

## Characteristics of Newborns Treated for Acute Omphalitis at the University Hospital of Split 2015 – 2019

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### Abstract

**Objectives** – The aim of the study was to retrospectively evaluate the clinical and laboratory data in neonates treated for acute omphalitis at the time of admission at the University Hospital of Split. **Patients and Methods** – All neonates treated for acute omphalitis from January 1st 2015 to December 31st 2019 were included in this study. **Results** – There were 97 neonates included, of whom 58 (59.79%) were males. The median age at admission was 7 days. The most common clinical sign was periumbilical redness in 70 (72.16%), followed by umbilical discharge in 49 (50.52%) neonates. In 62 (63.92%) neonates bacteria were isolated from the umbilical stump swab. The most common microorganism isolated was methicilin-sensitive *Staphylococcus aureus* (MSSA) in 21 (33.87%) neonates followed by *Klebsiella pneumoniae* in 15 (24.19%), and *Escherichia coli* in 14 (22.58%) cases. Antibiotics were given to all neonates. In all neonates treatment and clinical course were uneventful, without mortality. **Conclusion** – Neonatal omphalitis was not a frequent cause of hospitalization in the entire group of hospitalized patients at the Department of Pediatrics of the University Hospital of Split (0.75%). Acute omphalitis had a mild clinical course and redness of the periumbilical area, together with the presence of umbilical cord discharge, predominated in the clinical presentation. It is necessary to educate the population and medical staff continuously on the importance of maintaining newborn hygiene and proper umbilical cord care.

**Key Words:** Neonate ■ Umbilical Cord ■ Infection ■ Omphalitis ■ *Staphylococcus Aureus*.

### Introduction

Omphalitis is an infection of the umbilical stump and/or surrounding tissues, occurring primarily in the neonatal period more frequently in developed (6 to 8%) than in developing countries (0.2 to 0.7%) (1-4). Most neonates with omphalitis present with a mild disease. However, it can also pose a significant risk for sepsis, other serious bacterial infections or neonatal mortality since the devitalized umbilical cord provides an ideal medium for bacterial growth (5). The staging of omphalitis is proposed as follows: Grade 1: Funisitis with

malodorous purulent umbilical discharge; Grade 2: as Grade 1 together with periumbilical abdominal wall cellulitis; Grade 3: as Grade 2 with systemic signs of infection, including sepsis, shock, disseminated intravascular coagulation, multiple organ dysfunction; Grade 4: as Grade 3 and ecchymoses, crepitus, bullae; with evidence of involvement of superficial and deep fascia and associated muscle (6). The process of bacterial colonization of the navel starts after birth, mostly with Gram-positive cocci and different enteral bacteria. Risk factors for omphalitis include: low birth weight, maternal infection, umbilical catheterization, prolonged labor, unplanned home birth and improper cord

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care (3, 4, 7). Patients usually present with local signs of infection. It might start as localized cellulitis, but it can spread to the whole abdominal wall. Purulent discharge or bleeding may be seen (8). Systemic symptoms, such as fatigue, poor feeding, fever, and irritability, can be an indication of sepsis. Necrotizing fasciitis is noted in umbilical infections caused by anaerobic bacteria (8).

Laboratory work-up in most of the patients with omphalitis is similar to the work-up for suspected serious bacterial infection. A comprehensive set of tests includes complete blood count, white blood cell count (WBC) with differential, C-reactive protein (CRP), procalcitonin (PCT), and microbiologic cultures (9). Whenever possible, blood culture and cultures of the discharge should be obtained prior to the start of antibiotic therapy. In cases of systemic symptoms, diagnostic work-up should be more extensive, including urine culture, chest X-ray, lumbar tap and some other indicated procedures to exclude severe infections (10). Broad-spectrum parenteral antibiotics against Gram positive and Gram negative bacteria are usually used to treat omphalitis. The initially recommended empirical antibiotic is antistaphylococcal penicillin and aminoglycoside (11). In the case of a high incidence of methicillin-resistant *Staphylococcus aureus*, vancomycin should be administered before the culture results are available. If there is a suspicion of anaerobic infection, clindamycin or metronidazole are indicated (11).

The main objective of this research was to analyze retrospectively the clinical signs and laboratory parameters at the time of admission in neonates hospitalized for acute omphalitis at the Department of Pediatrics of the University Hospital of Split.

## **Patients and Methods**

All the data were taken from the medical records for retrospective analysis. Inclusion criteria were: Neonates (age ≤ 28 days at the time of admission) who were discharged home with the diagnosis of acute omphalitis and treated at the Department of Pediatrics of the University Hospital of Split in

the period from January 1<sup>st</sup> 2015 to December 31<sup>st</sup> 2019. Neonates with prior umbilical canalization were excluded from the study.

## ***Ethical Considerations***

The research was in line with the provisions on the protection of the rights and personal data of respondents from the Patients' Rights Protection Act (OG 169/04, 37/08), the Act on Implementation of the General Data Protection Regulation (OG 42/18), and the rules of the HMA Declaration on its 1964-2013 revisions. The study was approved by Ethics Committee of the University Hospital of Split (2181-147-01/06/M.S.-20-2) on November 26<sup>th</sup> 2019.

## ***Statistical Analysis***

Statistical analyses were conducted using Microsoft Office Excel and MedCalc (v.11.5.1.0, MedCalc Software, Ostend, Belgium). Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation or as a median. The comparison of categorical variables was performed using the Chi-square test. A P value < 0.05 was considered statistically significant.

## **Results**

In the period from 2015 to 2019, 97 children were treated for acute omphalitis at the Department of Pediatrics of the University Hospital of Split, Croatia, which is 0.75% of the total number of hospitalized patients during that period (Table 1). There were more hospitalized males (58, 59.79%) than females. The highest number of hospitalizations was observed in 2016 and 2017, which was a significant difference ( $P < 0.0001$ ).

The age of the neonates at admission was between 0.88 days and 28 days (median = 7 days). Omphalitis developed in 98.97% of infants born between 37 and 42 gestational weeks, and only in one case (1.03%) in a preterm infant (<37 gestational weeks) born with a low birth weight (<2500 g).

Table 1. Number of Neonates Diagnosed with Acute Omphalitis and Their Gender in Relation to the Total Number of Hospitalizations at the Department of Pediatrics of the University Hospital of Split, Croatia in 2015-2019

Year	Number of newborns hospitalized for acute omphalitis by gender N (%)			Total number of hospitalizations
	Female	Male	Total	
2015	7 (7.22)	13 (13.4)	20 (0.79)	2520
2016	11 (11.34)	18 (18.56)	29 (1.11)	2609
2017	16 (16.49)	16 (16.49)	32 (1.12)	2854
2018	3 (3.09)	5 (5.15)	8 (0.31)	2562
2019	2 (2.06)	6 (6.19)	8 (0.34)	2376
Total	39 (40.21)	58 (59.79)	97 (0.75)	12 921

Table 2. Clinical Presentation of Acute Omphalitis at Admission in 97 Neonates Treated at the Department of Pediatrics of the University Hospital of Split, Croatia in 2015-2019

Clinical sign	Observed years					Total N (%)
	2015 (N=20)	2016 (N=29)	2017 (N=32)	2018 (N=8)	2019 (N=8)	
Redness of skin around the umbilicus	14	22	24	5	5	70 (72.16)
Discharge from the umbilical stump	13	13	14	3	6	49 (50.52)
Bleeding	2	3	2	1	1	9 (9.28)
Granuloma	2	1	3	2	0	8 (8.25)
Malodor	0	2	0	1	1	4 (4.12)

Table 3. Laboratory Findings of Neonates at Admission to the Department of Pediatrics of the University Hospital of Split, Croatia due to Acute Omphalitis (n=97)

Findings	Mean±SD*	Minimum	Maximum
Leukocytes (10 <sup>9</sup> /L)	11.77±3.12	3.8	24.5
CRP (mg/L)†	2.86±5.18	0.2	39.9
Thrombocytes (g/L)	353.77±119.73	61	711

\*Standard deviation; †C-reactive protein.

The clinical presentation of acute omphalitis was analyzed. The most common sign was redness of the skin around the umbilicus. Redness was described as marginal redness, periumbilical redness, erythematous area, or local hyperemia. In slightly more than half the cases, discharge or secretion from the umbilicus was noted, described as purulent discharge, yellowish and serous secretion. Umbilical cord bleeding, umbilical granuloma and malodor were found in <10% neonates (Table 2).

Table 3 shows the laboratory findings in neonates treated for acute omphalitis at admission.

An umbilical cord swab was taken in 76 (78.35%) out of 97 patients. The results of 62 (63.92%) were available. The most common agent isolated was methicillin-sensitive *Staphylococcus aureus* (MSSA), found in 21 (33.87%) patients, alone or in combination with other bacteria, followed by *Klebsiella pneumoniae* and *Escherichia coli*. A single pathogen was isolated in 39 out of 62 (62.9%) cases. In patients with multiple isolates, the following bacteria were found: coagulase-negative *Staphylococcus* (CoNS), methicillin-sensitive and methicillin-resistant *Staphylococcus epidermidis*

Table 4. Bacterial Isolates from the Umbilical Stump Swab Taken at Admission in 62 out of 97 Neonates Treated for Acute Omphalitis at the Department of Pediatrics of the University Hospital of Split, Croatia in 2015-2019

Isolates	Observed years					Total N (%)
	2015	2016	2017	2018	2019	
Single isolate	5	13	16	1	4	39 (62.9)
Multiple isolates	2	8	10	2	1	23 (37.1)
MSSA <sup>*</sup>	2	7	8	2	2	21 (33.87)
<i>Klebsiella pneumoniae</i>	3	4	4	2	2	15 (24.19)
<i>Escherichia coli</i>	0	7	6	0	1	14 (22.58)
<i>Enterococcus spp.</i>	1	5	2	0	0	8 (12.9)
<i>Proteus mirabilis</i>	0	4	2	0	0	6 (9.68)
<i>Enterobacter cloacae</i>	1	0	2	0	1	4 (6.45)
<i>Acinetobacter baumannii</i>	0	2	1	0	0	3 (4.84)
MRSE <sup>†</sup>	3	0	0	0	0	3 (4.84)
<i>Pseudomonas aeruginosa</i>	2	0	1	0	0	3 (4.84)
FF <sup>‡</sup>	0	1	1	0	0	2 (3.23)
CoNS <sup>§</sup>	0	0	2	0	0	2 (3.23)
<i>Staphylococcus aureus</i>	0	0	1	0	1	2 (3.23)
MSSE <sup>  </sup>	1	0	0	0	0	1 (1.61)
<i>Enterobacter aerogenes</i>	0	1	0	0	0	1 (1.61)
<i>Morganella Morganii</i>	0	0	1	0	0	1 (1.61)
<i>Streptococcus viridians</i>	0	0	1	0	0	1 (1.61)

<sup>\*</sup>Methicillin sensitive *Staphylococcus aureus*; <sup>†</sup>Methicillin resistant *Staphylococcus epidermidis*; <sup>‡</sup>Physiological flora; <sup>§</sup>Coagulase negative Staphylococcus; <sup>||</sup>Methicillin sensitive *Staphylococcus epidermidis*.

(MSSE and MRSE), *Enterococcus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Enterobacter aerogenes*, and *Acetivibrio* (Table 4). Blood cultures were taken in only 15 (15.46%) neonates and all of them were sterile.

Out of the 14 isolated, one sample of *Escherichia coli* isolated in 2017 was extended spectrum beta-lactamase positive (ESBL+). Four out of the 15 isolates of *Klebsiella pneumoniae* were ESBL+. Only one patient was treated with oral cephalexin, while all the others were treated with parenteral antibiotics. The antibiotic used most often was intravenous ceftriaxone in 94 (97.92%) out of 96 neonates. Almost half the patients (45, 46.39%) had only one diagnosis, of acute omphalitis, at discharge. The most common comorbidities were hyperbilirubinemia (18, 18.56%), patent foramen ovale (13, 13.4%) and conjunctivitis (9, 9.28%). The average hospital stay of patients treated for only acute

omphalitis was 5.51±2.4 days, while the average hospital stay of all the patients was 6.94±5.84 days.

## Discussion

The aim of this study was to analyze the demographic data, clinical characteristics and laboratory parameters of children treated for acute omphalitis at the Department of Pediatrics of the University Hospital of Split, Croatia. We found that in the period from 2015 to 2019, 97 children were treated for acute omphalitis, which is <1% of the total number of patients hospitalized at our Department. There was a higher number of hospitalized patients in 2016 and 2017, while in 2018 and 2019 there was a noticeable decrease in the number of hospitalized children. In our institution, clean, dry cord care is recommended for newborns born in health facilities, according to the recommendations (12).

The same practice is followed at home, as well. After discharge, neonates are supervised by nurses from the local outpatient facility who conduct home visits minimally 3 times in the first month after birth for care of the mother and newborn. After the increase in the number of hospitalizations the frequency of home visits was increased to 3-7 in the first month after birth. There was also a rise in awareness of proper umbilical cord treatment. However, the recommendations for home care remained the same. The majority of patients were males. Data on the incidence of infection by sex obtained in this study are similar to data from a study conducted in Michigan, USA, where the proportion of boys was 61% (13). Male gender has been identified in previous studies as one of the risk factors that suggest poorer prognosis of omphalitis treatment outcomes (14).

The mean age at which acute omphalitis was diagnosed was  $8.84 \pm 5.73$  days, with a median of 7 days. In the period of two weeks after birth, the process of drying and falling off of the umbilical cord takes place, and the devitalized tissue is susceptible to infection, so this result is expected.

Redness predominated in the clinical presentation at admission, and was described in more than 70% neonates. Redness is described as marginal skin redness, periumbilical skin redness, erythematous area, or local hyperemia. One study tried to facilitate the diagnosis of acute omphalitis on the basis of the clinical picture, that is, on the basis of two items from the clinical picture. According to the algorithms from that study, the presence of intense redness or moderate redness with the presence of pus is sufficient for the diagnosis (15). From the above, it may be concluded that the diagnosis cannot be made without the presence of redness. As stated before, among our patients, the majority (70.71%) had redness in the clinical picture, while in others this sign was missing. It is possible that redness was present in the clinical picture without being noted or acute omphalitis did not present with redness. Purulent discharge, yellowish secretion or serous secretion in half of the neonates. Umbilical granuloma was noted as the only feature

in eight subjects. This is classified separately under code no. P83.81 in the International Classification of Diseases – 10 revision (16), in contrast to acute omphalitis with or without bleeding, which is marked as P38. Therefore, the term umbilical granuloma should not be used to describe the clinical picture of acute omphalitis. A subject in whom the umbilical granuloma is visible in the clinical picture should be admitted to hospital with this diagnosis separately, or this diagnosis should be accompanied by a diagnosis of acute omphalitis.

Umbilical stump swabs were not taken in all the patients admitted. According to the National Institute for Health and Care Excellence (NICE) instructions, for newborns with clinical signs of umbilical infection, it is necessary to make a blood culture, take an umbilical cord swab, and start antibiotic treatment immediately (17). In our study, subjects who did not have an umbilical cord swab were started on antibiotics, based solely on the clinical presentation and laboratory findings. It is important to change this practice in our institution in the future, so that all appropriate cultures are taken in patients hospitalized with a diagnosis of omphalitis.

The most common isolate in newborns treated for acute omphalitis was *Staphylococcus aureus*. *Staphylococcus aureus* was also shown to be the most common microbial agent in a study conducted in Tanzania, as well as in studies conducted in Pakistan, and Turkey (18-20). In a study from Pakistan, 95.7% of all *Staphylococcus aureus* isolates were methicillin sensitive strains (19). This proportion corresponds roughly to our study, in contrast to studies showing a predominance of methicillin-resistant *Staphylococcus aureus* (18, 21, 22). Regarding our results, we were very pleased that from 2015 to 2019 there was no case of acute omphalitis treated at our Department caused by MRSA.

The second most commonly isolated pathogen in our study was *Klebsiella pneumoniae*, similar to other studies (19, 21). In our study, four isolated *Klebsiella pneumoniae* were ESBL positive. In the period from 2014 to 2017, the resistance of bacteria

to antibiotics was monitored throughout Europe, including Croatia. It was then observed that most *Klebsiella pneumoniae* that are resistant to third-generation cephalosporins produce the ESBL strain (23). All four cases at our hospital were successfully treated with intravenous ceftriaxone. The third most common causative agent was *Escherichia coli*. In only one subject in our study was *Escherichia coli* ESBL positive, and it was treated successfully with intravenous ceftriaxone. According to some authors, acute omphalitis is a polymicrobial infection (24). In our study, polymicrobial infection was detected in only 23 (37.1%) cases.

According to various guidelines and research, treatment with parenteral antibiotics is recommended in patients diagnosed with omphalitis. A combination of flucloxacillin and an aminoglycoside antibiotic (gentamicin) is recommended. The treatment for the development of complications in the form of necrotizing fasciitis should include antibiotics that act on anaerobic organisms: metronidazole or clindamycin. Treatment for at least seven to ten days is recommended (17). All the subjects in our study were started on antibiotic treatment. Only one patient received the antibiotic orally. The remaining were treated parenterally. In the vast majority of cases, ceftriaxone was the antibiotic of choice, and cefuroxime was used in only two cases. Ceftriaxone is a third-generation cephalosporin, which as such acts on gram-positive and gram-negative bacteria. Katzung's Basic and Clinical Pharmacology states that broad-spectrum lactamase-producing strains are not susceptible to them, but this study showed that parenteral ceftriaxone led to a clinically favorable treatment outcome in all subjects, including those with ESBL + omphalitis (25).

Of all the patients, almost half were treated exclusively for acute omphalitis, while the rest had some other diseases in addition to acute omphalitis. The most common comorbidities recorded in the study period was hyperbilirubinemia, which was observed in 18.56% neonates. From the results of our research, we saw that the presence of comorbidities prolonged the duration of hospital stay. The

average hospital stay of subjects treated exclusively for acute omphalitis was 5.5 days, while the average hospital stay of all study subjects was 7 days. Since the recommended treatment for omphalitis should last for seven to ten days (17), it seems that the duration of treatment in our Department was shorter. However, after discharge from the hospital, antibiotic therapy at home was prescribed for all of them, including a topical treatment.

Umbilical cord care methods have been investigated in several meta-analyses (26-30). Dry umbilical cord care was compared with the use of 4% chlorhexidine. It was concluded that in deliveries outside the hospital and areas with a high infant mortality rate, it is desirable to apply a solution or gel of 4% chlorhexidine to the umbilical cord within 24 hours after birth (31-33). This procedure significantly reduces the incidence of omphalitis and neonatal mortality, compared with dry umbilical cord care (27). The use of traditional umbilical cord care materials, such as various plants or human milk, can lead to contamination by pathogenic bacteria, including *Clostridium tetani* (34). The proven efficacy of 4% chlorhexidine in deliveries outside a hospital cannot be applied to hospitals (26,27,31). In healthy newborns and in deliveries in hospitals, there is evidence to support dry cord care for effective and rapid separation of the cord (30, 35). As mentioned above, the WHO has recommended dry umbilical cord care in high-resource facilities (12). Dry care involves keeping the battalion clean, leaving it in the air as much as possible, or covering it lightly with a clean cloth. For newborns who are born at home in settings with high neonatal mortality, the WHO recommends the use of chlorhexidine. Although the use of chlorhexidine was marked as safe, traces of the drug were found in the blood of newborns after topical application (36,37).

Our results support others who found dry care quite effective. The incidence of acute omphalitis at the Department of Pediatrics of the University Hospital of Split, Croatia, in the period from 2015 to 2019 was low, especially in the last two years analyzed. The infection had a mild clinical course,

did not lead to the development of complications, and responded to treatment with ceftriaxone. Therefore, it would be the best to continue to apply dry umbilical care.

Although acute omphalitis has a mild clinical course and is not life-threatening for the newborn, it still represents a stressful event for both mother and child: hospitalization, separation from parents, various diagnostic procedures, fear of complications, etc. From an economic point of view, reducing the number of hospitalizations would save hospital resources and reduce the burden on the already overburdened system. That is why it is important to educate mothers and medical staff continuously about the importance of maintaining newborn hygiene and umbilical cord care.

### Limitations of the Study

The main limitation of this study is the retrospective collection of data from the medical records, which may make them incomplete. A relatively small number of patients were also included in the study, which may be one of the limiting factors.

### Conclusions

It is necessary to educate the population and medical staff continuously on the importance of maintaining newborn hygiene and umbilical cord care. Although the incidence of acute omphalitis in our institution is low, it is important continuously to monitor the frequency of hospitalized neonates with suspicion of omphalitis and to respond promptly if needed by increasing nurse home visits or improving education. Redness of the periumbilical area, together with the presence of umbilical cord discharge, predominates in the clinical picture. The most frequently isolated pathogen was methicillin-susceptible *Staphylococcus aureus* (MSSA) and the parenteral administration of ceftriaxone led to a positive treatment outcome.

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important intellectual content: JeM, ICC, JoM; Approved final version of the manuscript: JeM, EG, ICC and JoM.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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