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Lumbar puncture in infants with urinary tract infection: assessment of infant management in the emergency department

Short title: Bacterial meningitis in infants with urinary tract infection

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Declaration of interest:

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Abstract

Background: Neonatal bacterial infections must be bacteriologically confirmed from laboratory samples to best adjust antibiotic therapy. Lumbar puncture (LP) has been recommended for infants younger than 1 month with suspected serious bacterial infection (SBI) to manage possible meningitis. However, the incidence of bacterial meningitis associated with other infections and particularly with urinary tract infections (UTIs) is low. Recourse to systematic LP may be less essential if infants have a UTI.

We aimed (a) to determine the management and frequency of bacterial meningitis coexisting with a documented diagnosis of UTI in infants aged < 1 month who had an LP, and (b) to evaluate the management of infants in emergency admissions with suspected SBI while assessing antibiotic treatment. *Methods:* We conducted a retrospective single-center study from January 2010 to April 2019 including all cases of neonatal bacterial infections, and collected data on the clinical, laboratory, and radiological features.

Results: In all, 409 infants were included in the study. Of these, 162 (39.6%) presented with a UTI and eight (2%) had bacterial meningitis. Of the infants diagnosed with UTI, 74.7% had an LP, of whom 34.7% experienced LP complications. No coexistence of UTI and bacterial meningitis was found among infants who had an LP and a documented UTI.

Conclusion: Although not all infants had an LP and a urine culture at the same time, these results show that bacterial meningitis coexisting with a confirmed UTI diagnosis in infants is rare. Furthermore, LP can be traumatic in some cases and therefore its utility should be assessed according to the clinical context.

Keywords: Bacterial meningitis, urinary tract infection, neonatal bacterial infection, lumbar puncture.

1. Introduction

The diagnosis and management of neonatal infections are major activities in pediatric emergency departments. On examination, most infants do not have specific clinical symptoms that point to a particular tissue infection [1]. Viral infections are the most common [2], but serious bacterial infections (SBIs) including urinary tract infections (UTIs), meningitis, and septicemia are the causes of 5–10% of cases of neonatal fever [3]. The frequency of SBI is inversely proportional to age: 21.6% before 1 week and 12% before 1 month of age [3,4].

The most frequent bacteria responsible for SBIs in infants younger than 3 months are *Escherichia coli* (56–61%) and group B *Streptococcus* (6–21%) [5]. UTIs make up 65% of SBIs, bacteriemia 16%, meningitis 2%, UTI and bacteriemia 6%, meningitis and bacteriemia 5%, and UTI and meningitis 1% [6]. UTIs, the most frequent SBIs, predominate in boys, can give rise to atypical or nonspecific symptoms of infection (icterus, isolated digestive disorders, isolated fever, sepsis) [7], and in 80% of cases are due to *E. coli* [6].

Concerns about a possible SBI lead to many invasive procedures in newborns (infants aged under 1 month) such as venipuncture, lumbar puncture (LP), probabilistic intravenous antibiotic therapy, and hospitalization to await the laboratory results [8].

In the current guidelines, LP is performed systematically for suspected SBIs in newborns to rule out meningitis and adjust the dose of antibiotics, even when a UTI has been documented with no clinical signs of severity. However, the association of UTI and bacterial meningitis is rare [9]. Moreover, LP can be traumatic, hemorrhagic, difficult to interpret, fallible, and operator-dependent. Systematic recourse to LP with center-dependent procedures has led to debate among clinicians [10]. According to the literature, systematic LP is probably less essential in infants with a UTI.

The main objective of this retrospective study was to determine the management and frequency of bacterial meningitis coexisting with a documented diagnosis of UTI in infants younger than 1 month in our hospital. The secondary objectives were to determine the number of LPs, LP complications, and subsequent adjustment of antibiotic doses, and review the diagnostic procedures for infants with suspected infection.

2. Patients and methods

2.1 Population and study design

This single-center retrospective study included data of neonates examined in the pediatric emergency department for suspected SBI at the University Hospital of Clermont-Ferrand from January 2010 to April 2019. Inclusion criteria for clinically suspected SBI were: infants younger than 1 month with fever, diarrhea, vomiting, nutritional difficulties, weight gain insufficiency, weight loss, icterus, hemodynamic and respiratory and/or neurological failure. Exclusion criteria were premature birth, cardiac or digestive malformation, anoxic–ischemic encephalopathy or neonatal stroke, nosocomial infection, and absence of medical record data.

For each patient, the following features were recorded: age; risk factors for early-onset neonatal infection (EONI); clinical symptoms on admission; clinical severity criteria (hemodynamic, respiratory, or neurological failure); results of laboratory and radiological examinations; list, dose, and duration of antibiotics; LP procedure; and LP complications (hemorrhagic, insufficient or coagulated sample, or LP failure). Risk factors of EONI were: maternal group B *Streptococcus* colonization (in the setting of inadequate prophylactic treatment), chorioamnionitis, maternal fever higher than 38 °C, prolonged rupture of membranes > 12 h, meconium or tinted staining, and fetal heart rate abnormality. We considered hemodynamic failure as: low blood pressure (<60 mmHg systolic), heart rate <

80 bpm, use of vasopressors or vascular filling, perfusion abnormality or shock clearly stated in the patient's file. Respiratory failure was considered if there was: ventilator support (intubation, continuous or bilevel positive airway pressure), respiratory frequency > 60 breaths/min or respiratory distress. Urine cultures were considered positive if: leukocyte count > 10 cells/mm³ and bacteriuria $\geq 10^4$ colony-forming units (CFU)/mL [9] or if it was recorded as positive in the hospital report even when multiple microorganisms were found on culture. Urine samples were collected by urine bag or urinary tract catheter. Cerebrospinal fluid (CSF) was considered inflammatory when CSF white blood cells (WBC) > 20 cells/mm³ and hemorrhagic when red blood cells (RDB) > 5000 cells/mm³. A CSF WBC/RBC ratio of 1/1000 was used for interpretation of hemorrhagic CSF as recommended by Lyons et al. [11]. Viral meningitis was considered when a polymerase chain reaction (PCR) test was positive for virus detection. A diagnosis of bacterial meningitis was retained in the presence of a pathogenic bacteria on CSF direct examination or culture with or without inflammatory CSF or in the case of an inflammatory CSF with predominant polynuclear neutrophils in the WBC count. A positive hemoculture for coagulase-negative *Staphylococcus* was not considered as an invasive bacterial infection but was considered as probably contaminant.

2.2 Data collection, statistical analyses, and ethical considerations

Medical records were selected using the local software CORA with the keywords “pyelonephritis,” “urinary tract infection,” “meningitis,” “bacterial infection,” “sepsis,” “fever,” “lumbar puncture,” and “neonatal infection” for infants aged < 1 month.

Statistical analyses were performed using Stata software (version 13, StataCorp, College Station, US). Categorical data are presented as absolute values and percentages. Continuous data are expressed as mean and standard deviation (SD) or median and interquartile range (IQR) according to their statistical distribution. The assumption of normality was assessed using the Shapiro–Wilk test.

This single-center retrospective study complied with the ethical standards of the institutional research committee. Non-opposition to retrospective collection of clinical data was obtained from parents.

3. Results

3.1 Population, laboratory, and radiological results

A total of 1036 medical records were listed in the initial search request. Subsequently, 627 records were excluded because of other pathological conditions ($n=621$) or missing data ($n=6$) (**Fig. 1**). A total of 409 patients were included; the median age was 18 days (interquartile range [IQR]: 11–25).

Risk factors for EONI were present in 47.4% ($n=194$) of cases, with vaginal or neonatal samples positive for group B *Streptococcus* in 36% of cases and for *E. coli* in 19% of cases; the samples were negative in 38% of cases. At admission, of all the infants included, 21.5% ($n=88$) had no fever, 45.5% ($n=186$) had isolated fever, and 17.4% ($n=71$) had infection by contagium. Clinical severity criteria were identified in 18.8% of cases ($n=77$) (**Table 1**).

Microbiological samples comprised LP ($n=267$, 65.3%), viral respiratory tract sample ($n=153$, 37.4%), urine culture ($n=404$, 98.9%), and blood culture ($n=304$, 74.3%). Overall, 74 patients (27.7%) who had an LP met the clinical severity criteria (**Tables 1 and 2**).

C-reactive protein (CRP) was assayed in 392 neonates (96%) and procalcitonin in 328 neonates (80%) (**Table 1**).

A viral infection (viral culture PCR positive) was confirmed in 201 neonates (49.1%) (**Table 1**). Of these, 27 (13.4%) met the clinical severity criteria on admission.

A bacterial infection was documented for 186 infants (45.5%), with a majority of UTI ($n=162$, 39.6%). *E. coli* was the main germ identified in the case of UTI (95.6%) (**Table 3**).

Among the infants with a UTI, multiple microorganisms were found in the culture in three cases and two germs were found in 22 cases. Bacterial meningitis was diagnosed in eight patients (2.0%). The bacteria identified in CSF were Group B *Streptococcus* ($n=4$), *E. coli* ($n=3$), and *Enterococcus faecalis* ($n=1$). Thirteen patients (3.1%) had a probable bacterial infection with no identified germ. There was no laboratory evidence of an infection in 22 cases (5.4%) (**Table 1**). Overall, 37 patients (22.8%) with a UTI and six patients (75%) with bacterial meningitis met the clinical severity criteria on admission.

Of those patients with confirmed UTI, eight had viral meningitis coexisting with enterovirus and eight had coexisting elevated white cell count in the CSF but without predominant polynuclear neutrophils, without elevated protein in the CSF and without positive bacterial culture. Bacteremia was identified in 24 patients (5.9%) and was associated with UTI in 9.9% of cases ($n=16$) and with four out of the eight cases of meningitis (**Table 2**). Of the infants with confirmed meningitis, two did not meet the clinical severity criteria nor did they have bacteremia.

Ultrasound examinations of urinary tracts were performed on 154 of 162 infants with UTI (95.1%) and 46 of 154 (29.9%) showed malformative uropathy or vesicoureteral reflux.

3.2 Failed lumbar puncture and complications

Of the total of 267 LPs, 84 (31.7%) failed: 44 CSFs were hemorrhagic, 26 CSFs were coagulated, 12 LP procedures failed to obtain CSF, and one analysis was not feasible owing to insufficient CSF. One patient became ill during the LP procedure. Among the 162 patients with confirmed UTI, 121 (74.7%) had an LP, of whom 42 (34.7%) had complications or failed LP, 73 (60.3%) had a urine culture before the LP procedure, and 37 (22.8%) presented with clinical severity criteria on admission (**Table 2**). Among the 84 cases of failed LPs, 21

(25%) infants met the clinical severity criteria and of the available LPs, 52 (28%) infants met the clinical severity criteria.

3.3 Antibiotic therapy

A total of 288 infants (70.4%) had received intravenous antibiotic therapy (**Table 2**). The most frequently prescribed antibiotic combination was cefotaxime and gentamycin, in 183 of the 288 infants (63.5%) (**Table 4**). The mean duration of antibiotic therapy was 8.9 days (SD=5.4). A meningeal dose of cephalosporin was initially prescribed to 75 patients (18.3%). Of these, 30 (40%) met clinical severity criteria and 11 patients had a secondary adjusted dose after a negative CSF culture (**Table 2**). A viral infection was finally identified in 98 of the 288 treated infants (34.0%), and 46 of the 288 patients (16.0%) had cessation of antibiotic therapy in the 3 days following the first prescription, due to a viral etiology or negative microbiological test results. A meningeal dose of cephalosporin was initially prescribed to six of eight patients with bacterial meningitis. Of 162 patients with a UTI, 34 (20.9%) had a meningeal dose initially prescribed, but only eight had an adjusted dose (**Table 2**).

3.4 Prevalence of meningitis in infants with UTI

Of the 186 neonates with invasive bacterial infection, eight had isolated meningitis, two had isolated bacteremia, and 162 had isolated UTI. Four infants had meningitis and bacteremia, 12 had UTI and bacteremia, and none had coexisting UTI and bacterial meningitis. However, only four of eight patients (50%) with bacterial meningitis had an initial urine culture before antibiotic therapy and only 121 of 162 patients with confirmed UTI (74.7%) had an LP.

4. Discussion

In this study we set out to retrospectively identify bacterial meningitis coexisting with a confirmed diagnosis of UTI in infants, and to review the management of these infants with suspected SBI in emergency admissions, with assessment of antibiotic treatment. To this end, all the infants admitted for a suspected neonatal infection were included in the study over a period of 9 years.

Of the 409 patients included, 186 had a bacterial infection and 87.1% had UTIs. In the literature, the rate of UTIs among bacterial neonatal infections has been reported to be 65% [6]. In our study a UTI was also the most frequent form of bacterial neonatal infection. The number of UTIs was probably overestimated because of the urine collection mode and also because we took into account urine culture with multiple microorganisms. In our hospital we principally use a urine bag, which can generate many false-positive results [12] and a high contamination rate [13]. Urinary tract catheter is only used after urine bag failure. According to the guidelines of the European Association of Urology [14], urine sampling by suprapubic aspiration or catheterization is the best urinary collection mode and has a low contamination rate. This method is not used in current practice because it is invasive and painful.

A total of 288 infants (70.4%) had received intravenous antibiotic therapy. A meningeal dose of cephalosporin was initially prescribed to 75 patients (18.3%). Of these, 30 (40%) met the clinical severity criteria and 11 had a secondary adjusted dose after a negative CSF culture. Of the infants with a UTI, 37 met the clinical severity criteria, two of 37 had no LP, and nine of 37 had a non-contributory LP.

Addressing the risk of bacterial neonatal meningitis is important for avoiding mortality and morbidity and for adjusting the dose and duration of antibiotic therapy [15]. In our study,

eight of 186 patients with a bacterial infection (4.3%) had bacterial meningitis, versus 2% reported in the literature [6]. Six of these patients met clinical severity criteria and received an initial meningeal dose of antibiotics. However, we did not identify coexisting bacterial meningitis in patients with a confirmed UTI who had an LP. We note that not all infants with a UTI had an LP, which can distort our results insofar as many infants had a non-contributory LP.

The meta-analysis by Tebruegge et al. [15] and Thomson et al. [16] reported less than 2% of coexisting bacterial meningitis and UTI in infants aged under 2 months Schnadower et al. [17] found only 0.1% of multiple localizations of infection, while Wang et al. found no coexisting bacterial meningitis in infants with UTI [18]. This confirms that the occurrence of bacterial meningitis in young infants with documented UTI is unusual.

Besides being painful, an LP can be source of various complications [19]: 10–30% of LPs can be traumatic [11]. In our study, 267 neonates had an LP, and complications or failure occurred in 20.5%. Complications may also have been underestimated, as pain induced by the LP procedure was summarily reported in the records, even when pain management was applied.

The latest American [4], British [20], and French [21] national guidelines for the management of suspected neonatal bacterial infection do not state LP indications, and not for confirmed UTI. In this study, urine culture was carried out on 42% patients before the LP procedure. This suggests that the LP procedure could be avoided when UTI is strongly suspected and there are no clinical severity criteria.

This would also allow for an initial adjusted dose of antibiotics to be prescribed for UTIs. The latest guidelines of the French Pediatric Society for antibiotic doses in cases of suspected bacterial meningitis in infants is 200 mg/kg/day of cefotaxime in association with an aminoglycoside +/- amoxicillin with secondary adjustment according to the antibiogram, versus

the conventional dose of 100 mg/kg/day in other SBIs [22]. When antibiotic therapy is initiated at the meningeal dose, a secondary adjustment according to the conventional dose is recommended in the case of a negative CSF culture [10]. The recommended duration of antibiotic therapy in bacterial meningitis can range from 7 to 21 days, versus 10 days in a UTI. In our study, 75 patients had an initial meningeal dose of antibiotics, including 30 patients meeting clinical severity criteria. Eight of these 75 cases had confirmed bacterial meningitis. Of the 67 patients without confirmed bacterial meningitis, only 11 had a secondary adjusted dose of antibiotics, resulting in an excessive dose being taken for several days.

A viral infection was finally identified in 98 of 288 treated infants (34.0%), and 46 of 288 patients (16.0%) had cessation of antibiotic therapy in the 3 days following the first prescription, due to a viral etiology or negative microbiological test result. Of the 162 patients with a UTI, 34 (20.9%) had a meningeal dose initially prescribed, but only eight had an adjusted dose.

These results show that excessive antibiotic therapy is used even when viral infections were confirmed. Adherence to recommendations for management of young infants suspected of SBI seems difficult to apply, possibly because evaluation and treatment differ among hospital practitioners. A study of 573 office-based practitioners across the United States showed that pediatric clinicians used individualized clinical judgment when treating febrile infants younger than 3 months, including neonates [3]. The pursuit of antibiotic therapy can also be due to the clinical evolution or the laboratory results during hospitalization, but this information was not sought. The deviation of practitioners' strategies from established guidelines may also reflect their fear of underestimating or undertreating young infants with an IBS, especially meningitis.

Elevated white cell count in the CSF without bacterial meningitis has been previously reported in UTIs in infants. Shah et al. [23] found 18.5% of inflammatory CSF among 1025 infants with UTI and Schnadower et al. report a similar level of 18% in 1190 infants [24]. Tebruegge et al. [15] did not find a higher evolutive risk in these infants than in those with isolated UTI, suggesting the use of a conventional dose of antibiotics in this condition. We found a lower level of this association in our cohort (6.6%), possibly due in part to a nonsystematic LP procedure or an overestimation of UTI. The cause of this associated CSF inflammation is still debated (associated viral meningitis or mediated neuroinflammation) [19].

Our study has several limitations typical of retrospective studies and due to many selection biases. These include potential biases in data collection. First, the number of UTIs was probably overestimated because some urine cultures were interpreted as UTIs when there were multiple microorganisms. As we did not want to change the diagnoses of UTI already made, we took these cases into account. Not all infants who had bacterial meningitis had a urine culture, and not all infants with a documented UTI had an LP. We also considered bacterial meningitis with positive CSF cultures without taking into account glycorrachia, which can lead to an underestimation of the number of bacterial meningitis cases.

The results of the literature thus suggest that bacterial meningitis rarely occurs in neonates with UTI, but because of the several biases of our study and the small number of patients, we cannot argue for or against systematic LP procedure in neonates with a UTI who do not meet clinical severity criteria. Our study also reveals unsatisfactory management among some practitioners.

To guide practice, there are various recommendations to be made in different areas: the urine collection mode [13], the diagnosis, and use of antibiotics in cases of meningitis [25] or in UTI [15].

The overuse of antibiotics must also be considered because of their side effects such as allergic reactions, bacterial resistance, diarrhea, *Clostridium difficile* infection, renal insufficiency, etc. [26,27]

To improve our practice, the performance of clinicians, particularly the management of neonates with a suspected IBS, should be analyzed in detail to evaluate how well the guidelines are followed and whether care is truly optimized.

Several avenues for further improvement can be considered: better teamwork, renewal and training of practitioners, control of prescriptions, regular referral to guidelines [28], antibiotic vigilance, and re-evaluation of antibiotic therapy.

Our purpose was also to propose a strategy for the management of neonatal infections (**Figure 2**) justified by the very low incidence of associated bacterial meningitis in patients with a confirmed UTI, combined with the risk of complications of LP.

However, a larger prospective study will be needed to help validate this procedure.

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Table 1. Patient characteristics and microbiological diagnoses

Clinical data and procedures	
Total number of patients	409
Median age (days) (interquartile range)	18 (11–25)
Risk factors of EONI, <i>n</i> (%)	194 (47.4)
Fever, <i>n</i> (%)	321 (78.5)
Isolated fever, <i>n</i> (%)	186 (45.5)
Infection by contagium, <i>n</i> (%)	71 (17.4)
Clinical severity criteria, <i>n</i> (%)	77 (18.8)
CRP, <i>n</i> (%)	392 (95.8)
• Median (mg/L) (interquartile range)	41 (1.45–26.7)
• CRP < 3 mg/L, <i>n</i> (%)	159 (40.6)
• Maximum (mg/L)	285
PCT, <i>n</i> (%)	328 (80.2)
• Median (µg/L) (interquartile range)	14 (0.1–0.44)
• PCT < 0.1 µg/L, <i>n</i> (%)	70 (21.3)
• PCT < 0.5 µg/L, <i>n</i> (%)	165 (50.3)
• Maximum (µg/L)	204
LP, <i>n</i> (%)	267 (65.3)
• Positive viral PCR	52 (19.5)
➤ Enterovirus	46 (88.5)
➤ Parechovirus	5 (9.6)
➤ Coxsackie virus	1 (1.9)
Virus of respiratory tract, <i>n</i> (%)	153 (37.4)
Urine culture, <i>n</i> (%)	404 (98.8)

Blood culture, <i>n</i> (%)	304 (74.3)
Viral infections (standard PCR), <i>n</i> (%)	201 (49.1)
• Enterovirus	54 (26.8)
• Rhinovirus	33 (16.4)
• Rotavirus	9 (4.4)
• Influenza A virus	8 (3.9)
• Coxsackie virus	1 (0.5)
• Respiratory syncytial virus	8 (3.9)
• Parechovirus	4 (1.9)
• Influenza B virus	2 (0.9)
• <i>Herpes simplex</i> virus 1	1 (0.5)
Bacterial infections, <i>n</i> (%)	186 (45.5)
• UTI	162 (39.6)
• Meningitis	8 (2.0)
• Osteo-arthritis	1 (0.2)
• Parotiditis	1 (0.2)
• Pneumonia	1 (0.2)
• Septicemia	2 (0.5)
• Infection with no identified germ	13 (3.1)
No bacterial or viral infection identified, <i>n</i> (%)	22 (5.4)

n: Number of patients,; EONI: early-onset neonatal infection; CRP: C-reactive protein; PCT: procalcitonin; PCR: polymerase chain reaction; LP: lumbar puncture; UTI: urinary tract infection.

Table 2. Combined results of procedures and diagnoses in all patients and in patients with UTI

Condition	Total patients	Patients with
	<i>n</i> (%)	UTI <i>n</i> (%)
Total	409	162
Viral meningitis	52 (20)	8 (4.9)
Bacterial meningitis	8 (2.0)	0
Bacterial meningitis + clinical severity criteria	6 (75)	0
Clinical severity criteria	77 (18.8)	37 (22.8)
Urine culture	404 (98.8)	162 (100)
LP	265 (64.8)	121 (74.7)
Complicated or failed LP	84 (20.5)	42 (25.5)
LP + clinical severity criteria	74 (27.7)	37 (22.8)
Urine culture before LP procedure	169 (42)	73 (60.3)
Isolated inflammatory CSF	22 (8.2)	8 (6.6)
Bacteremia	24 (5.9)	16 (9.9)
Antibiotic therapy	288 (70.4)	162 (100)
Initial meningeal dose of antibiotics	75 (18.3)	34 (20.9)
Initial meningeal dose of antibiotics + clinical severity criteria	30 (40)	37 (22.8)
Secondary adjustment of dose of antibiotics after negative CSF culture	11 (2.7)	8 (23.5)

n: Number of patients; UTI: urinary tract infection; LP: lumbar puncture; CSF: cerebrospinal fluid.

Table 3. Results of urine culture in 162 confirmed UTIs

Bacteria found in UTI	n (%)
<i>Escherichia coli</i>	155 (95.6)
<i>Enterococcus faecalis</i>	27 (16.6)
Group B <i>Streptococcus</i>	12 (7.4)
<i>Enterobacter cloacae</i>	7 (4.3)
<i>Klebsiella pneumoniae</i>	6 (3.7)
<i>Klebsiella oxytoca</i>	1 (0.6)
<i>Citrobacter koseri</i>	1 (0.6)
<i>Enterobacter aerogenes</i>	1 (0.6)
UC with two germs	22 (13.6)
Multiple microorganisms (at least three germs)	3 (1.8)

n: Number of cases; , UTI: urinary tract infection, UC: urine culture.

Table 4. Probabilistic antibiotic therapy

Probabilistic antibiotic combination	<i>n</i> (%)
Total number of probabilistic antibiotic therapies	288
Cefotaxime + gentamycin	183 (63.5)
Cefotaxime + gentamycin + amoxicillin	61 (21.2)
Ceftriaxone + gentamycin	18 (6.3)
Amoxicillin + gentamycin	13 (4.5)
Other combinations	13 (4.5)

n: Number of antibiotic therapies.

Legends to figures

Figure 1. Scheme of case inclusions.

Distribution of included and excluded patients is shown together with the distribution of final diagnoses.

n: number; UTI: urinary tract infection; CSF: cerebrospinal fluid; CBU: cytobacteriological examination of urine

Figure 2. Proposal for management of neonatal infections.

A proposal for the management of neonatal infections, including urinary tract infection (UTI) without clinical severity criteria is presented.

CRP: C-reactive protein; PCT: procalcitonin; PCR: polymerase chain reaction; LP: lumbar puncture.

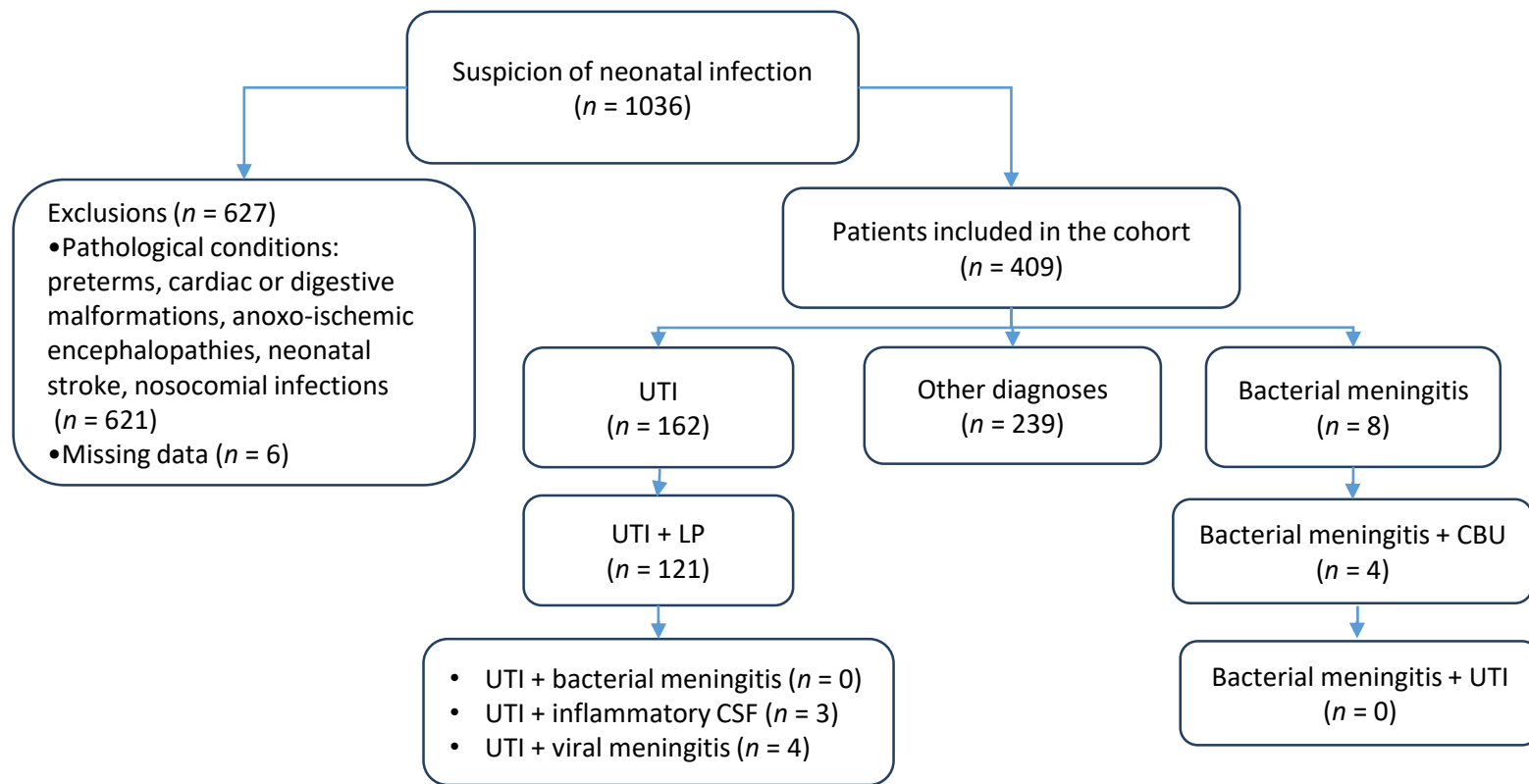


Figure 1. Scheme of inclusions

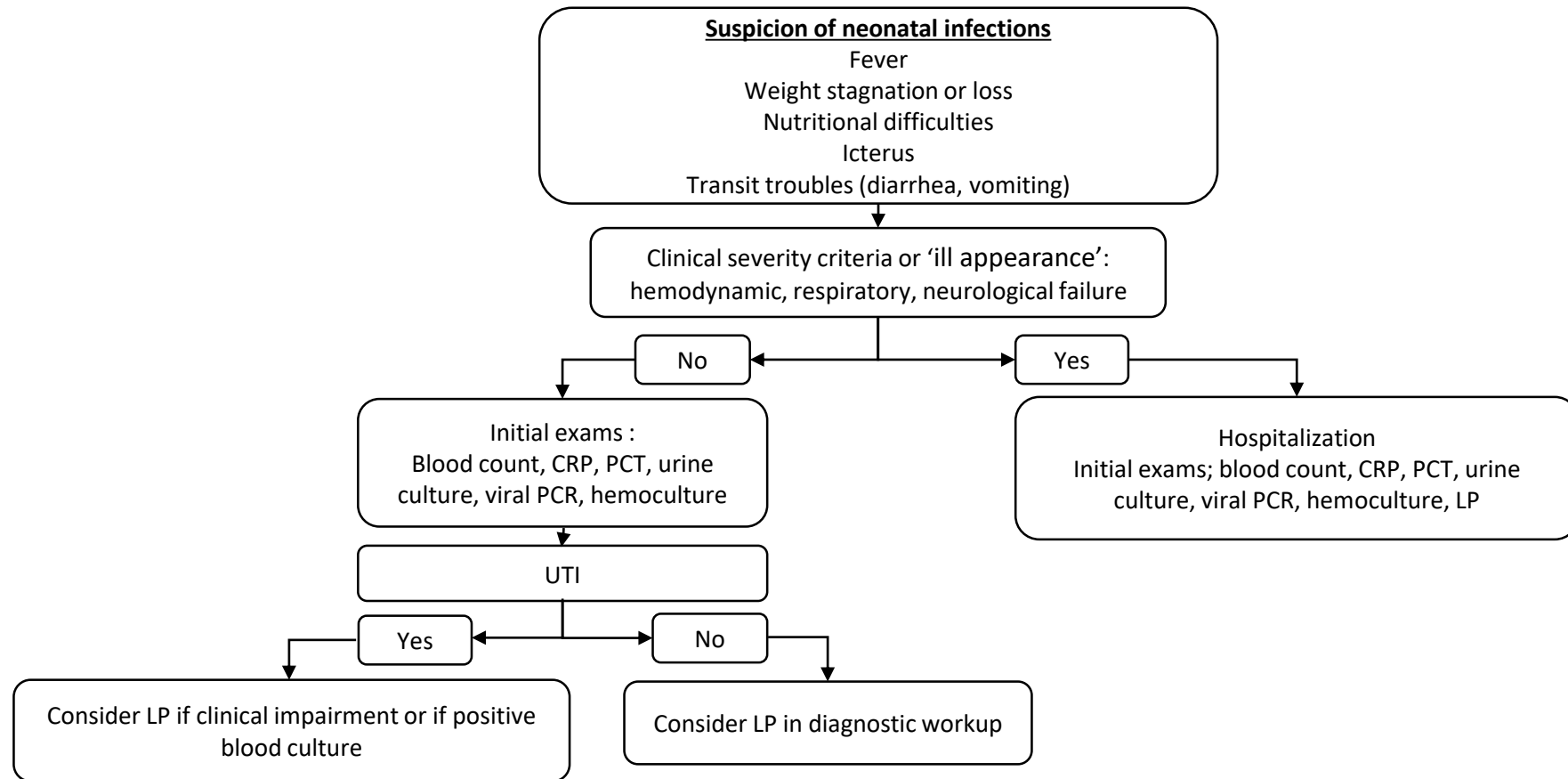


Figure 2. Proposition for a diagnostic procedure in neonates suspected of bacterial infections