THE JOURNAL OF BONE & JOINT SURGERY (BRITISH)

Septic arthritis or transient synovitis of the hip in children

THE VALUE OF CLINICAL PREDICTION ALGORITHMS

J. Sultan,
P. J. Hughes

From Lancashire Teaching Hospitals NHS Foundation Trust, Preston, United Kingdom

The crucial differentiation between septic arthritis and transient synovitis of the hip in children can be difficult. In 1999, Kocher et al introduced four clinical predictors which were highly predictive (99.6%) of septic arthritis. These included fever (temperature ≥ 38.5°C), inability to bear weight, white blood-cell count > 12.0 × 10^9 cells/L and ESR ≥ 40 mm/hr; CRP ≥ 20 mg/L was later added as a fifth predictor. We retrospectively evaluated these predictors to differentiate septic arthritis from transient synovitis of the hip in children over a four-year period in a primary referral general hospital. When all five were positive, the predicted probability of septic arthritis in this study was only 59.9%, with fever being the best predictor. When applied to low-prevalence diseases, even highly specific tests yield a high number of false positives and the predictive value is thereby diminished.

Clinical predictors should be applied with caution when assessing a child with an irritable hip, and a high index of suspicion, and close observation of patients at risk should be maintained.

A child with an acutely irritable hip is a common diagnostic challenge for general practitioners, emergency physicians, paediatricians and orthopaedic surgeons. Along with septic arthritis and transient synovitis, there are a variety of other possible causes, such as Perthes' disease, fracture, tumour and slipped upper femoral epiphysis.[1-5] A history, physical examination and a plain radiograph of the hip usually leave septic arthritis and transient synovitis as the two most probable diagnoses. Their initial presentation is similar, namely non-traumatic progressive pain in the hip, limp, fever and irritability.[1-9] The early differentiation between septic arthritis and transient synovitis is therefore difficult, but crucial. Whereas transient synovitis is self-limiting, septic arthritis needs urgent decompression of the hip and intravenous antibiotics.[1,10-13] Delays in treatment increase the risk of complications, including osteonecrosis of the capital femoral epiphysis, osteomyelitis, chondrolysis, systemic sepsis and secondary osteoarthritis.[1,5,9-12,14-16]

There have been several attempts to differentiate the early stages of septic arthritis and transient synovitis.[2-4,6-8] Most of these studies concentrated on the clinical findings and laboratory investigations which may be used to identify high-risk patients who require invasive investigations and/or treatment.[2-4,6-8] In 1999, Kocher et al[2] suggested a clinical algorithm based on a retrospective study of four clinical predictors, and prospectively validated those in 2004.[7] The predictors were: fever ≥ 38.5°C, inability to bear weight even with support, a white cell count > 12 × 10^9 cells/L and an ESR ≥ 40 mm/hr. When all predictors were positive, the probability of septic arthritis was 99.6% in the retrospective study and 93.0% in the prospective study.[2,7] However, when Luhmann et al,[6] retrospectively applied the same criteria, the predicted probability of septic arthritis was only 59% when all four predictors were positive. In 2006, Caird et al[8] added a raised CRP level of ≥ 20 mg/L as a fifth predictor, with a 98% predicted probability of septic arthritis.

The aim of this study was to investigate the value of these clinical predictors when applied to a cohort of patients presenting to a primary referral general hospital.

Patients and Methods

A retrospective study of all children under the age of 16 years admitted to hospital with an irritable hip between February 2003 and February 2007 was undertaken. We identified 137 admissions; 15 patients were excluded because of insufficient data and 26 were excluded as they were diagnosed with conditions other than septic arthritis or transient synovitis of the hip. This left 96 patients in the study.

J. Sultan, MBBS, MRCS(Ed), Specialty Registrar (ST3) in Trauma and Orthopaedics Blackpool Victoria Hospital, Whinney Heys Road, Blackpool, Lancashire, FY3 8NR, UK.

P. J. Hughes, BSc(Hons), MBChB, FRCS(Trauma&Orth), Consultant Orthopaedic Surgeon Lancashire Teaching Hospitals NHS Foundation Trust, Royal Preston Hospital, Sharoe Green Lane, Fulwood, Preston PR2 9HT, UK.

Correspondence should be sent to Mr J. Sultan; e-mail: jsultan@hotmail.co.uk

doi:10.1302/0301-620X.92B9.24286 $2.00

J Bone Joint Surg [Br] 2010;92-B:1289-93.
Received 15 December 2009; Accepted after revision 22 April 2010

Table I. Positive predictors in the transient synovitis group

Number of positive predictors	Number of patients (%)
0	47 (*51.6*)
1	30 (*33.0*)
2	8 (*8.8*)
3	3 (*3.3*)
4	2 (*2.2*)
5	1 (*1.1*)

Table II. Septic arthritic group: microbiology results

Joint fluid culture	Blood culture
Group A β-haemolytic streptococci	Group A β-haemolytic streptococci
Streptococci pneumoniae	No growth
Staphylococcus aureus	Not done
Staphylococcus aureus	No growth
Numerous WBCs, no growth*	*Staphylococcus aureus*

* this patient was already on antibiotics started empirically by the paediatricians at the time of the washout. Blood cultures were taken before starting the antibiotics; WBC, white blood cells

The records were reviewed for age, gender, date of presentation, history and physical findings, including the presence of fever and ability to bear weight, radiological interpretation; laboratory investigations, including white cell count, ESR, CRP, and the results of blood and joint aspirate cultures. Additional investigations, including ultrasound scans, the treatment, the clinical course, the final diagnosis and the outcome were recorded.

The diagnosis of septic arthritis was defined as a positive culture of aspirate from the hip joint, or positive blood cultures with numerous white blood cells on high-power microscopy of the hip aspirate and no other identified source of infection. The diagnosis of transient synovitis was given to patients who had negative cultures, total resolution of symptoms during follow-up and no other identified pathology of the hip. Fever was defined as a temperature ≥ 38.5°C using oral or tympanic thermometers at initial presentation. The weight-bearing status was the inability or refusal to bear weight even with support. A limping child was considered to be partially weight-bearing. A raised white cell count was defined as $> 12 \times 10^9$ cells/L, a raised ESR as ≥ 40 mm/hr and a raised CRP as ≥ 20 mg/L. These definitions were in line with the work of Kocher et al[2] and other relevant literature.[6-8]

Statistical analysis. Univariate analysis was performed using Fisher's exact test for the five predictors. A two-sample Student's *t*-test was used to compare continuous variables. The sensitivity, specificity, false-positive rate and predicted probability were calculated using standard formulae.[17] Comparisons were made between the septic arthritis and transient synovitis groups, and a difference was considered to be statistically significant when the p-value was < 0.05. Statistical analysis was carried out using SPSS (version 16.0; SPSS Inc., Chicago, Illinois).

Results

Of the 96 cases (62 boys), 91 (94.8%) were diagnosed with transient synovitis, and five (5.2%) with septic arthritis.

In the transient synovitis group, the mean age was 5.7 years (1 to 12). In 47 patients all five predictors were negative (51.6%). However, six (6.6%) had three or more positive predictors, and all five predictors were positive in one patient (Table I). He had chickenpox two weeks prior to admission. An urgent bone scan was normal and his symptoms settled with analgesia. Urine and blood cultures were negative.

Five patients (5.5%) underwent aspiration of the hip. All these cultures were negative and the symptoms resolved spontaneously without antibiotics. None of the patients in the transient synovitis group had positive blood cultures.

In the septic arthritis group (five patients, three boys), the mean age was 6.5 years (2 to 10). Four patients had positive cultures from the joint aspirate and one had numerous white blood cells in the aspirate, but no growth on culture. This patient was already on antibiotics when the joint was aspirated. However, blood cultures taken before starting the antibiotics were positive. The causative organisms for these patients are listed in Table II. Only one patient in the septic arthritis group had five positive predictors. One had four, one had three, and two had only one (Table III).

The temperature and the CRP level were significantly different between the groups when compared as continuous variables. The difference was also significant when fever and a raised CRP were compared categorically as positive *versus* negative predictors (Table IV).

The difference between the groups with regard to age, gender, white cell count, ESR and ability to bear weight was not statistically significant, whether these variables were

Table III. Positive predictors (bold) in the septic arthritis group

Number of predictors	Age (yrs)	Gender	Weight-bearing	Fever	White cell count	Erythrocyte sedimentation rate	C-reactive protein
5	5	Male	**None**	**39.3**	**14.4**	**50**	**255.4**
4	9	Female	Partial	**38.9**	**17.9**	**46**	**139.9**
3	7	Female	**None**	**39.0**	10.9	18	**98.4**
1*	10	Male	Partial	**39.3**	8.4	19	11.9
4*			**None**	**38.9**	**9.0**	**70**	**44**
1	2	Male	**None**	38.3	8.0	10	10.7

* this patient presented initially with only one positive predictor. He was discharged home after a senior review by a consultant orthopaedic surgeon. He re-presented next morning with four positive predictors and had an urgent hip arthrotomy and washout, which confirmed septic arthritis on joint fluid cultures

Table IV. Univariate analysis: septic arthritis compared with transient synovitis

Variable*	Transient synovitis (n = 91)	Septic arthritis (n = 5)	p-value
Age in years (range)	5.7 (1 to 12)	6.5 (2 to 10)	0.564
Male gender (%)	62 (*68*)	3 (*60*)	0.657
Fever (%)			
≥ 38.5°C‡	4 (*4.4*)	4 (*80*)	< 0.001
≥ 38.0°C‡§	9 (*9.9*)	5 (*100*)	< 0.001
Temperature in °C† (range)	36.88 (35.0 to 40.3)	38.96 (38.3 to 39.3)	< 0.001
Non-weight-bearing (%)	26 (*28.6*)	3 (*60*)	0.160
WCC			
> 12.0 × 10^9 cells/l‡ (%)	17 (*18.7*)	2 (*40*)	0.256
×10^9 cells/L† (SD)	9.87 (3.30)	11.92 (4.20)	0.187
ESR			
≥ 40 mm/hr‡ (%)	11 (*12.1*)	2 (*40*)	0.134
mm/hr† (range)	21.13 (2.0 to 116.0)	28.60 (10.0 to 70.0)	0.543
CRP			
≥ 20 mg/L‡ (%)	9 (9.9)	3 (60)	0.013
mg/L† (SD)	11.10 (1.0 to 133.5)	103.08 (10.7 to 255.4)	< 0.001

* WCC, white cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

† values are given as means

‡ fever/temperature, WCC, ESR and CRP were compared both as continuous variables using two-sample Student's *t*-test and as categorical variables (positive or negative predictors) using Fisher's exact test

§ if fever is considered positive when the temperature is ≥ 38.0°C instead of ≥ 38.5°C, all patients with septic arthritis will have this predictor positve, and the p-value remains < 0.001

categorical (Fisher's exact test) or continuous (two-sample Student's *t*-test, Table IV).

If the threshold for fever, to be considered as a positive predictor, is reduced from ≥ 38.5°C to ≥ 38.0°C, the number of patients with septic arthritis and fever as a positive predictor rises from four (80%) to five (100%). The difference between the groups, however, remains significant, with $p < 0.001$ in either case (Table IV).

The correlation between the number of positive predictors and sensitivity, specificity, false positives and predicted probability of septic arthritis is shown in Tables V and VI.

When all five predictors were negative, septic arthritis was absent. However, when all five predictors were positive, the sensitivity was 20% and the predicted probability of septic arthritis was only 59.9%.

Discussion

When considering the four earlier studies, it is notable that all were carried out in tertiary referral centres.[2,6-8] The patients were at high risk for septic arthritis and all, regardless of which group they were in, required aspiration of the hip and/or arthrotomy as part of their management.[2,6-8] Furthermore, the percentage of children with septic arthritis was high in the studies of Kocher et al[2] and Caird et al[8] (49% and 71%, respectively). When the percentage of septic arthritis patients fell to 28% in the study of Luhmann et al,[6] the predicted probability of septic arthritis fell to 59.1%.

Table V. Distribution of number of positive predictors for sensitivity, specificity and false-positive ratio

Positive predictors	Transient synovitis (n = 91)	Septic arthritis (n = 5)	Sensitivity	Specificity	False positive
At least					
1	44	5	1.00	0.516	0.484
2	14	3	0.600	0.846	0.154
3	6	3	0.600	0.934	0.066
4	3	2	0.400	0.967	0.033
5	1	1	0.200	0.989	0.011

Table VI. Predicted probability of septic arthritis

			Predicted probability of septic arthritis (%)				
Number of predictors	Transient synovitis (this study, n = 91)	Septic arthritis (this study, n = 5)	This study	Kocher et al[2] original	Luhmann et al[6]	Kocher et al[7] validation	Caird et al[8]
0	47	0	*2.3*	*< 0.2*	-	*2.0*	*16.9*
1	30	2	*5.1*	*3.0*	-	*9.5*	*36.7*
2	8	0	*10.9*	*40.0*	-	*35.0*	*62.4*
3	3	1	*22.0*	*93.1*	-	*72.8*	*82.6*
4	2	1	*39.4*	*99.6*	*59.1*	*93.0*	*93.1*
5	1	1	*59.9*	-	-	-	*97.5*

In our study, we included children with sufficient clinical suspicion of septic arthritis to warrant admission for close observation. Children who were discharged home after initial assessment were not included. All our patients were primary referrals from the emergency department or GP practices, rather than by other hospitals to a tertiary referral centre. The number of children with septic arthritis in our study was only five (5.2%), but we believe this represents the true prevalence of septic arthritis.[15-20]

Only five patients (5.5%) in the transient synovitis group required aspiration of the hip in our study, whereas all transient synovitis patients in the previously quoted studies underwent hip aspiration.[2,6-8] The demographics of our patients were similar to the previously quoted studies.[2,6-8]

The role of a clinical prediction algorithm is to avoid the need to use invasive investigations such as ultrasound-guided aspiration. An algorithm should therefore be useful in selecting patients for these invasive investigations from a general population. When applied to a high-risk group with a high prevalence of septic arthritis, as in the case of the studies of Kocher et al[2,7] and Caird et al,[8] the predictive value of the algorithm would be expected to be high, as would apply in a tertiary referral centre. However, in a primary referral general hospital, where the prevalence of septic arthritis is lower and patients admitted for observation do not necessarily require aspiration, the predictive value of the algorithm is adversely affected by the lower prevalence of the disease.

When calculating the predictive value of any test, it is important to note the prevalence of the disease. Even highly specific tests, when applied to low-prevalence events, yield a high number of false-positive results and the predictive value of the test is diminished.[21] This can be observed in the study of Luhmann et al,[6] where the percentage of patients with septic arthritis was lower than that of Kocher et al[2,7] and Caird et al[8] (28% *versus* 49% and 71%, respectively) and the predicted probability of septic arthritis observed in those studies was 59% *versus* 99.6% and 98%. In our study, the predicted probability of septic arthritis when all five predictors were positive was only 59.9%. This supports our hypothesis that the value of these predictors diminishes with the decreasing percentage of patients with septic arthritis in the group being studied.

Furthermore, we found that fever was the most significant predictor. When the threshold for fever is reduced to 38.0°C rather than 38.5°C as originally proposed by Kocher et al,[7] the sensitivity increased from 80% to 100% whilst maintaining the p-value < 0.001, (Table IV). A CRP ≥ 20 mg/L was also found to be significantly different between the groups. This is in agreement with Caird et al,[8] who found fever to be the best predictor, followed by a raised CRP. The other variables between the groups were not significantly different in our study.

One patient in the septic arthritis group presented initially with only one positive predictor, a fever of 39.3°C. The other predictors, although raised, did not meet Kocher's criteria (Table III). The temperature returned to normal following administration of paracetamol. A provisional diagnosis of transient synovitis was made and the child was discharged home. He returned the next morning with four positive predictors (Table III). An urgent arthrotomy and washout confirmed septic arthritis with positive cultures of the joint fluid. This case illustrates the sensitivity of fever as a predictor and the importance of monitoring the trend of changes in the clinical and biochemical picture. It also highlights the importance of keeping a high index of

suspicion of septic arthritis if any of the predictors are raised, regardless of whether or not they meet Kocher's criteria.

The limitations of this study include its retrospective nature and the small number of patients with septic arthritis. Nevertheless, the study has the advantage of testing the clinical predictors in a general population, rather than a carefully selected group of patients referred to a tertiary centre. The low percentage of septic arthritis in this study (5.2%) represents more closely the actual prevalance of septic arthritis in children with irritable hips.

Although clinical predictors are helpful in distinguishing septic arthritis from transient synovitis of the hip in children, they are not as predictive of the disease in a general population as initially described. Therefore, they should be applied with caution. A high index of suspicion should be maintained if any of the predictors are raised, with close observation of children at risk, especially those with fever. Further research is required to determine which combination of clinical predictors is more sensitive, and at what values.

The authors wish to thank Mr A. Owais for his assistance in amending the script.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

1. **De Boeck H.** Osteomyelitis and septic arthritis in children. *Acta Orthop Belg* 2005;71:505-15.
2. **Kocher MS, Zurakowski D, Kasser JR.** Differentiating between septic arthritis and transient synovitis of the hip in children: an evidence-based clinical prediction algorithm. *J Bone Joint Surg [Am]* 1999;81-A:1662-70.
3. **Eich GF, Superti-Furga A, Umbricht FS, Willi UV.** The painful hip: evaluation of criteria for clinical decision-making. *Eur J Pediatr* 1999;158:923-8.
4. **Del Beccaro MA, Champoux AN, Bockers T, Mendelman PM.** Septic arthritis versus transient synovitis of the hip: the value of screening laboratory tests. *Ann Emerg Med* 1992;21:1418-22.
5. **Bennett OM, Namnyak SS.** Acute septic arthritis of the hip joint in infancy and childhood. *Clin Orthop* 1992;281:123-32.
6. **Luhmann SJ, Jones A, Schootman M, et al.** Differentiation between septic arthritis and transient synovitis of the hip in children with clinical prediction algorithms. *J Bone Joint Surg [Am]* 2004;86-A:956-62.
7. **Kocher MS, Mandiga R, Zurakowski D, Barnewolt C, Kasser JR.** Validation of a clinical prediction rule for the differentiation between septic arthritis and transient synovitis of the hip in children. *J Bone Joint Surg [Am]* 2004;86-A:1629-35.
8. **Caird MS, Flynn JM, Leung YL, et al.** Factors distinguishing septic arthritis from transient synovitis of the hip in children: a prospective study. *J Bone Joint Surg [Am]* 2006;88-A:1251-7.
9. **Nunn TR, Cheung WY, Rollinson PD.** A prospective study of pyogenic sepsis of the hip in childhood. *J Bone Joint Surg [Br]* 2007;89-B:100-6.
10. **Hunka L, Said SE, MacKenzie DA, Rogala EJ, Cruess RL.** Classification and surgical management of the severe sequelae of septic hips in children. *Clin Orthop* 1982;171:30-6.
11. **Waldvogel FA.** Treatment of osteomyelitis and septic arthritis. *Bull N Y Acad Med* 1982;58:733-49.
12. **Kang SN, Sanghera T, Mangwani J, Paterson JM, Ramachandran M.** The management of septic arthritis in children: systematic review of the English language literature. *J Bone Joint Surg [Br]* 2009;91-B:1127-33.
13. **Skinner J, Glancy S, Beattie TF, Hendry GM.** Transient synovitis: is there a need to aspirate hip joint effusions? *Eur J Emerg Med* 2002;9:15-18.
14. **Lunseth PA, Heiple KG.** Prognosis in septic arthritis of the hip in children. *Clin Orthop* 1979;139:81-5.
15. **Wilson NI, Paola M.** Acute septic arthritis in infancy and childhood: 10 years' experience. *J Bone Joint Surg [Br]* 1986;68-B:584-7.
16. **Petersen S, Knudsen FU, Andersen EA, Egeblad M.** Acute haematogenous osteomyelitis and septic arthritis in childhood: a 10-year review and follow-up. *Acta Orthop Scand* 1980;51:451-7.
17. **Nade S.** Acute septic arthritis in infancy and childhood. *J Bone Joint Surg [Br]* 1983;65-B:234-41.
18. **Gafur OA, Copley LA, Hollmig ST, et al.** The impact of the current epidemiology of pediatric musculoskeletal infection on evaluation and treatment guidelines. *J Pediatr Orthop* 2008;28:777-85.
19. **Landin LA, Danielsson LG, Wattsgård C.** Transient synovitis of the hip: its incidence, epidemiology and relation to Perthes' disease. *J Bone Joint Surg [Br]* 1987;69-B:238-42.
20. **Lavy CB.** Septic arthritis in Western and sub-Saharan African children: a review. *Int Orthop* 2007;31:137-44.
21. **Bland JM.** *An introduction to medical statistics*. Second ed. New York: Oxford University Press, 1995.