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Epidemiological, Clinical, and Diagnostic Aspects of Urinary Tract Infection in Newborns at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A) in Benin

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Abstract

To study epidemiological and diagnostic aspects of urinary tract infection (UTI) in newborns at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A). This was a cross-sectional study conducted from April 1, 2019 to September 30, 2019 and concerned all newborns admitted to the neonatal unit of DTH-B/A. According to the National Agency for Health Accreditation and Evaluation (NAHAE)recommendations of 2002, all symptomatic newborns who did not have a visible malformation outside the genitourinary system and whose parents gave their consent were included in the study. The census was exhaustive despite the calculated minimum size of 109 newborns. Urine sedimentation and cytobacteriological examination of urine samples, taken in adhesive bags after local disinfection, demonstrated presence of pathogenic microbes. Sensitivity of detected microbes was studied to different antibiotics. Interpretive reading of antibiograms was established according to the Standards of the French Society of Microbiology (FEMS), edition 2012. If UTI was confirmed, an abdominopelvic ultrasound was performed in search for a malformative uropathy as a contributing factor in newborns. A standardized survey was developed for data collection. The data entered were analyzed using the Epi info software, version 3.5.4. In all, 124 newborns were included in the study. UTI accounted for 8.06% of all neonatal infections and 2.15% of admissions. The average age of onset was 7.8 days, with a gender ratio of 1:1. The main clinical manifestations were jaundice and respiratory distress. Microbes involved were *Staphylococcus aureus* (6/10), *Escherichia coli* (2/10), and *Klebsiella oxytoca* (2/10). The resistance of microbes to antibiotics was generally high. No abnormalities were revealed in the ultrasound. Although neonatal UTI is not a rare infection, bacterial resistance is of concern.

Keywords: Benin, newborn, urinary tract infection

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Introduction

One of the serious bacterial infections in pediatrics is urinary tract infection (UTI) (1). It often goes unnoticed in newborns due to difficulties in diagnosis, as its symptoms are embedded in the group of overt neonatal sepsis (NNS). In Africa, little data are available on the subject. In fact, only a few hospital series covering a limited number of cases are available. In Madagascar, Robinson et al. (2) found pediatric prevalence of UTI in less than 2% cases. This is because clinical manifestations of UTI are often nonspecific in newborns, not forgetting the high cost that limits access to the cytobacteriological examination of urine (CBEU), a key examination for positive diagnosis (2), and unavailability of the study of urine sedimentation. Moreover, even though the CBEU is done, there are difficulties in collecting urine samples (3).

It has been established in young children that reducing the morbidity associated with UTI and preventing its complications, including kidney scarring, requires early diagnosis and effective treatment of the infection (3,4). In several African countries in the south of Sahara, few teams of pediatricians routinely screen symptomatic newborns for UTI (5). In addition, even if the diagnosis is made, it is rare that further investigations are performed to make etiologic diagnosis or to look for complications that could be severe. The present study was undertaken in 2019 to enrich literature; to make available the data on UTI in newborns not accessible in our country; and to study epidemiological, clinical, etiological, and progressive aspects of UTI in newborns at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A).

Patients and Methods

This was a cross-sectional study with prospective data collection carried out in the neonatology unit of the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A) in Parakou, Benin, over a period of 5 months (from April 03, 2019 to September 26, 2019). It pertained to all newborns admitted to the neonatal unit of DTH-B/A in 2019 during the study period and meeting study's inclusion criteria. According to the National Agency for Health Accreditation and Evaluation (NAHAE)recommendations of 2002 (6), all symptomatic newborns whose parents gave their informed consent were included in this study. Newborns with a defect visible from outside the genitourinary system that could be the cause of UTI symptoms were excluded from the study. The sampling was done on non-probability basis by an exhaustive census and involved all newborns admitted to the neonatal unit of DTH-B/A during the study period and meeting inclusion criteria. In addition, a minimum size of 109 newborns was retained on the basis of hospital frequency of UTI in newborns of 7.7% at the Teaching Hospital of Cocody in 2006 (7).

The dependent variable was UTI in the newborn and retained according to the results of CBEU, that is, presence of at least 10,000 leukocytes/mm³ and 1,000,000 bacteria/mm³ National Agency for Health Accreditation and Evaluation (NAHAE) 2002 (6).

The independent variables were socio-demographic aspects (age, gender, and ethnicity), clinical aspects (reason for consultation, gestational history, and physical signs), and paraclinical aspects (urine sedimentation, C-reactive protein, white blood cell [WBC] count, and CBEU).

Urine was collected in an adhesive bag after local disinfection and breastfeeding if possible; the bag was replaced every 30 min even if the newborn did not pass urine. The samples were taken before any antibiotic treatment and sent within 2 h of collection to laboratory for analysis. The urine collected was inoculated on a culture medium; the three culture mediums used were as follows: CLED (Cystine-Lactose-Electrolyte-Deficient) agar, for counting of germs; CHAPMAN agar; and EMB agar.

Urinary sedimentation: Urine sedimentation was carried out with 10 mL of the second urine passed in the morning. The collected urine sample was centrifuged at 2000 revolutions per minute (rpm) for 10 min. Field-by-field analysis under a microscope was conducted with 50 µL of the pellet spread on a slide covered with a cover slip. The cylinders were sought at 200× magnification and all other elements were shown at 400× magnification (8).

Data were collected through an individual face-to-face interview with a parent of the newborn (father or mother) using a developed and pre-tested standardized survey.

Quality control was done on a daily basis. Interpretative reading of antibiograms was made according to the Standards of the French Society of Microbiology (FEMS), edition 2012 (8). If UTI was confirmed, an abdominopelvic ultrasound was performed to search malformative uropathy as a contributing factor in newborn patients.

Sample analysis was carried out in the hospital, and the data were taken and completed from patients' files. The processing of files was completed manually. Double data entry and analysis were carried out using the Epi info software, version 3.5.4. Tables and figures were produced using the Microsoft Word and Excel software, version 2013. Proportions were calculated for qualitative variables. Quantitative variables were expressed as mean values and standard deviation for those with normal distribution, while median and inter-quartile range (Q1 and Q3) were calculated for quantitative variables with skewed distribution. The proportions were compared using the Chi-square test or Fisher's exact test. For different associations, the significance threshold used was 5%. This research work was initiated at the Faculty of Medicine of the Teaching Hospital of Borgou-Alibori (DTH-B/A) Written and oral informed consent of a parent (mother or father) of a newborn was obtained before administration of

a questionnaire. The rules of anonymity and confidentiality of the information collected were respected.

Results

Frequency

Of the 466 newborns admitted during the study period, 124 were symptomatic, including 10 CBEU positive cases, with a relative frequency of 8.06% and a hospital frequency of 2.15%.

Sociodemographic aspects

The average age of newborns was 7.8 days (range: 1–26 days). There were five baby boys and five baby girls with a gender ratio of 1:1. Of these 10 newborns, two were premature, and seven were born vaginally. In the 6-month study, six cases were recorded in July 2019.

Clinical aspects

In three newborn patients, the first reason for consultation was fever and jaundice. The most frequent general signs in newborns with a positive urine culture were fever and polypnea, which were found in two of the 10 cases. The most frequent physical signs in newborns with a positive urine culture were jaundice and respiratory distress (five patients each). The obvious urinary tract abnormalities found in neonates with positive urine culture included one case of hypospadias and one case of phimosis. On macroscopy, urine samples were cloudy in all 10 cases. Urinary dipstick leukocyturia was found in eight of the 10 cases. Table 1 summarizes the results of clinical data.

Table 1: Distribution of newborns at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A) with a positive uroculture according to clinical data (n = 10) in 2019.

	(n = 10)
Reasons for consultation	
Fever	3
Jaundice	3
Respiratory distress	2
Neurological signs	2
General signs	
Fever	2
Polypnea	2
Physical signs	
Fever	5
Jaundice	5
Neurological signs	4
Obvious device anomalies	
Hypospadias	1
Phimosis	1
Macroscopic examination of urine	
Cloudy urine	10
Dipstick	
Hypodense urine	2
Normal density	5
Hyperdense urine	3
Urine at acidic pH	2
Urine at normal pH	5
Urine at alkaline pH	3
Leukocyturia	8

Paraclinical aspects

In 10 newborn patients with positive urine culture, blood tests demonstrated normal leukocyte counts, and six had positive *C-reactive protein* (CRP).

The urine sediment demonstrated the presence of superficial transitional cells in two newborns. The organisms isolated on CBEU were:

- *Staphylococcus aureus* (Gram-positive cocci) was detected in six cases.
- Gram-negative bacilli, two cases each of *Escherichia coli* and *Klebsiella oxytoca* were detected.

In terms of sensitivity of the antibiotics tested, the microbes were more susceptible to imipenem in eight of the nine cases. *Staphylococcus aureus* was resistant to all third-generation cephalosporins tested and was susceptible to imipenem for all urine samples of the cases tested. Enterobacteriaceae isolated were resistant to 100% amoxicillin and clavulanic acid, and in 50% of the cases to ceftazidime and quinolones. Table 2 shows sensitivity of the organisms isolated to the tested antibiotic susceptibility (ATBs).

Therapeutic aspects

Of the 10 cases, three newborns received the combination of cefotaxime–gentamicin, three received the combination of cefotaxime–gentamicin–ampicillin, and one

Table 2: Distribution of germs isolated from newborns at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A) in 2019 presenting urinary tract infection according to their sensitivity to antibiotics.

	Number of times tested	*Staphylococcus aureus*			Enterobacteriaceae (*Escherichia coli* and *Klebsiella oxytoca*)		
		Sensitive N	Intermediate N	Resistant N	Sensitive N	Intermediate N	Résistant N
Amoxicillin and clavulanicacid	08	00	00	06	00	00	02
Cefixime	08	00	00	06	00	01	01
Ceftriaxone	08	00	00	06	00	01	01
Ceftazidime	08	00	00	06	01	00	01
Imipeneme	08	05	01	00	02	00	00
Norfloxacin	06	00	01	03	01	00	01
Lévofloxacin	06	00	01	03	01	00	01
Ciprofloxacin	06	00	00	04	01	00	01
Gentamicin	08	00	00	06	00	01	01

newborn received cefotaxime alone. The following combinations: ceftriaxone–gentamicin, cefotaxime–gentamicin–ciprofloxacin, and ceftriaxone–gentamicin–ampicillin were administered to one newborn each.

Combinations of ceftriaxone–gentamicin and cefotaxime–gentamicin–ciprofloxacin were replaced by imipenem on the 4th day of hospitalization in one newborn each.

The mean hospital stay of newborns treated for UTI was 7.2 days ± 5.69 days. The average length of hospital stay for *Escherichia coli* was 12.5 days; it was 6.6 days for *Staphylococcus aureus* and 3.5 days for *Klebsiella oxytoca*. Table 3 shows the distribution of the length of hospitalization according to the germs isolated.

Table 3: Distribution of the length of hospitalization (in days) according to the germs isolated from newborns with urinary tract infection at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A) in 2019 (n = 10).

	Escherichia coli N	*Klebsiella oxytoca* N	*Staphylococcus aureus* N
2	00	01	00
4	01	00	01
5	00	01	03
8	00	00	01
13	00	00	01
21	01	00	00

Evolution

Concerning *Staphylococcus aureus*, the outcome was favorable in four of the six cases and the remaining two patients left against medical advice. It was favorable in both cases of *Escherichia coli*. One case of *Klebsiella oxytoca* left against medical advice and the second one died.

Identification of associated factors

Factors associated with positive urine culture in newborns were age (P = 0.00), and hypospadias in baby boys (P = 0.00; Table 4)

Discussion

This was a descriptive and analytical observational study conducted in 2019 to examine epidemiological, clinical, etiological, and evolutionary aspects of UTI in newborns at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A).

Bias and limitations of the study

The urine collection method used was the source of false positives and multi-bacterial contamination. However, other methods were not common in practice because they were invasive. Since neonatal infections are already taking heavy toll in neonatal mortality, the team of researchers

Table 4: Factors associated with the onset of urine tract infection in newborns at the Departmental Teaching Hospital of Borgou-Alibori (DTH-B/A) in 2019.

	Positive CBEU		Negative CBEU		P-value
	n	%	n	%	
Position of urethralmeatus					0.00
Apical	04	80.00	06	98.51	
Hypospadias	01	20.00	00	00.00	
Epispadias	00	00.00	01	01.49	
Age group (days)					0.00
1–8	07	70	100	87.72	
8–15	01	10	08	07.02	
15–22	00	00	05	04.39	
22–28	02	20	01	0.88	

CBEU: cytobacteriological examination of urine.

did not want to put the newborns surveyed at additional risk. The results of urine dipstick could also be affected by urine pH. On the other hand, the choice of inclusion criteria allowed not to consider any cases of asymptomatic bacteriuria.

A small sample size did not allow us to have effectiveness to study and detect other significant features associated with neonatal UTI.

Newborns sometimes passed small amounts of urine, which did not allow urinary dipstik test and urine sedimentation. Urine sedimentation was not done with the second morning urine as recommended (7).

Comparison of results

Frequency of urinary tract infection

In this series, during the study period, the frequency of UTI was 8.06% of neonatal infections. The hospital frequency was 2.15%, which was similar to 1.94%, found by Kemeze et al. (9) in Douala, Cameroon, in 2015. On the other hand, other authors have found higher frequencies. Atmani et al. (10) in 2007 found a hospital frequency of 4.2% in Fez, Morocco. Amorissani et al. (7) in 2006 reported a hospital frequency of 7.7% in Cocody, Ivory Coast. This difference could be due to the sample size and the short study period used in the present study, and to the criteria of National Nanotechnology Initiative (NNI) used in each of the mentioned studies.

Cytobacteriological examination of urine and antibiogram

Isolated germs

The bacteria identified in the present study were dominated by Gram-positive cocci in six of the 10 cases, followed by Enterobacteriaceae in rest of the four cases. *Staphylococcus aureus* was the only isolated Gram-positive cocci. Enterobacteriaceae consisted of equal parts of *Escherichia coli* and *Klebsiella oxytoca*. In a 2012 study conducted by Ouédraogo et al. (11) in Burkina Faso with children aged 3 days to 15 years reported *Escherichia coli* in 4 of the 10 cases, *Staphylococcus aureus* in 1 of the 10 cases, and *Klebsiella oxytoca* in 1 in 10 cases. In 2004, Adjei et al. (12) conducted a study in Ghana with children aged less than 12 months and noted *Escherichia coli* in three and *Staphylococcus aureus* in one of the 10 cases. The predominance of *Staphylococcus aureus* in the present study could be due to multiple vaginal examinations compared to potential ascending contamination. N'guessan et al. (13) reported, in 2008 at Ivory Coast that three risk factors for amniotic infection during labor were identified: namely number of vaginal examinations, use of internal sensors for the duration of egg opening, and the duration of labor . The only instance of death in the present study was that of a premature born infant because of *Klebsiella Oxytoca*. This suggests *Klebsiella oxytoca* and prematurity as factors of poor prognosis. It could also be a case of sepsis favored by a fragile terrain of prematurity. It could also be a nosocomial infection.

Sensitivity of microbes to antibiotics

Sensitivity of *Staphylococcus aureus*: The isolated strains of *Staphylococcus aureus* in all patients were resistant to amoxicillin + clavulanic acid, third-generation cephalosporins, and gentamicin. They were resistant to quinolones in 75% of patients. There was no resistance to imipenem. In 2004, Adjei et al. (12) found 20% resistance to amoxicillin + clavulanic acid in a study conducted in Kumassi, Ghana. In 2003, the National Neonatal-Perinatal Database report (14) in New Delhi, India, accounted a resistance of 65.80% to gentamicin, 67.80% to ciprofloxacin, and 80.40% to ceftriaxone and ceftazidime.

Sensitivity of *Escherichia coli*: In 2004, Amorissani et al. (15) in a study conducted in Cocody, Côte d'Ivoire, reported resistance of *Escherichia coli* in 45.85% cases to ceftriaxone, and 16.67% cases to gentamicin. In 2015, Duong et al. (16) in a study conducted in Vietnam found resistance of *Escherichia coli* in 20% of cases to amoxicillin + clavulanic acid, 62.30% to ceftriaxone, 38% to ciprofloxacin, and 48% to gentamicin. Touat et al. (17) in 2019, reported an average resistance of E. coli of 47% to fluoroquinolones and 41.60% to 3rd generation cephalosporins

In 2018, the World Health Organization (18) reported 36.5% resistance of *Escherichia coli* to ciprofloxacin.

Sensitivity of *Klebsiella Oxytoca*: In 2012, Ouédraogo et al. (11) in a study conducted in Ouagadougou, Burkina Faso, established 33.30% resistance of *Klebsiella oxytoca* to amoxicillin plus clavulanic acid and gentamicin, and 11.10% resistance to ceftriaxone.

In recent years, bacterial resistance to antibiotics has increased to worrying proportions globally. According to WHO (18),the problem is more acute in Africa because of the almost total absence of resistance surveillance system in our work context, anarchic prescriptions, inappropriate use of antibiotics and their sale outside legal structures or without prescription, modification of ecosystems attributable to humans, and use of antibiotics for prophylaxis as "anti-stress" or as stimulators of animal growth.

Associated factors

The associated factors selected were age (P = 0.00), and hypospadias in boys (P = 0.00). Gankpé (19) in 2018 while conducting study in the same department of the present study found vaginal delivery as a factor associated with maternal–fetal infection. In fact, maternal–fetal infection is transmitted through the following three routes: hematogenous route, amniotic contamination, and during passage through the birth canal (20).

The following three abnormalities are associated with hypospadias: ectopic meatus, hypoplasia of spongy bodies, and the skin tissue causing more or less pronounced "bend" and the dorsal preputial apron. These abnormalities of the penis interfere with urination (incomplete emptying), causing microbial overgrowth and leading to urinary infections (21).

Conclusion

One of the serious bacterial infections in pediatrics is UTI. The present study demonstrated that 2% of newborns hospitalized presented with UTI without relation to gender. UTI therefore does not appear to be the primary location for neonatal infection. UTI was more common in the early neonatal period. The clinical manifestations were dominated by respiratory distress and jaundice. The germ most frequently involved was *Staphylococcus aureus* followed by *Escherichia coli* and *Klebsiella oxytoca*. Age and position of the urethral meatus were identified as associated factors. No urinary tract malformation was detected on ultrasound. The overall level of resistance of microbes to antibiotics remains very high, which could raise the issue of nosocomial infections.

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