SEUP
SOCIEDAD ESPAÑOLA DE URGENCIAS DE PEDIATRÍA

EMERGENCIASPediátricas
Vol. 1. Nº 2. Mayo - Agosto 2022

Emerg Pediatr. 2022; 1(2): 78-82

ORIGINAL

Prevalence of bacterial meningitis in febrile infants younger than 90 days of age with urinary tract infection

Tomás Giménez, María Eugenia Malin

Emergencies and Emergency Service. Victor J Vilela Children´s Hospital. Rosario. Argentina

Received on June 13, 2022
Accepted on August 31, 2022

Key words:
Fever
Infant
Serious bacterial infection
Urinary tract infection
Meningitis
Lumbar puncture

Palabras clave:
Fiebre
Niño
Infección bacteriana severa
Infección del tracto urinario
Meningitis
Punción lumbar

Abstract

Introduction: Infants younger than three months are susceptible to serious bacterial infections (SBI). Urinary tract infection (UTI) is the most common cause of SBI in this age range. SBI may lead to bacteremia and some authors recommend to routinely test the cerebrospinal fluid in order to rule out bacterial meningitis. Nevertheless, several studies have shown that this association is less common than previously thought.

Objective: To determine the prevalence of bacterial meningitis in febrile infants between 28 and 90 days of life with a diagnosis of UTI at a tertiary pediatric hospital between 2008 to 2020.

Method: An observational, retrospective, and cross-sectional study was conducted. The medical records of patients younger than 90 days who were admitted between 2008 and 2020 were reviewed.

Results: 93 patients were included, of whom 62% were male, and median age was 55 days (IQR 45-60). Lumbar puncture and cerebrospinal fluid analysis were performed in 44% of the patients. Meningitis was diagnosed in one patient of the total study population (1%).

Conclusions: The prevalence of meningitis in children younger than 90 days with UTI was 1%. The suspicion of central nervous system infection in these patients currently depends on the use of risk stratification tools and clinical judgment. Further studies are still needed to better understand the risk of meningitis and UTI in these patients.

PREVALENCIA DE MENINGITIS BACTERIANA EN NIÑOS FEBRILES ENTRE 28 Y 90 DÍAS DE VIDA CON DIAGNÓSTICO DE INFECCIÓN URINARIA

Resumen

Introducción: *Los niños menores de tres meses son susceptibles a padecer infecciones bacterianas severas (IBS). La IBS más frecuente en este rango etario es la infección urinaria. Comprende un proceso potencialmente bacteriémico por lo que algunos autores consideran necesario el estudio rutinario de líquido cefalorraquídeo para descartar meningitis bacteriana. Sin embargo, diversos estudios han mostrado que esta asociación tiene una frecuencia menor de lo esperado.*

Objetivo: *Determinar la prevalencia de meningitis bacteriana en lactantes febriles entre 28 y 90 días de vida con diagnóstico de infección urinaria durante el periodo 2008 a 2020 en un hospital pediátrico de tercer nivel.*

Metodología: *Se realizó un estudio observacional, retrospectivo y transversal. Se utilizó como unidad de estudio las historias clínicas de pacientes menores a 90 días que cursaron internación entre los años 2008 y 2020.*

Corresponding author:
Dr. Tomás Giménez
Correo electrónico:
Tomigimenez91@gmail.com

© 2022 Sociedad Española de Urgencias de Pediatría — Sociedad Latinoamericana de Emergencia Pediátrica

Resultados: *Se incluyeron 93 pacientes de los cuales el 62% fueron varones y la mediana de edad fue de 55 días (RIC 45-60). Se indicó punción lumbar y estudio del líquido cefalorraquídeo al 44% de los pacientes. Se realizó diagnóstico de meningitis en 1 paciente del total de la población estudiada (1%).*

Conclusiones: *La prevalencia de meningitis en niños con infección urinaria menores a 90 días de vida fue del 1%. La presunción de infección del sistema nervioso central en estos pacientes depende actualmente de la utilización de herramientas para estratificación de riesgo y del juicio clínico. Aún se requieren más estudios para conocer el riesgo de meningitis e infección urinaria en estos pacientes.*

INTRODUCTION

Infants younger than three months are susceptible to serious bacterial infections (SBI). Urinary tract infection (UTI) is the most common cause of SBI in this age range. In our setting, we use predictive tools such as the Rochester criteria to identify children at increased risk of SBI[1-4].

UTI may lead to bacteremia and has been associated with the presence of meningitis, especially in children under 60 days of age. This has led to the routine use of invasive tests to rule out central nervous system (CNS) infection[5].

In recent years, research has suggested that the occurrence of concomitant meningitis in infants with UTI is lower than previously thought[6-9]. Nevertheless, there is still no gold standard for identifying low-risk patients to avoid unnecessary invasive procedures[10,11]. There are currently no data on this subject in our setting.

The main aim of this study was to determine the prevalence of meningitis in patients younger than 90 days with UTI at a tertiary pediatric hospital. The secondary aim was to stratify the risk of these patients according to the Rochester Criteria.

METHODS

An observational, retrospective, cross-sectional study was conducted. The medical records of patients between 28 and 90 days of life admitted to the Víctor J. Vilela Children's Hospital in the city of Rosario, Argentina, between 2008 and 2020 were reviewed. The discharge diagnosis "urinary tract infection" (N39.0) coded according to ICD 10 was used. We also searched for patients with a discharge diagnosis of "meningitis" (G03.9) to identify patients who had UTI as a secondary diagnosis. The data search was conducted by the Statistical Department of our center. The data were collected from the medical records of the patients and processed in Microsoft Excel. To categorize patients at low risk for SBI, the following parameters were considered according to the Rochester Criteria:

- Well-appearing.
- Previously healthy: for patients that met all the following criteria:
  - Term newborn.
  - No chronic or underlying diseases.
  - Not hospitalized longer than the mother after delivery.
  - No previous hospitalizations.
  - No previous or current antibiotic treatment.
- No signs of local infection.
- Laboratory criteria: white blood cell count (WBC) 5,000 to 15,000 cells/mm^3; absolute neutrophil count (ANC) 1500-10,000 cells/mm^3; ≤ 10 leukocytes per high power field on urinalysis.

UTI was defined as the presence of an inflammatory reaction in the urine and/or positive urine culture. An inflammatory reaction in urine was defined as the presence of significant leukocyturia (> 10 cells per high power field) and/or the presence of nitrites and esterasas (≥ 1+). A urine culture was considered to be positive if the colony count was greater than 10^5 CFU in urine collected by clean catch, greater than 10^4 CFU in samples collected by bladder catheterization, and any colony count in a sample obtained by suprapubic aspiration.

Bacteremia associated with UTI was defined as positive blood cultures with growth of a single microorganism corresponding to the microorganism recovered from the urine culture.

The diagnosis of meningitis was made when growth of a microorganism in the cerebrospinal fluid (CSF) was detected or in the presence of bacteremia with abnormal CSF. CSF was considered to be abnormal when > 10 cells/mm^3 were found or results on direct examination were positive.

A traumatic lumbar puncture was defined as a CSF sample with red blood cells.

The medical records were searched for evidence of complications of the initial infection, defined as worsening fever, septic shock, alteration of the neurological status, as well as procedure-related complications.

RESULTS

Overall, 255 medical records of patients seen between 1/1/2008 and 1/1/2020 were reviewed; 208 had a discharge diagnosis of "urinary tract infection" (N39.0) and 47 of "meningitis" (G03.9). 162 patients were excluded for the following reasons: diagnosis of meningitis not associated with UTI (n= 46), healthcare-associated UTI in critically ill patients hospitalized for another reason (n= 97), contaminated urine sample (n= 12), and negative urine culture result (n= 7). A total of 93 patients were included in the analysis.

Of all the patients, 58 (62%) were male and median age was 55 days (IQR 45-60). Fifty-three (57%) patients were between 28 and 59 days of life.

When the Rochester criteria were retrospectively applied in each situation, it was found that of the total sample, three

TABLE 1. Rochester Criteria.

High-risk SBI	90 (96.7%)
Altered general status	5 (5.5%)
Abnormal WBC only	1 (1.1%)
Inflammatory reaction in urine only	39 (43.3%)
Abnormal WBC and inflammatory reaction in urine	45 (50%)
Low-risk SBI	3 (3.3%)

TABLE 2. Pathogens in urine cultures.

Pathogens	n (%)
Escherichia coli	78 (74.2)
Klebsiella pneumoniae	7 (6.6)
Enterococcus faecalis	4 (3.8)
Proteus mirabilis	2 (1.9)
Klebsiella oxytoca	2 (1.9)
Contaminated	12 (12.3)

TABLE 3. Details of the patient with Meningitis.

Previously healthy, 39-day-old infant that presented with a 24-hour history of fever (peak 39.5°C) associated with mild upper respiratory symptoms. Good general status, alert and reactive on examination.

Complementary studies:
- RWBC 10,300 cells/mm^3 (50% ANC) ESR 97 – Urinalysis: abundant leukocytes; direct examination: positive for gram-negative bacilli
- Cytochemical CFS: 2 elements, Proteins 50 mg/dl, Glucose 59 mg/dl (glycemia 110 mg/dl)
- Urine culture: *E. coli* > 10^5 CFU
- Blood culture: *E. coli*
- CSF culture: *E. coli*

Outcome: The patient received IV antibiotics without complications; follow-up study after discharge of the urinary tract showed pyelocaliceal dilation of 8.5 mm on renovesical ultrasound. No record of other studies was found.

(3.3%) patients were low risk and 90 (96.7%) were high risk as they did not meet at least one of the criteria (Table 1).

Eighty-four patients (90%) had an inflammatory reaction in the urinalysis. The urine culture was normal in eight (7%) but showed a significant colony count. Of the patients identified as high risk for SBI, 43.3% (n= 39) had urinary sediment alteration as the only criterion.

E. coli was the predominant microorganism isolated in the urine culture. The remaining urine culture results are detailed in Table 2.

Of the total number of patients, seven (7.5%) had bacteremia with the recovery of the same microorganism from the urine culture. The isolated microorganism was *E. coli* in all cases. No other microorganisms were found in blood cultures.

Lumbar puncture was performed in 41 (44%) patients, 12 of which were traumatic (29.2%); 75.5% corresponded to the age group of 28 to 59 days; 91% had one or more criteria to be stratified as high risk for SBI.

Of these infants, 42% had altered urinary sediment as the only risk factor for developing SBI. Of all the CSF samples studied, one was positive for *E. coli* and urine and blood cultures were also positive for the same microorganism, confirming the diagnosis of bacterial meningitis associated with UTI (Table 3). This case accounted for 1% of the total sample studied. In two patients Enterovirus was detected by polymerase chain reaction. No other pathogenic microorganisms were isolated from the remaining CSF samples and no sterile pleocytosis was observed in any of the cases. No procedure-related complications were reported in the medical records.

The most commonly used inflammatory marker was erythrocyte sedimentation rate (ESR) in all patients, which was positive in 83% of the cases. Of these patients, only seven also presented with bacteremia and one with meningitis. PCR was requested in 22 patients and was positive in 50%, none of whom developed bacteremia or meningitis.

All patients received empirical parenteral antibiotic therapy. The mean hospital stay was 6.1 days with a median of 5 days. No complications of the infection were reported in any of the cases. No patient with a discharge diagnosis of UTI was readmitted to the study center. No death was reported in any of the medical records reviewed.

DISCUSSION

The frequency of meningitis in patients with UTI found in this study is similar to the results reported in the literature, showing a prevalence between 0.2 and 1.1%[6,8,12,13]. On the other hand, of the patients who did not undergo lumbar puncture and were treated presumptively as having UTI without meningitis, none evolved unfavorably or was readmitted to our institution due to inadequately treated meningitis. Similar results were found in other studies with a multicenter study design allowing for the possibility to detect readmissions to other institutions[8,9,14].

The finding of bacteremia coincided with the frequency reported in previous studies[15]. The patient who presented with meningitis also had associated bacteremia. Due to the potential of UTIs to become bacteremic, blood cultures continue to be part of the routine study of infants in this age group.

In our study, in which we retrospectively applied the Rochester criteria to a series of patients, we found that most corresponded to the high-risk group and were studied as such. The only patient who had meningitis and concomitant UTI was categorized as high risk according to the Rochester criteria. Nevertheless, almost half (43%) of the patients who

were classified as high risk had urinary sediment alteration as the only criterion, including the patient who developed meningitis. Unlike previous reports, no sterile pleocytosis was observed in any of the patients with UTI in whom CSF was tested, while it was found in almost 20% in some series published in the literature[16]. The risk scores on which we base our clinical practice were designed more than 30 years ago[3]. Due to improved perinatal controls and the advent of conjugate vaccines, the epidemiology of SBI in infants has changed, with a decrease in Group B *Streptococcus* and *Listeria* as well as a decrease in *Pneumococcus* and *Haemophilus* isolates, with a consequent increase in *E. coli* infections[17]. The specificity of these algorithms is insufficient to limit the use of lumbar punctures, empirical antibiotic therapy, and hospital admission[18,19].

New protocols, validated and compared with the Rochester criteria, challenge the traditional approach to the febrile infant. The use of acute phase reactants, such as procalcitonin or c-reactive protein, would allow more accurate identification of invasive bacterial infections, including bacteremia and bacterial meningitis. The Step-by-Step protocol published in 2019 and supported by the Spanish Society of Pediatric Emergencies recommends a sequential and rational approach for the study of the child younger than 90 days with fever. This score has shown greater accuracy than the Rochester criteria for SBI risk stratification[20,21]. The 2021 guidelines for the management of the febrile infant with fever without apparent focus proposed by the American Academy of Pediatrics consist of evidence-based recommendations to reduce the interventions in these patients and include the use of laboratory resources, such as procalcitonin, or other care tools, including telemonitoring of patients, that have not been fully developed in our setting[22].

SBI risk stratification in febrile infants is a common topic of discussion in Pediatric Emergency Departments. The problem is not to overlook a high-risk patient while avoiding overdiagnosis, which may lead to unnecessary complementary studies that generate stress in the child and their families. In our setting, in addition to the scarcity of diagnostic resources, a barrier to the rational care for these children is the difficulty to incorporate the family in the decision-making process due to geographic, economic, and educational limitations.

This study has certain limitations. First, lumbar puncture and CSF study were not performed in all the infants included in the study. Although patients that only received antibiotic treatment for UTI evolved favorably and did not require readmission, it is not possible to rule out the presence of meningitis in these children. The scarce data on the prevalence of the association between UTI and meningitis, together with the fact that there is still no gold standard method to identify infants at risk of developing SBI, may have led to the heterogeneous management of these patients. Second, this is a single-center retrospective study where noncomputerized medical records were reviewed and no record was kept on the criteria used by the treating clinician to assess the infant's risk of SBI. In addition, the search for patients was conducted solely on the basis of ICD-10 diagnosis, and miscoded medical records may have been missed.

CONCLUSIONS

The prevalence of bacterial meningitis in patients less than 90 days of life with UTI was 1%. Of the children who were studied to rule out CNS infection, two thirds were in the 28–59-day age group and 96% had at least one risk criterion for SBI according to Rochester criteria. The presumption of CNS infection and, therefore, the performance of lumbar puncture in these patients was based on the combination of the Rochester criteria and the clinical judgment of the treating physicians. Although the frequency of the association between UTI and meningitis in infants younger than 90 days of age appears to be low, further studies are needed to better understand the risk of meningitis and UTI in these infants.

REFERENCES

1. Bruno M, Ellis A, Ferolla FM, de Cristófano A, Ervitti A, Ferolla F, et al. Consensus for the proper use of antibiotics in children under 36 months with fever without source of infection. Arch Argent Pediatr. 2017; 115(2): S27-37.
2. Dagan R, Powell KR, Hall CB, Menegus MA. Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis. J Pediatr. 1985; 107(6): 855-60.
3. Jaskiewicz JA, McCarthy CA, Richardson AC, White KC, Fisher DJ, Dagan R, et al. Febrile Infants at Low Risk for Serious Bacterial Infection-An Appraisal of the Rochester Criteria and Implications for Management. Pediatrics. 1994; 94(3): 390-6.
4. Adragna M, Exeni A. Comité de Nefrología. Nuevas recomendaciones frente a las actuales controversias en infección urinaria. Arch Argent Pediatr. 2015; 113(6): 579-81.
5. Bergstrom T, Larson H, Lincoln K, Winberg J. Studies of urinary tract infections in infancy and childhood. XII. Eighty consecutive patients with neonatal infection. J. Pediatr. 1972; 80: 858-66.
6. Nugent J, Childers M, Singh-Miller N, Howard R, Allard R, Eberly M. Risk of Meningitis in Infants Aged 29 to 90 Days with Urinary Tract Infection: A Systematic Review and Meta-Analysis. J Pediatr. 2019; 212: 102-10.e5.
7. Tebruegge M, Pantazidou A, Clifford V, Gonis G, Ritz N, Connell T, et al. The age-related risk of co-existing meningitis in children with urinary tract infection. PLoS One. 2011; 6(11): e26576.
8. Vuillermin PJ, Starr M. Investigation of the rate of meningitis in association with urinary tract infection in infants 90 days of age or younger. Emerg Med Australas. 2007; 19(5): 464-9.
9. Paquette K, Cheng MP, McGillivray D, Lam C, Quach C. Is a Lumbar Puncture Necessary When Evaluating Febrile Infants (30 to 90 Days of Age) With an Abnormal Urinalysis? Pediatr Emerg Care. 2011; 27(11): 1057-61.
10. Lee TJ, Aronson PL. To Spinal Tap or Not To Spinal Tap, That Is the Question. Hosp Pediatr. 2018; 8(4): 236-8.
11. Martinez E, Mintegi S, Vilar B, Martinez MJ, Lopez A, Catediano E, et al. Prevalence and predictors of bacterial meningitis in young infants with fever without a source. Pediatr Infect Dis J. 2015; 34(5): 494-8.
12. Poletto E, Zanetto L, Velasco R, da Dalt L, Bressan S. Bacterial meningitis in febrile young infants acutely assessed for presumed urinary tract infection: a systematic review. Eur J Pediatr. 2019; 178(10): 1577-87.
13. Burstein B, Sabhaney V, Bone JN, Doan Q, Mansouri FF, Meckler GD. Prevalence of bacterial meningitis among febrile infants

aged 29-60 days with positive urinalysis results: a systematic review and meta-analysis. JAMA Netw Open. 2021; 4(5): e214544.

14. Wang ME, Biondi EA, Mcculloh RJ, Garber MD, Natt BC, Lucas BP, et al. Testing for Meningitis in Febrile Well-Appearing Young Infants with a Positive Urinalysis. Pediatrics. 2019; 144(3): e20183979.
15. Gomez B, Mintegi S, Benito J, Egireun A, Garcia D, Astobiza E. Blood culture and bacteremia predictors in infants less than three months of age with fever without source. Pediatr Infect Dis J. 2010; 29(1): 43-7.
16. Mintegi S, Benito J, Astobiza J, Capape S, Gomez B, Eguireun A. Well appearing young infants with fever without known source in the Emergency Department: Are lumbar punctures always necessary? Eur J Emerg Med. 2010; 17(3): 167-9.
17. Elgoibar B, Gangoiti I, Garcia-Garcia JJ, Hernandez-Bou S, Gomez B, Martinez Indart L, et al. Paediatric Escherichia coli bacteraemia presentations and high-risk factors in the emergency department. Acta Paediatr. 2021; 110(3): 1032-7.
18. Kuppermann N, Mahajan P, Ramilo O. Prediction models for febrile infants: Time for a unified field theory. Pediatrics. 2019; 144(1): e20191375.
19. Rogers AJ, Kuppermann N, Anders J, Roosevelt G, Hoyle JD, Ruddy RM, et al. Practice Variation in the Evaluation and Disposition of Febrile Infants ≤ 60 Days of Age. J Emerg Med. 2019; 56(6): 583-91.
20. Gomez B, Mintegi S, Bressan S, da Dalt L, Gervaix A, Lacroix L. Validation of the "step-by-step" approach in the management of young febrile infants. Pediatrics. 2016; 138(2): e20154381.
21. Kuppermann N, Dayan PS, Levine DA, Vitale M, Tzimenatos L, Tunik MG, et al. A Clinical Prediction Rule to Identify Febrile Infants 60 Days and Younger at Low Risk for Serious Bacterial Infections. JAMA Pediatr. 2019; 173(4): 342-51.
22. Pantell RH, Roberts KB, Adams WG, Dreyer BP, Kuppermann N, O'Leary ST, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. Pediatrics. 2021; 148(2): e2021052228.