URINARY TRACT INFECTION IN FULL-TERM NEWBORN INFANTS: RISK FACTOR ANALYSIS

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SUMMARY: **Objective:** To analyze the correlation of risk factors to the occurrence of urinary tract infection in full-term newborn infants.

Patients and methods: Retrospective study (1997) including full-term infants having a positive urine culture by bag specimen. Urine collection was based on: fever, weight loss > 10% of birth weight, nonspecific symptoms (feeding intolerance, failure to thrive, hypoactivity, debilitate suction, irritability), or renal and urinary tract malformations. In these cases, another urine culture by suprapubic bladder aspiration was collected to confirm the diagnosis. To compare and validate the risk factors in each group, the selected cases were divided into two groups: Group I – positive urine culture by bag specimen collection and negative urine culture by suprapubic aspiration, and Group II – positive urine culture by bag specimen collection and positive urine culture by suprapubic aspiration .

Results: Sixty one infants were studied, Group I, n = 42 (68.9%) and Group II, n = 19 (31.1%). The selected risk factors (associated infectious diseases, use of broad-spectrum antibiotics, renal and urinary tract malformations, mechanical ventilation, parenteral nutrition and intravascular catheter) were more frequent in Group II ($p<0.05$). Through relative risk analysis, risk factors were, in decreasing importance: parenteral nutrition, intravascular catheter, associated infectious diseases, use of broad-spectrum antibiotics, mechanical ventilation, and renal and urinary tract malformations.

Conclusion: The results showed that parenteral nutrition, intravascular catheter, and associated infectious diseases contributed to increase the frequency of neonatal urinary tract infection, and in the presence of more than one risk factor, the occurrence of urinary tract infection rose up to 11 times.

DESCRIPTORS: **Urinary tract infection. Risk factor. Newborn infant.**

Usually, urinary tract infection in the neonatal period manifests after 72 hours of life. The incidence is between 0.1 to 10% in all infants. It is more frequent in male and preterm newborn infants, and may be as high as 10% in low birth weight infants[17,20]. This incidence is directly proportional to the presence of several risk factors for this disease. Among the risk factors, beside those previously mentioned, are the presence of associated infectious diseases (sepsis, bronchopneumonia, septic arthritis, osteomyelitis, meningitis, etc.), the use of broad-spectrum antibiotics, mechanical ventilation, parenteral nutrition, intravascular catheter, and prolonged stay in the intensive care unit[1,7,20]. Renal and urinary tract malformations may be present in neonates with a urinary tract infection[8].

Urinary tract infections are of interest to neonatologists for several reasons. First, they can be asymptomatic, so the diagnosis must be made by the examination and culture of a properly obtained specimen of urine[7,11]. Second, they may indicate a serious underlying abnormality of the urinary tract, such as obstructive uropathy. Third, they may have long-term consequences insofar as they may produce kidney damage, which may lead later in life to hypertension, recurrent infections, and kidney failure.

The knowledge of neonatal urinary tract infection risk factors or predisposing factors is important for identifying appropriate situations for performing serial urine culture to obtain an early diagnosis and adequate treatment[13]. The knowledge of the most important risk factors in a neonatal lower risk population is also important.

The purpose of this study was to analyze the contribution of the risk factors to the occurence of urinary tract infection in full-term newborn infants.

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PATIENTS AND METHOD

We conducted a retrospective study in the Child Institute "Prof. Pedro Alcântara" of the Hospital das Clínicas, University of São Paulo, Faculty of Medicine, including all full-term newborn infants (gestational age – 37 to 42 weeks) presenting positive urine culture by bag specimen collection.

Urine collection was based on clinical data as follows: fever (T>37.8º C)[24], weight loss > 10% of birth weight, or nonspecific symptoms (feeding intolerance, failure to thrive, hypoactivity, debilitate suction, irritability). In these cases, another urine culture was collected by suprapubic bladder aspiration to confirm diagnosis.

To compare and validate the risk factors in each group, the selected cases were divided into two groups: Group I – positive urine culture by bag specimen collection and negative urine culture by suprapubic aspiration, and Group II – positive urine culture by bag specimen collection and positive urine culture by suprapubic aspiration. The selected risk factors were: associated infectious pathologies, use of broad-spectrum antibiotics, renal and urinary tract malformations, mechanical ventilation, parenteral nutrition, and intravascular catheter[3,6,17].

Figure 1 shows the design of the study.

The finding of 100 000 CFU/ml of the same microorganisms defined the positivity of the bag specimen collection[26]. A suprapubic aspiration specimen was defined as positive at any CFU/ml rate[26].

The population of study was characterized by gestational age, birth weight, sex, perinatal asphyxia (Apgar score < 6 at 5 minute), and membrane rupture time (<24 hours and ≥ 24 hours). Symptoms were: fever (T>37.8º C), weight loss > 10% of birth weight or nonspecific symptoms (feeding intolerance, failure to thrive, hypoactivity, debilitate suction, or irritability).

The technique of bag specimen collection was: antisepsy and sterile plastic bag fitted on the genitalia[25]. If diuresis would not occur within 30 minutes, procedure would have been repeated until success[25].

The suprapubic aspiration specimen required a full bladder[16,23]. The overlying skin was disinfected, the bladder was punctured above the symphysis pubis with a 25-gauge needle on a syringe, and about 2 ml of urine was aspirated[2,21].

All urine specimens were transported promptly to the laboratory[9]. Urine specimens were processed onto CLED, MacConkey, Thayer-Martin, thioglicolate, and blood agar plates. Culture plates were incubated at 35–37º C and read at 24–48 hours; if results were positive, the antibiogram was determinated[9]. The absence of microorganisms within 48 hours characterized the culture as negative[9].

Data were analyzed through chi-square, Fischer exact test, Student *t* test, and relative risk. Significance was defined as $p<0.05$.

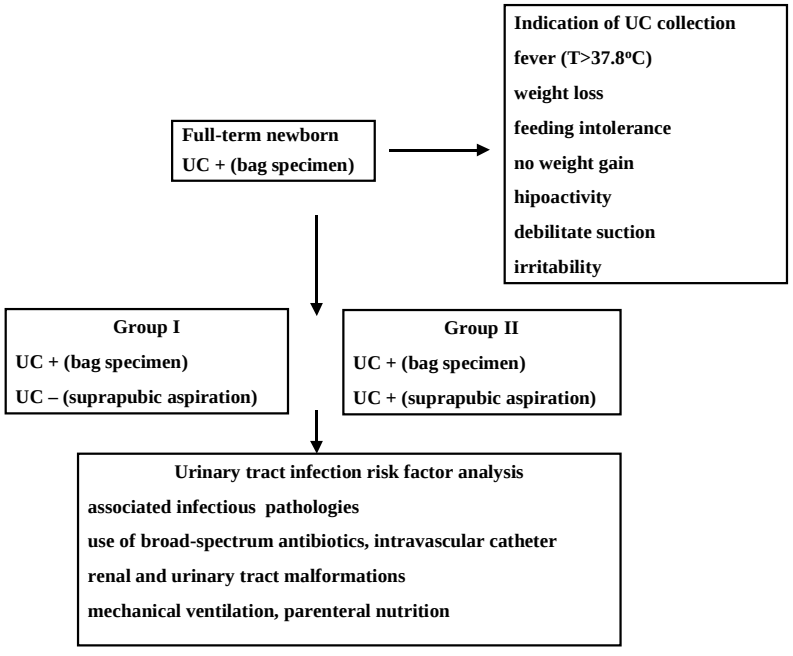

Figure 1 - Design of the study.
UC = urine culture

Table 1 - Population of the study – Group I and Group II.

	Group I n=42	Group II n=19	P	Test
Birth weight (g)	Average 3399.52 Variation 2560-4270 SD 418.36	3171.05 2420-4260 515.08	0.07	Student *t*
Sex	n (%)	n (%)		
Male	16 (38.1)	10 (52.6)	0.28	chi-square
Female	26 (61.9)	9 (47.4)	0.28	chi-square
Asphyxia Apgar 5' < 6	1 (2.4)	3 (15.8)	0.14	chi-square
Membrane Rupture time ≥ 24h	7(16.7)	5 (26.3)	0.47	chi-square

Table 2 - Clinical data – Group I and Group II.

	Group I N=42	Group II n=19	P	Test
	n (%)	n (%)		
Fever (T > 37.8°C)	38 (90.5)	15 (78.9)	0.31	chi-square
Weight loss > 10% of birth weight	20 (47.6)	3 (15.8)	0.01	chi-square
Nonspecific symptoms	4 (9.5)	10 (52.6)	0.0004	chi-square

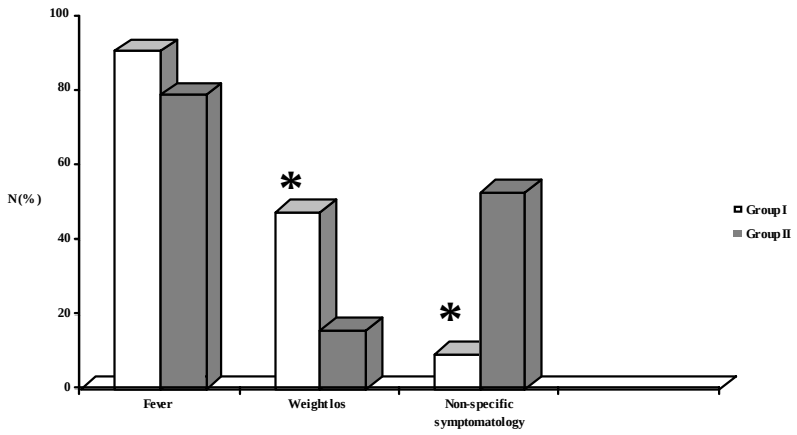

Figure 2 - Clinical data (%) – Group I and Group II.

RESULTS

Sixty-one full-term newborn infants were included in this study, representing 5.1% of the total infants born alive in the study period. The diagnosis was confirmed (positive urine culture by suprapubic aspiration) on 19/61 (31.1%) of full-term infants included in the study (1.6% of the total infants born alive).

The infants were distributed in two groups according to the positivity of urine culture collected by suprapubic aspiration. Group I had 42 infants (68.9%) and Group II had 19 infants (31.1%).

The population of the study is shown in the Table 1 and clinical manifestations are shown in Table 2 and Fig. 2.

No complication occurred from specimen collection by the suprapubic method.

The microbial content of cultures of urine specimens was: *Escherichia coli* (42.9%), *Staphylococcus aureus* (10.5%) *Staphylococcus* coagulase - negative (26.3%), *Enterococcus faecalis* (15.8%) and *Klebsiela pneumoniae* (5.3%).

The studied risk factors (associated infectious pathologies, use of broad-spectrum antibiotics, renal and urinary tract malformations, mechanical ventilation, parenteral nutrition, and intravascular catheter) were more frequent in Group II ($p<0.05$). These results are described in Table 3 and Fig. 3.

Nine newborn infants (21.5%) presented infectious pathologies: omphalitis (33.3%), pyodermitis (33.3%), bronchopneumonia (22.2%), and sepsis (11.1%) in the Group I. In Group II this value was increased to 63.2% (meningitis - 8.3%, omphalitis - 25%, bronchopneumonia - 25%, and sepsis - 41.6%).

The urological malformations were as follows: hydronephrosis (27.3% in Group I and 9.1% in Group II), ureteropelvic junction obstruction (27.3%

Table 3 - Risk factors for urinary tract infection.

Risk factor	Group I	Group II	P	Test
	n=42 n (%)	n=19 n (%)		
Associated infectious diseases	9 (21.4)	12 (63.2)	0.001	chi-square
Use of broad-spectrum antibiotics	3 (7.1)	6 (31.6)	0.02	chi-square
Renal and urinary tract malformations	4 (9.5)	7 (36.8)	0.01	chi-square
Mechanical ventilation	1 (2.4)	4 (21.1)	0.04	chi-square
Parenteral nutrition	1 (2.4)	10 (52.6)	0.0006	chi-square
Intravascular catheter	1 (2.4)	5 (26.3)	0.01	chi-square

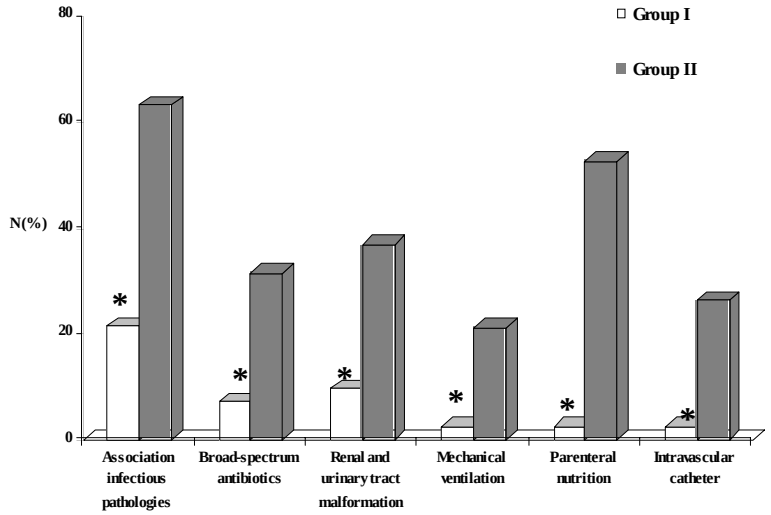

Figure 3 - Risk factors for urinary tract infection.

in Group II), posterior uretero valves (27.3% in Group II, and policystic kidney (9.1% in Group II).

Correlation between risk factors and urinary tract infection, in both studied groups, using relative risk analysis is shown in Table 4.

Table 5 shows the same analysis, drawing from more than one risk factor.

DISCUSSION

The first description of urinary tract infection in the neonatal period dates from the beginning of the century, and the observations made are still valid. Due to the absence of specific symptoms, the confirmation of diagnosis is based on laboratory data[4]. The clinical presentation may vary from fever and other signs of sepsis to minimal changes, or the infant may be without signs[4].

Until the decade of 1960, studies of urinary tract infection in the neonatal period were discrepant because they presented different criteria to define this infection and used divergent methodologies[17].

Currently, research indicates that urinary tract infection incidence is correlated to the presence of risk factors. The environment of the studied population, i.e., the intensive care unit or the nursery, should be taken into consideration.

The study population had a urinary tract infection frequency of 1.6%, a rate close to the low incidence limit of this disease in the neonatal period[12]. This finding may be due to the low risk in this study population, because in the absence of risk factors the full-term infant rarely develops urinary tract infection.

The population of this study (61 full-term infants) presented nonspecific symptoms (Table 2 – Fig. 2) and positive urine culture collected by bag specimen, which was considered to be the presumptive urinary tract infection diagnosis. Diagnosis (positive urine culture by suprapubic aspiration) was confirmed in 19 full-term newborn infants, emphasizing the need for this method to make accurate etiologic diagnosis.

Another consideration concerning the incidence of the urinary tract infection is its relationship to associated infectious pathologies; when newborn infants develop sepsis, for instance, there is a higher chance of developing urinary tract infection[5,6]. The results showed that in Group II, presence of infection was one of the most prevalent associated risk factors (63.2%), with significant statistical difference as compared to Group I (Table 3 – Fig. 3). Therefore, urinary tract infection should be considered in all infants who have signs of sepsis.

Prematurity and male gender are classically called risk factors[8]. There is also a proportional relationship with the presence of renal and urinary tract malformations[17]. Furthermore, a prolonged stay in the nursery may be con-

sidered as a risk factor, for instance, prematurity, perinatal asphyxia, mechanical ventilation, and inadequate nutrition. The incidence of neonatal urinary tract infection as a complication of intensive care has risen sharply in recent years.

Risk factors included in this research (associated infectious pathologies, use of broad-spectrum antibiotics, renal and urinary tract malformations, mechanical ventilation, and intravascular catheter) were more frequent ($p<0.05$) in Group II (Table 3 – Fig. 3).

Congenital renal and urinary tract defects, mainly the obstructive anomalies[17,19], exhibit a close relationship with urinary tract infection, and these were more frequent ($p<0.05$) in Group II (Table 3 – Fig. 3).

The male presents a high incidence of renal and urinary tract malformations and sepsis, leading us to believe that these malformations increase the frequency of urinary tract infections. Circumcision seems to reduce the overall incidence of urinary tract infections, although a few studies have suggested that this procedure may be a predisposing factor for urinary tract infection, mainly due to the complications encountered[10]. In this study group, the absence of circumcision led us to exclude this procedure as a risk factor or protector factor of neonatal urinary tract infection. In our study, Group II presented no difference related to gender. The low sample size is one of the factors that could explain this finding.

Natural defenses in the urinary tract include antibacterial properties of urine and urinary tract mucosa, anti-adherence mechanisms, machanical effects of urinary flow, presence of phagocytic cells, and immune mechanisms[22]. In the neonatal period, these mechanisms may fail, facilitating an urinary tract infection[3]. Furthermore, in the neonate, it is frequently difficult to know whether an urinary tract infection is the cause or the result of bacteremia[14].

Another factor to be considered is the use of broad-spectrum antibiotics, since use of these antibiotics is necessary for treatment of undetermined infection. Use of broad spectrum antibiotics may change neonate natural flora, increasing infections by opportunistic microorganisms[18]. Fungal urinary tract infections, mainly *Candida albicans* well exemplify this fact[15].

Table 3 and Fig. 3 reinforce that the use of broad-spectrum antibiotics (cefotaxime and vancomycin) can be considered as a factor risk, through analyzed data-frequency 31.6% ($p<0.05$).

All invasive procedures, even with antisepsy, could lead to a bacterial contamination, especially in the neonatal period. Intravascular catheterization, often necessary to deliver prescription drugs or parenteral nutrition, can facili-

Table 4 - Relative risk (RR) analysis of the risk factors for urinary tract infection.

Risk factors	RR	CI:95%	P	Test
Associated infectious pathologies	3.27	1.51-7.04	0.001	chi-square
Use of broad-spectrum antibiotics	3.03	1.51-6.08	0.012	Fisher exact
Renal and urinary tract malformations	2.97	1.57-5.64	0.007	Fisher exact
Mechanical ventilation	2.99	1.61-5.53	0.029	Fisher exact
Parenteral nutrition	5.05	2.72-9.39	0.0009	Fisher exact
Intravascular catheter	3.27	1.84-5.83	0.009	Fisher exact

Table 5 - Relative risk (RR) analysis using more than one risk factor for urinary tract infection.

Risk factor association	PR	CI:95%	P	Test
Associated infectious diseases + Use of broad-spectrum antibiotics	2.95	1.50-2.78	0.003	chi-square Yates' corrected
Parenteral nutrition + Intravascular catheter	11.05	2.68-45.64	0.00004	Fisher exact
Parenteral nutrition + Intravascular catheter + Mechanical ventilation	8.11	2.55-25.75	0.00004	Fisher exact
Associated infectious diseases + Renal and urinary tract malformations	3.54	1.99-6.29	0.00003	chi-square Yates' corrected
Parenteral nutrition + Intravascular catheter + Renal and urinary tract malformations	3.98	1.54-10.28	0.006	Fisher exact

tate a bacteremia and consequently a urinary tract infection. Also, intubation, a necessary mechanical ventilation procedure, can provoke infection.

The frequency of mechanical ventilation, intravascular catheterization, and parenteral nutrition (Table 3 – Fig. 3) was higher in Group II.

Finally, all analyzed risk factors in this research (associated infectious pathologies, use of broad-spectrum antibiotics, renal and urinary tract malformations, mechanical ventilation, parenteral nutrition, and intravascular catheter) were present at high frequencies in Group II (Table 3 – Fig. 3), with statistical significance ($p<0.05$). These findings support the relationship between risk factors and urinary tract infection in the neonatal period.

The relative risk of urinary tract infection risk factors was, in decreasing importance: parenteral nutrition, intravascular catheter, associated infectious diseases, use of broad-spectrum antibiotics, mechanical ventilation, and renal and urinary tract malformations (Table 4).

Analysis using more than one urinary tract infection risk factor (Table 5) revealed an increased relative risk, rising from 2.95 to 11.05. The combination of intravascular catheter and parenteral nutrition had the highest relationship with neonatal urinary tract infection frequency.

In conclusion, the results of this study showed that the presence of predisposing factors or risk factors (parenteral nutrition, intravascular catheter, associated infectious pathologies, use of broad-spectrum antibiotics, mechanical ventilation, and renal and urinary tract malformations) can contribute to increased urinary tract infection frequency in the neonatal period, and in the presence of more than one risk factor, the urinary tract infection occurrence rose up to 11 times.

RESUMO

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FALCÃO MC e col. - Infecção urinária em recém-nascido de termo: análise de fatores de risco. **Rev. Hosp. Clín. Fac. Med. S. Paulo 55** (1):9-16, 2000.

Objetivos: Analisar a contribuição dos fatores de risco para a ocorrência de infecção urinária em recém-nascidos de termo.

Casuística e metodologia: Estudo retrospectivo (1997), incluindo recém-nascidos de termo com urocultura positiva por saco coletor. A indicação desta coleta foi baseada em: hipertermia (T>37,8ºC), perda de peso>10% do peso de nascimento, alterações do estado geral (recusa alimentar, ganho insuficiente de peso e hipoatividade) ou presença de malformações nefro-urológicas. Nesses recém-nascidos foi realizada punção suprapúbica para confirmação diagnóstica. Os recém-nascidos foram divididos em dois grupos, segundo o resultado das uroculturas: Grupo I (diagnóstico presuntivo de infecção urinária) e Grupo II (diagnóstico confirmado de infecção urinária), para avaliação dos fatores de risco pela análise do risco relativo.

Resultados: Foram estudadas 61 crianças (5,1% dos recém-nascidos de termo) - Grupo I n=42 (68,9%) e Grupo II n=19 (31,1%). Os fatores de risco avaliados (patologias infecciosas associadas, uso prévio de antibióticos, malformações nefro-urológicas, ventilação mecânica, nutrição parenteral e o uso de cateteres) foram mais freqüentes no Grupo II ($p<0,05$). Analisando-se esses fatores, através de risco relativo, encontrou-se, em ordem decrescente de importância: nutrição parenteral, uso de cateteres, patologias infecciosas associadas, antibiótico prévio, ventilação mecânica e a presença de malformações nefro-urológicas.

Conclusões: Os resultados mostraram que a presença de nutrição

parenteral, uso de catéteres e patologias infecciosas associadas contribuiram para aumentar a freqüência da infecção do trato urinário no período analisado e, na presença de mais de um desses fatores, o risco elevou-se em até 11 vezes.

DESCRITORES: **Infecção urinária. Fatores de risco. Recém-nascido.**

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