of hospital charts as the gold standard (11–14):

- To measure the predictive positive value (PPV) of the case definition, a clinician specialized in infectious diseases read the complete medical reports on the BJI cases, which were selected from the administrative database in four hospitals, including two paediatric teaching hospitals. This covered the clinical data, all microbiological assays, X-rays or MRI scans, including the radiologist’s interpretation. The corresponding 202 medical records were then reviewed: 163 records were true BJIs, and 39 records were miscoded (false positive), corresponding to suspected septic arthritis, which was ultimately diagnosed as reactive arthritis or only joint pain. This gave a PPV of 81% [CI 95% 75–86%]. We also checked the microbiological identification in the sample.
- The second stage of validation involved measuring the predictive negative value (PNV) of the case definition among 196 children hospitalized for orthopaedic fractures. This yielded a PNV of 100%.

We calculated the sensitivity and specificity of the case definition using the overall checked medical reports (N = 398), with sensitivity = 100% and specificity = 80%, PPV = 81% and PNV = 100%.

**Study variables**

Variables used in the analysis for epidemiological and economical outcomes included:

- Demographic characteristics – age was presented as a continuous variable and categorized into age groups.
- Type of BJI.
- Most frequent comorbidities potentially linked to infectious diseases.
- Coded pathogens – monomicrobial or polymicrobial.
- Hospital characteristics – public or private.
- Type of stay – intensive care unit (ICU) medical or surgical with a surgical procedure code.
- Patient outcomes – discharge destination (home, transferred), death, rehospitalization (number of patients who were discharged and readmitted in 2008 divided by the total number who were discharged alive) and
- Economic outcomes – total length of stay (LOS), Diagnosis Related Group (DRG) assignments, severity index and total billed charges.

In France, DRGs are assigned a severity index (0–2) based on the presence of comorbidities, to adjust the cost for the most complicated hospital stays.

We calculated the incidence of BJIs in children under 15 years, by age and gender, using the 2008 population data from the French National Institute of Statistics and Economic Studies [www.insee.fr]. The overall HD cost reimbursed by the national health insurance system was measured in Euros using the direct hospitalization cost to the society, taking into account various components of the DRG, including fixed hospital stay charges adjusted for LOS and supplementary charges (for ICU, haemodialysis and other care) (11).

**Statistical analysis**

Statistical analysis was performed using SAS version 9.1 software for Microsoft Windows (SAS Institute, Cary, NC, USA). Results were presented as frequencies or means. The chi-square test was used to compare categories. Relative risk (RR) and 95% confidence intervals (CI) were calculated. The means of continuous variables were compared using the t-test and the Wilcoxon test. Statistical significance was defined as p < 0.05.

**RESULTS**

A total of 2592 children fulfilled the recruitment criteria for a paediatric native BJI, with 2911 hospital stays. More than half of the BJI patients were coded as septic arthritis (52.5%), followed by osteomyelitis (43.9%) and spondylodiscitis (3.7%) (Table 1; Fig. 1).

**Epidemiology**

The male/female ratio was 1.4:1. The overall mean age of BJI cases under the age of 15 was 5.6 years, with boys being significantly older (mean age 5.8 years) than girls (mean age 5.2 years). The incidence in children under 15 years of age was 21.7 cases per 100 000 population, with a predominance among boys (24.5 per 100 000 vs 18.7 per 100 000 in girls) regardless of age. The highest incidence was among toddlers aged 1–2 years (Fig. 2).

A total of 329 (12.7%) children had at least one comorbidity. The most frequently reported comorbidities included skin and soft tissues infections (185 cases, including subcutaneous tissue, dermatitis, ulcer sore), respiratory diseases (97 cases, including upper and lower respiratory
disorders), sickle cell (46 cases) and fractures (19 BJI consequences). Boys were twice as likely to have soft tissues infections and fractures as girls.

There were three deaths in the HD database, all with multiple BJI hospitalizations. The first was a 34-day-old infant (girl) with osteomyelitis of the leg, the second was a 13-year-old boy with septic arthritis of the elbow, a chronic ulcer sore and bacteremia, and the third was a 13-year-old girl with septic arthritis of the hip who was receiving concurrent chemotherapy for leukaemia. No micro-organisms were coded for the three dead patients; we only found imprecise bacterial sepsis codes.

Microbiology
Micro-organisms were reported in 482 (16.6%) of the HDs, and the majority of these (64.5%) implicated a single pathogen. *Staphylococcus* spp. was isolated in 60.8%, followed by *Streptococcus* spp. We only found three infections due to group B *Streptococcus*, and all of these were in infants <3 months of age. *Tuberculosis* was identified in 20 infections. Among the polymicrobial cases, 80% had two micro-organisms coded, with *Staphylococcus* spp. most often isolated in association with *Streptococci* or *Gram-negative Bacilli*.

In the case validation sample, we found 48 identified micro-organisms in the 163 true cases, which corresponded to 29% of cases with microbiological proof. There was no polymicrobial infection. *Staphylococcus* spp. was isolated in 50% of cases (including 75% MSSA and 8% MRSA). *Streptococci* corresponded to 23%, *Kingella kingae* to 13%.

Surgical treatment procedures
Twenty-six percent of patients had a surgical stay – defined as a hospital stay associated with a specific surgical procedure (defined by the type of DRG). A further 39.8% had a hospital stay associated with a specific orthopaedic procedure to diagnose or manage BJIs.

- In septic arthritis, procedures were performed in 59% (evacuations, washing out by arthrotomy or needle lavage, synovectomies and punctures).
- In osteomyelitis, 23% had at least one procedure (biopsies, evacuations, abscess drainage).

One hundred and forty-four children had repeated aspirations (119 cases had two interventions), and 13

<table>
<thead>
<tr>
<th>Patients</th>
<th>Hospital stays</th>
</tr>
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<tbody>
<tr>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Diagnosis coded</td>
<td></td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>1359</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>1136</td>
</tr>
<tr>
<td>Spondylodiscitis</td>
<td>95</td>
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<tr>
<td>Not indicated</td>
<td>1</td>
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<tr>
<td>Surgical ward stays*</td>
<td>785</td>
</tr>
<tr>
<td>Specific procedure for BJI*</td>
<td>785</td>
</tr>
<tr>
<td>Total</td>
<td>1591</td>
</tr>
</tbody>
</table>

*BJI, bone and joint infection.
*A 'surgical patient' is one who has undergone at least one surgical procedure.

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children had repeated surgeries during the same hospital stay (12 had two interventions).

**Economic burden**

The overall mean LOS for a BJI stay was 8.4 days, and the majority (96%) were in the public sector. Just under two-thirds (63%) of the public hospital stays were in teaching hospitals, with more frequent surgical stays, specific procedures and a longer LOS (Table 2). The average LOS was longer in public hospitals (8.7 days, 95% CI: 1–368) than in private hospitals (5.9 days, 95% CI: 1–27). The proportion of surgical stays was higher in the private sector (69% vs 26% in public hospitals). A total of 2,570 (89.0%) HDs involved an uncomplicated DRG (severity index = 0). A total of 57 (2.0%) stays had an ICU admission. The overall rehospitalization rate was 9.7%, the majority of which were for a single rehospitalization. Most of the BJI patients were discharged home (2803; 92%).

Expenses for the national health insurance system were estimated to be €16 million, with a mean cost of €5168 per HD and an extra-cost of €1200 for public sector hospitals.

**DISCUSSION**

Paediatric BJIs are an important public health issue, because of the need for hospitalization and the potential for growth disturbance (2–6). The annual BJI incidence in children under 15 years of age was 22 per 100 000 and highest among infants. We report a male predominance and a higher prevalence of BJIs among boys of all ages. Skin infections and trauma have been shown to be risk factors for BJIs in childhood (7,10,15). We also found that males had more skin disorders and fractures than females. Only three children died.

The paediatric orthopaedic infection guidelines emphasize that the management and treatment of BJIs should consist of a combined medical and surgical approach, where the site of infection is washed out (1,4,6,16,17,18,19,20,21). We found that less than 30% of hospitalizations involved a surgical stay, and only 40% involved a specific procedure (e.g. needle aspiration, puncture).

We categorized septic arthritis, osteomyelitis and spondylodiscitis in BJI in the same way as a number of other authors (1,15,16,22). However, Offiah et al. discussed the important clinical differences that have led many authors in the past to consider neonatal osteomyelitis a separate entity from osteomyelitis in the older child (16). Microbiologic information was sparsely reported in our population (17%) and less frequently than reported in the literature (4,6,8,10,20,22). Our case validation sample of medical charts, identified up to 29% with microbiological information. A large part of this underrepresentation was attributed to the lack of coding of microbiological data in the NHDD, due to the lack of financial allocation for pathogen coding prior to 2010 (13,21). Nonetheless, we found Staphylococci were implicated in the majority of cases where microbiological information was coded (61%). Although the prevalence of Kingella Kingae is not precisely known, recent

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Children with bone and joint infections: stays by teaching hospital, general hospital or other type of hospital</th>
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</thead>
<tbody>
<tr>
<td>Hospitalization centre of paediatric BJI patient</td>
<td>Teaching hospital</td>
</tr>
<tr>
<td>Patients N † (%)</td>
<td>1694 (100)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>979 (57.8)</td>
</tr>
<tr>
<td>Female</td>
<td>715 (42.2)</td>
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<tr>
<td>Comorbidity (at least one)</td>
<td>213 (12.6)</td>
</tr>
<tr>
<td>Mean age [year (CI 95%)]</td>
<td>4.5 (4.3–4.7)</td>
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<tr>
<td>Hospital stays N (%)</td>
<td>1824 (100)</td>
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<tr>
<td>Diagnosis coded</td>
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<tr>
<td>Septic arthritis</td>
<td>923 (50.6)</td>
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<tr>
<td>Osteomyelitis</td>
<td>825 (45.2)</td>
</tr>
<tr>
<td>Spondylodiscitis</td>
<td>76 (4.2)</td>
</tr>
<tr>
<td>Surgical ward stays†</td>
<td>537 (29.4)</td>
</tr>
<tr>
<td>Specific procedure for BJI</td>
<td>892 (48.9)</td>
</tr>
<tr>
<td>Micro-organism</td>
<td>206 (11.3)</td>
</tr>
<tr>
<td>LOS* [days (CI 95%)]</td>
<td>8.9 (8.3–9.3)</td>
</tr>
<tr>
<td>Mean cost of stay (euro€)</td>
<td>5389</td>
</tr>
</tbody>
</table>

BJI, Bone and joint infection; LOS, length of stay; CI, confidence interval.

*Mixed hospitals are a very particular type of organization: private hospitals that also work in the public hospital sector.

†One patient could be hospitalized in different types of hospitals and be counted in more than one category.

‡A ‘surgical patient’ is one who has undergone at least one surgical procedure.
ACKNOWLEDGEMENTS

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References


**SUPPORTING INFORMATION**

Additional Supporting Information may be found in the online version of this article:

**Appendix S1** Case definition.