

Research Paper:

The Epidemiological Study, Clinical Signs, Complications, and Treatment of Cellulites in Children



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ABSTRACT

Background and Aim: Cellulite is the most common soft tissue infection in children. Children are prone to cellulite because they are more disposed to trauma, insect or animal bites, wounds, and scratches. This study aimed to determine the frequency of causes, complications, and cellulite treatment in children referred to Hazrat Masoumeh Hospital in Qom City, Iran.

Materials and Methods: This descriptive study was performed on all patients admitted to Hazrat Masoumeh Hospital in Qom during 2013-2020. The study data were extracted from patients' medical records and statistically analyzed.

Results: The Mean±SD age of the patients was 42.94±38.15 months. Their male/female sex ratio was almost one. The most affected areas were the lower extremities (43%), the upper extremities (26.5%), and the face and eyes (6.6%). The most common clinical manifestations were edema (75%), redness (62%), and fever (38%). The most commonly prescribed antibiotics were ceftriaxone (47%), cloxacillin (34.7%), and clindamycin (28%). The most common underlying causes were bites (16%), trauma (10%), and previous wounds (9%). Complications were abscesses (10%) and osteomyelitis (1.6%). Their Mean±SD values of erythrocyte sedimentation rate, C-reactive protein, and white blood count were 32.46±26.03 (mm/h), 24.14±23.07 (mg/dl), 12261±4587 (cell/μL), respectively. Preference was seen with Polymorphonuclear leukocytes (PMNs) in 80.5% of the cases. Blood culture was positive in 8% of the patients. According to the antibiogram response, the highest resistance was seen against cefazolin and then ceftriaxone, and the highest sensitivity to imipenem and ceftazidime.

Conclusion: Finally, due to the limitations of retrospective research in collecting information, future research should focus on evaluating specific treatments and diagnostic methods for diseases such as cellulite in Iran. Future research can determine the prevalence of organisms involved in our country, as well as the type of appropriate treatment for all inpatients and outpatients.

Keywords:

Causes, Cellulites, Hospitals, Epidemiologic studies

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1. Introduction

Cellulite is the most common soft tissue infection in children. Children are prone to cellulite because they are more exposed to injury from trauma, insect bites, or animals, wounds, and scratches [1]. The cause of cellulite is often *Staphylococcus aureus* or group A streptococcus. Among different types of cellulite, orbital cellulite and pre-septal cellulite are more common in children than adults [2]. Symptoms include eye pain, eyelid swelling, and redness. Orbital cellulite can lead to blindness or even death. Pre-septal cellulite also has many complications. Typical organisms include *Streptococcus pneumoniae*, and others are *Staphylococcus aureus* and anaerobic microorganisms. Diagnosis of cellulite is mainly made based on clinical manifestations. Blood culture in cellulite is indicated.

However, in a small number of these patients, the result of hot staining and marginal culture is positive for the development of cellulite. Treatment of pre-septal cellulite includes clindamycin, cotrimoxazole, amoxicillin, cefpodoxime. Topical antibiotics do not treat infection [3]. Orbital cellulitis was treated by antibiotics such as vancomycin, ceftriaxone, cefotaxime, ampicillin-sulbactam, and piperacillin-tazobactam. In case of non-response to experimental therapy with antibiotics or reduction of visual acuity and other complications, surgery is necessary [4]. The course of cellulite treatment is usually 5 to 10 days. In newborns, the treat takes 7 to 10 days. In more severe types, the treatment period is longer [5].

So far, several studies have been conducted to study epidemiology, manifestations, and effective treatments for cellulite in different parts of the world on different age groups. However, there are limited studies in Iran, especially in Qom Province, on these patients. Therefore, since the patients are primarily children and due to the irreversible complications of this disease and this age group has been less studied, the need for such research is strongly felt. Also, there have been cases of drug resistance, but no study has been conducted in Qom Province on this topic. We decided to conduct this study because of the importance of the disease in terms of its relatively significant prevalence and risk of new complications and even death. Also, there are insufficient statistics in the country and Qom Province regarding the epidemiological and clinical features of the disease. We aimed to determine the frequency of causes, complications, and cellulite treatment in patients referred to Hazrat Masoumeh Hospital in Qom City from April 2009 to December 2014.

2. Materials and Methods

This research is a descriptive-analytical (cross-sectional) and epidemiological study. The study population included all patients admitted with the final diagnosis of cellulite in Hazrat Masoumeh Hospital in Qom City during 2013-2020. First, the names of patients hospitalized in infectious wards with the initial and definitive diagnosis of cellulite during 2013-2020 were extracted from the patient registry office. By referring to the hospital archive, the patients' files were received and studied. Then the files of 121 patients who had the final diagnosis of cellulite were evaluated. Demographic information, including age and sex, site of involvement, seasonal prevalence, clinical manifestations, clinical course, effective antibiograms, blood culture, and laboratory results of these patients, were extracted and entered a checklist. The principles of the Helsinki Declaration were observed in all stages of this study. The patients' personal information was kept confidential and not published anywhere. Also, due to the retrospective nature of the research and the use of patients' medical records, no additional costs were imposed on patients for the study. Descriptive analysis was performed to calculate the frequency of variables by SPSS version 20. The relationships between quantitative variables were examined by t test and qualitative variables by the Pearson correlation test.

3. Results

Out of 121 hospitalized patients, 63(52%) were male, and 58(47.9%) were female. Their mean age was 42.94 months (between 3 and 4 years) with a standard deviation of 38.15 months; their age range was 1 to 200 months. The lesions were around the eye and surrounding tissues in 8 cases (6.61%), facial part in 19(15.7%), upper limbs in 32(26.45%), the axillary area in 2(1.65%), and lower limbs in 53 cases (43.8%). The location of involvement of 5 cases (4.13%) was unregistered. The head and neck each had 1 case (0.83%) involvement (Table 1).

The number of patients who were referred in spring was 32(27%), summer 30(25%), autumn 38(32%), and winter 19(16%). In terms of clinical manifestations at the beginning of hospitalization, edema was reported in 91 patients (75%), warmth 36 patients (29%), redness in 76 patients (62%), pain in 28 patients (23%), tenderness in 26 patients (21%) and purulent discharge in 9 patients (7%). Fever has also been reported in 47 cases (38%). Five cases (4%) had gastrointestinal symptoms and 4 (3%) mild respiratory symptoms. Two patients (1.6%) had preauricular lymphadenopathy, one of whom also had parotiditis (Table 2). The mean length of hospital

Table 1. Frequency distribution of cellulite involvement site in patients

Location of Involvement	No. (%)
Eyes and around it	8(6.61)
Upper limbs	32(26.45)
Lower limbs	53(43.7)
Axilla	2(1.65)
Face	19(15.7)
Neck	1(0.8)
Head	1(0.8)

stay was 3.5 days. The patients were hospitalized from 1 to 13 days, but 32 were discharged with personal consent and received outpatient treatment. In this study, ceftriaxone for 57 patients (47%), vancomycin for 18(14.87%), imipenem for 5(4.13%), ceftazidime for 6(4.96%), clindamycin for 34(28.1%), cefazolin for 8(6.61%), cephalothin for 7(5.78%), cloxacillin for 42(34.71%), cefotaxime for 1(0.8%), mupirocin for 1(0.8%), metronidazole for 2(1.65%) were prescribed.

Most cases in which the primary antibiotic was changed included the change of ceftriaxone to cloxacillin in 23 patients (19%), change of ceftriaxone to clindamycin in

19(15.7%), and change of ceftriaxone to vancomycin in 11(9.1%). Other items are listed in [Table 3](#).

Regarding the treatment choice, in 115 cases (95%), only injectable antibiotics were used. Six patients (5%) underwent surgery. Regarding the underlying cause, 12 cases (9.9%) had a history of trauma, and 4 cases (3.3%) had a history of immunodeficiency. Three of the immunodeficiency cases were neuroblastoma, and one was leukemia and had cellulite at the injection site for chemotherapy. Eleven patients (9.09%) also had previous ulcers that led to cellulite. In 8 cases (6.6%), cellulite was developed at the site of intravenous or intramuscular injection of drug or vaccine, of which 1 case was relat-

Table 2. Frequency distribution of clinical manifestations in patients

Clinical Manifestations	No. (%)
Edema	91(75)
Warmth	36(29)
Redness	76(62)
Pain	28(23)
Tenderness	26(21)
Purulent discharge	9(7)
Fever	47(38)
Gastrointestinal symptoms	5(4)
Respiratory symptoms	4(3)
Peripheral lymphadenopathy	2(1.6)
Parotiditis	1(0.8)

Table 3. Frequency distribution of antibiotics prescribed to patients

Prescribed Antibiotics	No. (%)
Ceftriaxone	57(47)
Vancomycin	18(14.87)
Imipenem	5(4.13)
Ceftazidime	6(4.96)
Clindamycin	34(28.1)
Cefazolin	8(6.61)
Cephalothin	7(5.78)
Cloxacillin	42(34.71)
Cefotaxime	1(0.8)
Mupirocin	1(0.8)
Metronidazole	2(1.65)

ed to the injection of Boston Consulting Group (BCG) vaccine, 1 case to the injection of ceftriaxone, 1 case to the injection of penicillin, 1 case to dexamethasone injection, and 3 cases to venipuncture. One patient with thalassemia also has cellulite at the transfusion site. Dental infection was the cause in 3 cases (2.48%), and 19 cases (15.7%) had a history of insect bites. Four patients (3.32%) had a history of skin lesions in the affected area, of which 1 patient (0.83%) reported acne manipulation,

1 (0.83%) chickenpox, and 1 patient (0.83%) eczema in that area. Three patients (2.48%) also had a history of burns in the affected area. The bite was reported in 2 cases (1.65%). In 55 (45.4%) cases, no specific cause had been mentioned ([Table 4](#)).

The mean Erythrocyte Sedimentation Rate (ESR) was 32.46 mm/h in 25 patients (20.6%). The Complete Blood Count (CBC) count was higher than normal (15000 cell/ μ L) in 14 patients (19.44%) with lymphocytes domi-

Table 4. Frequency distribution of underlying causes in patients

Underlying Cause	No. (%)
Trauma	12(9.9)
Immunodeficiency	4(3.3)
Previous wound	11(9.0)
Injection site	8(6.6)
Tooth infection	3(2.48)
Bite	19(15.7)
Skin lesion	4(3.32)
Burns	3(1.48)
Bitten	2(1.65)
Unknown cause	55(45.5)

nance. C-Reactive Protein (CRP) was recorded in 97 cases, of which 33(34%) were below 10 mg/dL.

According to the blood culture response, 10 cultures were positive. The resistance and susceptibility of microorganisms to various antibiotics were evaluated. The highest resistance was seen toward cefazolin in 4 cases and ceftriaxone in 3 cases. According to antibiograms effective in blood culture, the highest sensitivity was to imipenem (Table 3).

4. Discussion

A total of 121 patients were studied with an average age of 43 months (between 3 and 4 years); the age range was 1 to 200 months. Zhong et al. also reported a mean age of 3.5 years in their study [6]. However, this result was not consistent with the results of some other studies. In Gomes et al. study of 218 children, the mean age was 2 years [7]. According to research by Fanella et al., the average age of children with orbital cellulite was 7.5 years [8]. In Daniel et al. study, more than half of the patients (13 of 22 patients) were less than 9 years old, with a Mean $\pm$ SD age of 2.68 $\pm$ 2.28 years [9]. The mean age of children under 9 years in the Daniel study was close to our mean age, but due to the different methods of selecting patients in that study (dividing them into two groups less than 9 years and older), their study cannot be compared in terms of age with this study [9]. In the Berger study, the Mean $\pm$ SD age was 6.2 $\pm$ 5 years. In terms of gender, 58 patients (47.9%) were female, and 63 patients (52%) were male. The number of girls to boys in our study was almost equal [10]. In the Gomes study, 56.9% of the patients were boys, close to the results we obtained [7]. While these results were contrary to the results of other studies. In the Fanella study, which examined only orbital cellulite, the ratio of boys to girls was 2.2 [8]. In the Zhong study on orbital cellulite, boys were 65%, and girls were 35% [6]. In Bagheri et al. study on patients with cellulite regardless of age group, the prevalence of orbital cellulite was twice as high in men as in women, but the frequency of pre-septal cellulite was almost the same in both sexes [11].

Regarding the location of involvement, the most involved area was the lower extremities, with 53 cases (43.7%). In Upile et al. study on skin infections in children, the results were somewhat close to ours because they reported the most common sites of infection in the head, neck, and lower extremity [12], i.e., about 33% in the face and neck and 32% lower limb involvement. Lazzarini also studied adults who reported the most affected areas in their legs (66%), arms (24%), and face

(6%) [13]. In Berger et al. study, as in our and other studies, limbs (34%) and face and neck (20%) were the most involved sites [10]. In both Hahn and Fleisher's studies, the most involved areas were the legs [14, 15].

Regarding the season, 32 cases (27%) happened in spring, 30 cases (25%) in summer, 38 cases (32%) in autumn, and 19 cases (16%) in winter. The prevalence of the disease in the cold seasons of the year was 47%, and in the warm seasons of the year, 51%, which is almost no apparent difference in terms of season. This finding is contrary to the results of the Fanella study [8]. Their study showed 66% of cases in autumn and winter and 34% in spring and summer. In Dr Bagheri study, the highest incidence of the disease was reported in spring and the lowest in summer [11], but in our research, the highest seasonal prevalence occurred with a slight difference in autumn.

In terms of clinical manifestations at the beginning of hospitalization, edema was seen in 91 patients (75%), redness in 76 patients (62%), warmth in 36 patients (29%), pain in 28 patients (23%), tenderness in 26 patients (21%) and purulent discharge in 9 patients (7%). Also, 47 cases (38%) had a temperature. Five cases (4%) had gastrointestinal symptoms, and 4 cases (3%) had mild respiratory symptoms. Two patients (1.6%) had preauricular lymphadenopathy, one of whom also had parotiditis. The order of symptom prevalence is consistent with the results of Gomes et al. In Gomes study, the prevalence of swelling was 91.3%, redness was 81.7%, warmth was 47.2%, and tenderness was 31.7% [7]. On the first day of hospitalization, 42.2% of patients had a fever. In Dr Bagheri study, the most common complaints of patients were changes in appearance, and the most common clinical findings were swelling and redness of the eyelids [11]. In Murphy et al. study, 47% of children had symptoms of an upper respiratory infection, which was contrary to our results [16, 17].

In this study, the most commonly changed antibiotics during treatment were ceftriaxone to clindamycin in 19 cases (15.7%), ceftriaxone to cloxacillin in 23 cases (19%), and ceftriaxone to vancomycin in 11 cases (9.1%). Fanella reported that injectable antibiotics were used for all patients [8]. The main antibiotic was changed in 12 cases, either as a change from generation 2 to 3 of cephalosporins or with the addition of clindamycin. Ceftriaxone was the most common antibiotic in our study, but in the Fanella study, cefuroxime with 9 cases (24%) was more commonly used than other antibiotics [8]. In his research, other antibiotics such as cephalosporin with clindamycin (21%), cefotaxime and cloxacillin (21%),

cefotaxime (18%), vancomycin and cefotaxime (5%), metronidazole and cefuroxime (5%), penicillin (3%), ampicillin, and cefuroxime (3%) were used. Regarding the choice of treatment method, antibiotics have been used in all cases, of which 6 (5%) have undergone surgery due to the need for abscess drainage or debridement. In the Upile study, all patients were treated with antibiotics, and 7 children (3%) also needed surgery [12]. In Dr Bagheri study, patients were treated with an average of 2 antibiotics, and according to the type of cellulite they examined, they concluded that surgery was needed in 48.7% of cases with orbital cellulite and 14.8% of cases with pre-septal cellulite [11]. This finding did not agree with our results. In the Murphy study, all patients were treated with injectable antibiotics, and children with orbital abscesses underwent surgery.

In terms of complications, abscess was reported in 12 cases (10%), osteomyelitis was suspected in 2 cases (1.6%), and other complications such as blindness, limb loss, death, etc., were not reported [17]. In other studies, no death was reported. Only in Dr Bagheri's study, 1 case of ocular muscle paralysis due to orbital cellulite was observed [11]. In the Fanella study, no death was reported, and only one patient needed to be admitted to the intensive care unit [8]. No patients required readmission within three days of discharge. The prevalence of abscesses in patients was different in the other two studies and our study. In a study by Baker et al., who studied severe skin infections, abscesses were found in 36% of cases. In the Trenchs study, abscesses were seen in 17.5% of the patients [16]. In Murphy study, two people with orbital abscesses developed a severe complication, one of which was eye drainage, and one was the spread of infection to the intracranial space.

Regarding the underlying cause, 12 cases (9.9%) had a history of trauma, and 4 cases (3.3%) had a history of immunodeficiency. Eleven patients (9.09%) also had a previous wound that led to cellulite [17]. In 8 cases (6.6%), cellulite was developed at the site of venipuncture or the site of intramuscular injection. Three cases (2.48%) resulted from dental infection, and 19 cases (15.7%) had a history of insect bites. Four patients (3.32%) had a history of skin lesions in the affected area, of whom 1 (0.83%) was due to acne manipulation, 3 (2.48%) due to chickenpox, and 1 (0.83%) due to eczema in that area. Three patients (2.48%) also had a history of burns in the affected area. Bites were reported in 2 cases (1.65%). In 55 cases (45.4%), no specific cause was mentioned. A history of previous bites, trauma, and wounds were the most common underlying causes of childhood cellulite. In other studies, sinusitis was the most common

underlying cause in children since they only examined orbital cellulite. Murphy et al., who included adults in their research, found that children were more likely to develop orbital cellulitis following an upper respiratory infection and sinus disease. In contrast, adults often had a history of trauma or immunodeficiency [17]. In Berger et al. study, trauma (35%) and insects bites (9%) were the most common underlying causes [10]. In his research, Hahn also stated that trauma is the most common underlying cause [14]. In the Fanella study, asthma was the most common underlying disease in children with orbital cellulitis, seen in 4 of 38 children studied [8]. Three children had chronic sinusitis in the past, and two children had dental infections. In Dr Bagheri study, sinusitis was the most common underlying cause.

The Mean $\pm$ SD length of hospital stay was 3.5 $\pm$ 2.86 days [11]. The patients were hospitalized for 1 to 13 days, but 32 were discharged with personal consent and received outpatient treatment. In Fanella study, the Mean $\pm$ SD hospital stay was 2.5 $\pm$ 2.4 days [8]. In the Upile study, the mean hospital stay was two days [12].

The WBC reported a minimum of 400 and a maximum of 30600 cells/ μ L. The Mean $\pm$ SD value was 12261 $\pm$ 4587 cells/ μ L, and 78% had a normal WBC count from 5000 to 15000 cells/ μ L. Twenty-five cases (20.6%) also had leukocytosis. The results of the Fanella et al. study were also close to ours. Their result was 13400 $\pm$ 4500 cells/ μ L, but 67% were in the normal range, which is less than the results we obtained. In the Lazzarini study, the WBC count of half of the patients was higher than normal, which is higher than the percentage of leukocytosis in our study [13]. In the Hahn study, the WBC was higher than normal in 19% of cases, which was close to our result [14]. Fleisher et al. found 15% leukocytosis in their study [15]. The mean WBC count was 11900 cells/ μ L, which was almost equal to our result. ESR was requested in 103 cases, with the following results. The minimum value was 2 mm/h, the maximum was 125 mm/h, and the Mean $\pm$ SD was 32.46 $\pm$ 26.03 mm/h. Also, 38 patients (37%) had an ESR of less than 20 mm/h. In the Fanella study, the Mean $\pm$ SD ESR was 29.6 $\pm$ 6.1, which is almost two times what we obtained [8]. In his study, only one out of 12 patients (8%) had an ESR of less than 20, which is very different from ours. In the Lazzarini study, the ESR values of 50% of cases were higher than normal [13]. In the Hahn study, the ESR value was higher than normal in 94% of the patients [14]. Of the 97 cases of CRP recorded, 33 (34%) were below 10 mg/dL. Thirty-seven patients (38%) CPR levels were 10 to 40 mg/dL. Also, it was between 40 and to 100 mg/dL in 21 patients (21.6%) and above 100 mg/dL in 6 patients (6.2%). The

Mean±SD value was 24.14±23.07 mg/dL. In the study of Zhong et al., the Mean±SD CRP at the beginning of hospitalization was 22±29.8 mg/dL, which was close to our result [6]. In the Lazzarini study, 50% of CRP cases were higher than normal [13], and in Hahns study, positive CRP was 80% [14]. But in our study, this rate was 67%.

Blood cultures were requested for 60 patients. Of these, 10 were positive. Two of them were non-sterile. Eight cases (13%) of positive blood cultures were reported. *Klebsiella* was reported in 2 cases, *E. coli* in 2 cases, and *Serratia* in 2 other cases. Also, *Staphylococcus* in 1 case and *Pseudomonas* in 1 case. Blood positive culture results in other studies that have been reviewed were much fewer than our study, with only one person being positive for *Streptococcus pyogenes* (3.1%) in the Fanella study [8]. In the Trenchs study, blood cultures were requested for 79.3% of patients, of whom 0.6% were positive, and 2.8% were non-sterile and were grown in positive cultures of *S. aureus* and *Strep pyogenic* [16]. In the Berger study, 2% of patients had positive blood cultures, and 5.4% were non-sterile. Positive blood cultures included *Staphylococci* and *Streptococci* [10]. In the Lazzarini study, blood culture was positive in 2% of the specimens [13]. In the Fleisher study, blood cultures were also positive in 10 cases (2%) caused by *Haemophilus influenza*. The Mean±SD Polymorphonuclear leukocytes (PMNs) was 62.86±13.7 cells/μL [15]. In 72 patients, this test was requested; in 58 (80.55%) patients, PMN was preferred, while in 14 patients (19.44%), lymphocyte count was dominant. This variable has not been studied in the studies that have been presented. According to the blood culture response, 10 cultures were positive. The resistance and susceptibility of microorganisms to different antibiotics were evaluated. The highest resistance was to cefazolin in 4 cases and ceftriaxone in 3 cases. According to antibiograms effective in blood culture, the highest sensitivity was seen to imipenem in 6 cases, followed by ceftazidime in 5 cases. While Gomes et al. concluded that oxacillin or cefazolin is the drug of choice for uncomplicated cellulite [7].

Blood culture results were positive in a few cases, which is consistent with other study results. So requesting such a test should be reconsidered and only be requested if antibiotic resistance is seen. Although in this case, given the small percentage of positive blood cultures, it is not economical. According to the results of positive blood cultures, the highest sensitivity was related to imipenem, followed by ceftazidime, ciprofloxacin, and cefixime. Most resistance was observed against cefazolin and ceftriaxone. Given that ceftriaxone was mainly used to treat cellulite, it seems that the treatment of cellulite with

antibiotics such as cefazolin and ceftriaxone should be reconsidered.

5. Conclusion

Because of the limitations of retrospective research in collecting information, future research should focus on evaluating specific treatments and diagnostic methods for diseases such as cellulite in Iran. Future research should determine the prevalence of organisms involved in the disease in the area where we live, as well as the type of appropriate treatment for all inpatients and outpatients.

Ethical Considerations

Compliance with ethical guidelines

The Ethics Committee of Qom University of Medical Sciences approved this study (Code: IR.MUQ.REC.1394.70).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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