

## Results of treatment of Hip Septic Arthritis in Neonates

### Abstract

**Background & Aim:** Septic arthritis is one of the important childhood infections with a high number of complications. Given the rare occurrence of this infection in neonates and its low number of symptoms, the diagnosis of septic arthritis in infants is difficult and its prognosis is mainly affected by early diagnosis and treatment. This study aimed to evaluate the results of neonatal hip septic arthritis treatment results in two training hospitals during 2001-2016.

**Materials and Methods:** This cross-sectional and descriptive research was performed on infants who were referred to hospitals in the North of Iran due to hip septic arthritis during 2001-2016. Medical information was two recorded in a checklist based on demographic indicators and clinical findings in the laboratory. In addition, the presence of complications in the participants was assessed via a phone call or by in-person visit.

**Results:** In this study, the left hip joint was the most involved joint in terms of septic arthritis (72.2%). In addition, the most common bacteria responsible for the infection were *Klebsiella* (50%), *E.coli* (22.2%), and *Staphylococcus aureus* (27.8%). According to the results, 50% of the subjects were treated completely with no complications, whereas 11% of the right and 38.9% of left hips had limping ( $p=0.615$ ).

**Conclusion:** Given the high number of complications of neonatal hip infection, early diagnosis and timely treatment is needed to reduce the complications.

**Keywords:** Septic Arthritis, Neonates, Hip Joint, Infection, Treatment, Retrospective Study

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### Introduction

The Septic arthritis, an acute joint infection, is one of the most dangerous childhood infections. Joint infection occurs whenever pathogenic factors (e.g., bacteria, viruses, and fungi) reach the joint in some way and proliferate there <sup>(1)</sup>. For instance, infection in the throat, skin, nose, and even intestines can reach the patient's joint through the bloodstream. Insertion of sharp objects into the joint may also lead to the penetration of microbes into the injured site directly. The presence of infection in adjacent bone or osteomyelitis can result in joint infection through proximity to the shoulder, hip, and ankle joints. Injection into the joint and performing arthroscopy can lead to the entrance of pathogenic organisms into the joint <sup>(1, 2)</sup>.

The symptoms of the disease in infancy include restlessness, poor feeding, fever, and lethargy. However, specific symptoms of the disease include lack of movement of an organ by an infant due to joint pain, the restlessness of the infant during moving the baby, and irritability during touching the joint <sup>(3)</sup>. Sometimes, there are local symptoms such as redness and inflammation of the joint, which are mostly observed in peripheral joints, such as knees, wrists and ankles, elbows, fingers, and toes <sup>(4,5)</sup>.

At other ages, the disease's symptoms are high fever and sudden and severe pain in a joint, as well as redness and swelling of the joint. There might be a history of trauma, injuries, or injections (vaccines or medications) in the body part in the past few days, which can be the source of infection. At ages above three months, the disease mostly emerges as the involvement of a joint while several joints might be involved at lower ages<sup>(1-3)</sup>.

The infection is more prevalent in neonates and infants below the age of three-six months, compared to other ages, and shows more symptoms in the mentioned ages<sup>(6,7)</sup>. Overall, the infection is not that prevalent but it is crucial to focus on its symptoms in infants with chronic diseases and those with predisposing factors (e.g., immune deficiency, growth failure, and cancer). This is mainly due to the fact that the disease leads to the rapid spread of infection in blood and several complications. Therefore, septic arthritis is a rare but serious disease in neonates that can lead to permanent disabilities in patients<sup>(8-11)</sup>.

The worst complications caused by the spread of infection in blood and other systems are sepsis and death, and the survival of neonates may be associated with various complications, such as deafness and blindness. However, lack of bloodstream dissemination of infection may cause local complications, such as the spread of infection to the adjacent tissues (e.g., bone next to the joint). The complication can lead to the involvement of the growth plate and cause local organ growth disorder in the long-term. For instance, the involvement of a joint in the lower extremity may lead to a length difference between two members and permanent limping<sup>(12,13)</sup>. In addition, the presence of purulent fluid inside the joint and prolonged immobility may lead to an immobilized joint, and it will be very difficult to return its natural movement with the help of rehabilitation and physiotherapy. In fact, natural movement becomes irreversible in some cases<sup>(14,15)</sup>.

While no joint in the human body is safe from infection during infancy, the large joints are at a higher risk of infection. Among the large joints, the hip joint and to a lesser extent shoulder joint are important due to latent symptoms and fewer local symptoms in these regions. However, other joints such as knee, ankle, wrist, and elbow are at risk of infection and should be taken into consideration as well<sup>(1-4, 6)</sup>. Given the rare occurrence of the condition in neonates and the low number of symptoms of the disease, the diagnosis of septic arthritis in newborns is more difficult, compared to adults. Therefore, the prognosis of this disease is mainly affected by early diagnosis and timely intervention<sup>(2,5)</sup>. Diagnosis in these patients will be based on strong clinical suspicion and clinical results can be partial or even negative<sup>(3)</sup>. More common outcomes can include local swelling and limited movement in a joint or limb.

The primary lab examinations were also indicative of a higher erythrocyte sedimentation rate, c-reactive protein, neutrophil count, and red blood cells<sup>(4,5)</sup>. Joint aspiration procedure should be carried out on any suspicious joint or bone, and various assessments have shown that synovial fluid is positively detected in 82-85% of cases<sup>(6, 7)</sup>. Antibiotic treatment should be started for patients based on lab results and clinical suspicion of common and important organisms is essential<sup>(5, 8)</sup>. Given the rare observance of the disease in infants and the low number of symptoms and signs of the disease, its diagnosis is more difficult in neonates, compared to adults, and the prognosis of this disease is mainly affected by early diagnosis and lack of delay in treatment. All of these points indicate the extreme necessity of assessing and understanding the problem<sup>(9, 10)</sup>. With this background in mind, this study aimed to evaluate the results of the treatment of neonatal hip septic arthritis at Mazandaran University of Medical Sciences in Babol, Iran during 2001-2016. In other words, we assessed the results of the treatment of infants and

determined the presence or absence of complications in the samples in two important standard centers of Mazandaran.

### Methodology

This retrospective, cross-sectional, and descriptive study was performed to evaluate the outcomes of neonatal hip septic arthritis treatment in Mazandaran and Babol University of Medical Sciences during 2001-2016.

### Methods

The present study was performed on all neonates with hip septic arthritis who were referred to Bu-Ali Sina Hospital in Sari, Iran, and Amirkola Hospital in Babol, Iran (affiliated with Sari and Babol University of Medical Sciences) during 2001-2016, selected by census sampling. Inclusion criteria were metabolic diseases, autoimmune diseases, malignancies, immunodeficiency, any type of viral diseases (e.g., human immunodeficiency virus [HIV], hepatitis C virus [HCV], hepatitis B virus [HBV]), and lack of hypersensitivity diseases and allergy. On the other hand, the exclusion criteria were septic arthritis infection in a joint other than the hip joint, concomitant infections, incomplete medical files, and lack of giving informed consent. Meanwhile, those who provided consent via telephone were entered into the study.

In addition, all samples were telephoned to determine the outcome of treatment and the occurrence or non-occurrence of complications due to hip joint septic arthritis infection in the studied participants. The evaluated variables included the prevalence of septic arthritis, age, gender, weight, type of delivery, gestational age, vaccination status, involved joint, body temperature, white blood cell (WBC) count, reactive protein C, erythrocyte sedimentation rate, blood culture, articular fluid culture, the type of prescribed drug, the result of treatment, and the occurrence of possible complications (follow-up period for samples between 3-18 years after hospitalization).

Statistical analysis: data, coding, and statistical analysis were carried in SPSS version 16 using descriptive statistics, including frequency distribution table, central and dispersion indexes, and percentages (to describe demographic characteristics of subjects) and inferential statistics (Kolmogorov-Smirnov test, Levene's test, Chi-square, Fisher's exact test, independent t-test, and Mann-Whitney U (to compare the groups and test research hypothesis). Moreover, a P-value of 0.05 was considered statistically significant. It is noteworthy that the research was approved by the ethics committee of Mazandaran University of Medical Sciences with the code of IR.MAZUMS.RIB.REC.1399.007.

### Results

All participants were in the age range of the first 28 days of life (from birth to four weeks after birth, less than a month). The results demonstrated that 18 neonates with a mean age of  $21.72 \pm 5.54$  days were hospitalized in Bu-Ali Sina Hospital in Sari, Iran, and Amirkola Hospital in Babol, Iran during 2001-2016 due to hip septic arthritis. In total, 12 infants were male and six were female. Regarding the type of birth, 10 and 8 subjects were born by cesarean section and normal delivery, respectively. The gestational age of mothers was  $35.44 \pm 5.03$ , and all subjects in the two hospitals were fully vaccinated. Septic arthritis of the left and right hip was observed in 13 and 9 neonates, respectively.

The lab tests carried out estimated the mean WBC count and mean C-reactive protein serum level at  $7961 \pm 2023$  unit/ml and  $53.72 \pm 12.34$  mg/l, respectively. In addition, only five subjects (27.8%) had positive blood culture while 13 participants (72.2%) had negative blood culture. Moreover, the culture of the synovial fluid showed that nine subjects (50%) had *Klebsiella*, whereas two (22.2%) and five (27.8%) participants had *Escherichia coli*, and *staphylococcus aureus*, respectively.

The antibiotics used for the subjects were clindamycin in combination with cefixime in 11 cases (61.1%) and vancomycin in combination with cefixime in 7 patients (38.9%). According to the results of follow-ups conducted 3-18 years after the discharge of the patients, nine cases (50%) had no complications and gained complete health. After discharge, two patients (11.1%) had a limp in the right leg, whereas two individuals (33.3%) had the same condition in the left leg. In addition, one patient was discharged with personal consent and did not finish treatment, follow-up of whom showed a severe limp in the left leg. Most limps were caused by *Klebsiella* and *Staphylococcus aureus*. Nevertheless, no significant difference was observed between the type of bacteria and a limp in the right and left legs ( $P>0.05$ ).

According to the results, there was no significant relationship between the complications of septic arthritis infection and variables of age ( $P=0.664$ ), weight ( $P=0.940$ ), duration of pregnancy ( $P=0.265$ ), WBC count ( $P=0.286$ ), and C-reactive protein ( $P=0.273$ ). In addition, the results were indicative of no significant correlation between the complications of septic arthritis and variables of gender ( $P=0.124$ ), type of delivery ( $P=0.308$ ), antibiotic treatment ( $P=0.351$ ), blood culture results ( $P=0.136$ ), and culture of the synovial fluid ( $P=0.733$ ). However, a limp in neonates was significantly higher in those with left hip septic arthritis infection, compared to those with right hip septic arthritis infection ( $P=0.045$ ) (Table 1).

**Table 1. Frequency of qualitative variables assessed in the study based on treatment results and the emergence of complications**

Variables		Treatment Results								P-value
		No complications		Right leg limp		Left leg limp		Incomplete treatment of left leg limp		
		N	%	N	%	N	%	N	%	
Gender	Male	5	27.8	1	5.6	6	33.3	0	0	0.124
	Female	4	22.2	1	5.6	0	0	1	5.6	
Type of delivery	Natural	1	5.6	1	5.6	3	16.7	0	0	0.308
	Cesarean	8	44.4	1	5.6	3	16.7	1	5.6	
Antibiotic treatment	Cefixime/Clindamycin	6	33.3	2	11.1	3	16.7	0	0	0.315
	Cefixime/Vancomycin	3	16.7	0	0	3	16.7	1	5.6	
Blood culture	Positive	3	16.7	1	5.6	0	0	1	5.6	0.136
	Negative	6	33.3	1	5.6	6	33.3	0	0	
Culture of the synovial fluid	<i>Klebsiella</i>	3	16.7	1	5.6	4	22.2	1	5.6	0.733
	<i>E.coli</i>	3	16.7	0	0	1	5.6	0	0	
	<i>Staphylococcus aureus</i>	3	16.7	1	5.6	1	5.6	0	0	
Involved joint	Right hip	3	16.7	2	11.1	0	0	0	0	0.045
	Left hip	6	33.3	0	0	6	33.3	1	5.6	

## Discussion

The hip joint is one of the most important diarthroses, and hip joint injuries can cause a limp and poor gait by various mechanisms. The transfer of infection to the hip joint can lead to infectious arthritis in the hip joint<sup>(16,17)</sup>. The

symptoms of this disease are mostly high fever and sudden and severe pain in one joint. In addition, redness and joint swelling are significant symptoms of the disease. A history of trauma or injury or injections (vaccine or medicine) may be the source of infection in the limb<sup>(18-21)</sup>. According to the results of the

present study, the number of cesarean sections was significantly higher, compared to natural delivery, in all of the subjects with hip septic arthritis. In a research by Amini et al., 67.7% of the neonates were premature and 35.6% of them had a birth weight below 2500 gr. In addition, the mean body temperature of the subjects was 36.6°C, and the mean ESR was 85 mm Hg. Moreover, CRP was positive in all neonates<sup>(18)</sup>.

According to the studies conducted in this area, hip joint infection during infancy could be associated with symptoms such as restlessness, lack of feeding, fever, and lethargy in infants, similar to other neonatal infections. However, the specific symptoms of the disease include immobility of a limb by the infant due to joint pain, restlessness when moving the infant, or restlessness when touching the joint<sup>(21, 22)</sup>. Occasionally there are local symptoms such as redness and swelling of the joint, which is more common in peripheral joints including the knees, ankles, elbows, and fingers<sup>(18-21)</sup>. Given the rare occurrence of the disease in neonates and a low number of symptoms of the disease, diagnosis of septic arthritis in neonates is more difficult, compared to adults, and the prognosis of this disease is mainly affected by early diagnosis and lack of delay in treatment<sup>(2, 5)</sup>.

In total, 50% of the subjects were infected by *Klebsiella*, whereas 22.2% and 27.8% had *E.coli* and *Staphylococcus aureus*, respectively. In addition, the antibiotic treatment was clindamycin in combination with cefixime for 61.1% of the subjects and vancomycin in combination with cefixime for 38.9% of the subjects. In a study by Gramlich et al., *Staphylococcus aureus* and *Staphylococcus epidermidis* were the most common bacteria causing septic arthritis infection in shoulders and knees. In addition, *Propionibacterium* was only observed in shoulder septic arthritis infection<sup>(17)</sup>. In a research by Amini et al., the organisms isolated from hip and knee joint

fluid were *Klebsiella* (54%), *Staphylococcus aureus* (37%), and *E.coli* (9%)<sup>(18)</sup>.

In a study, Zamani et al. demonstrated that the hip joint was the most important joint with septic infection among the samples, and 65.6% of the subjects were infected by *Staphylococcus aureus*, whereas 12.3%, 12.3%, 4.1%, and 4.1% were infected by *Klebsiella*, *Streptococcus pneumoniae*, Group B *Streptococcus*, and *haemophilus influenza* type b, respectively<sup>(19)</sup>. In addition, Sedighi et al. introduced *Staphylococcus aureus* as the most common bacteria involved in joint infection following *haemophilus influenza*. Treatment results were favorable for those who underwent arthrotomy and concomitantly received antibiotic treatment promptly<sup>(20)</sup>. In a study by Yingtie et al. on the pathogens causing hip joint sepsis, out of 68 isolated microorganisms, 42 were gram-positive bacteria, 23 were negative bacteria and 3 were fungi. The results were indicative of a difference in the bacterial types of hip sepsis in children of different ages (5 days to 13 years). In neonates (less than one month), *Klebsiella pneumoniae* was the most common pathogen. At 1 month to 13 years of age, the most common pathogen was *Staphylococcus aureus*. Drug susceptibility test results showed that gram-positive bacteria were sensitive to vancomycin, teicoplanin, and linezolid. *Staphylococcus aureus* was up to 96% resistant to penicillin and *Klebsiella*, *E.coli*, *Haemophilus influenzae*, *Enterobacter cloacae*, and *Salmonella* were highly sensitive to meropenem and imipenem<sup>(23)</sup>.

In the present study, septic arthritis infection in the participants in two hospitals was observed in 27.8% of the right hip and 72.2% of the left hip. In the research by Amini et al., the most common joints involved were the hip joint (30.5%) and knee joint (23.72%), respectively. Gramlich et al. indicated that the rate of repair of infection in the knee and shoulder was 95% and 90%, respectively. Moreover, the mortality rate in shoulder septic infection was 10%. The results showed that

most knee infections can be controlled with an arthroscopic procedure, while all shoulder infections required surgery<sup>(17)</sup>. Our study was only about the hip joint. According to the results of the current research, 11.1% of the subjects had a limp in the right leg and 33.3 had a limp in the left leg during a 3-18-year follow-up. In addition, one patient was discharged with personal consent with did not complete the treatment, who had a severe limp in the left leg after follow-up. In the study of Zamani et al., the results demonstrated that all patients had joint pain and swelling at the time of referral, and there was limited joint movement in 80% of patients and a limp in 64% of the subjects. In addition, 80% of them had a fever, 80% had joint pain, and the rest had involved joints. The most common joint involved was the hip joint (62%)<sup>(19)</sup>.

One of the major limitations of this study was its retrospective nature and access to medical files of patients. Therefore, we could not examine the patients. Moreover, the patients were not seen and the reason for the limp of those with complications with radiography or other examination was not possible. Therefore, valuable clinical information was not available during hospitalization. In addition, the research was only performed in two hospitals. Therefore, it is recommended that further studies be performed in other hospitals with larger volumes. Furthermore, it is suggested that the results of paraclinical findings along with clinical findings be examined in a complementary study with much larger sample size.

## Conclusion

According to the results of the study, most bacteria responsible for hip septic arthritis infection were *Klebsiella*, *E.coli*, and *Staphylococcus aureus*. In addition, 50% of the infections caused a limp in the infants, especially in the left leg. Therefore, given the high number of complications of the disease, it is recommended to reduce the consequences

of this disease with early diagnosis and timely treatment.

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## Conflicts of Interest

None declared.

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