Role of urine culture in paediatric patients with cancer with fever and neutropenia: a prospective observational study

Jose Antonio Alonso-Cadenas ,[1,2] Monica Sancosmed Ron,[3] Blanca Herrero,[4] Esther Lera Carballo,[3] Alvaro Lassaletta,[5] Rocio Rodrigo,[3] Mercedes de la Torre,[1,2] On behalf of the Spanish Pediatric Emergency Research Group (RISeuP-SPERG)

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[1]Pediatric Emergency Department, Hospital Infantil Universitario Niño Jesús, Madrid, Spain
[2]Instituto de Investigación Sanitaria Hospital La Princesa, Madrid, Spain
[3]Paediatric Emergency Medicine, Hospital Vall d'Hebron, Barcelona, Spain
[4]Paediatric Oncology Department, Hospital Universitario Niño Jesús, Madrid, Spain
[5]Pediatric Neuro-oncology Unit, Hospital Infantil Universitario Niño Jesús, Madrid, Spain

Correspondence to
Dr Jose Antonio Alonso-Cadenas, Emergency Department, Hospital Infantil Universitario Niño Jesús, Madrid 28009, Spain; jalonsocadenas@gmail.com

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ABSTRACT

Objective To evaluate the need for routine urine studies in children with febrile neutropenia with cancer.

Design A prospective, observational study was conducted in two hospitals between November 2019 and October 2021.

Patients We recruited 205 patients in total.

Main outcome measures The primary outcome was presence of positive urine culture (UC). Urinary tract infection (UTI) was defined as urinary signs/symptoms and positive UC with or without pyuria. A descriptive analysis of data is provided.

We conducted a prospective study of paediatric patients with cancer with urinary continence. Data were analysed using descriptive statistics. The diagnostic performance of urinalysis was calculated using positive UC as the gold standard.

Results Positive UC was found in 7 of the 205 patients (3.4%; 95% CI 1.4% to 6.9%), 2 presenting urinary symptoms. UTI prevalence was 1.0% (95% CI 0.1% to 3.5%). A 23.8% prevalence of positive UC was found in patients with urinary symptoms and/or history of urinary tract disease (95% CI 8.2% to 47.2%) as compared with 1.1% of those without symptoms or history (95% CI 0.1% to 3.9%) (p<0.001). The sensitivity, specificity, negative predictive value, and area under the curve for urinalysis were 16.7% (95% CI 3.0% to 56.4%), 98.4% (95% CI 95.3% to 99.4%), 97.3% (95% CI 93.9% to 98.9%), and 0.65 (95% CI 0.51 to 0.79), respectively.

Conclusions UTI is an infrequent cause of infection in these patients. Urinalysis is indicated only in children with febrile neutropenia with urinary signs/symptoms and in asymptomatic patients with a history of urinary tract disease or unknown history. When urine is collected, UC should be requested regardless of the result of the urinalysis.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with neutropenia may develop no inflammatory response, and leucocytes may be absent from patient urine.
⇒ Lack of prospective studies in children that draw on data from an adequate sample size; the topic remains unclear in clinical practice.

WHAT THIS STUDY ADDS

⇒ Urinalysis is indicated in the presence of urinary signs/symptoms and/or history of urinary tract disease or unknown history.
⇒ Urine culture should be requested regardless of the result of the urinalysis.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results of this study could help to select children with febrile neutropenia in whom urinalysis and urine culture would be indicated.

INTRODUCTION

Fever during chemotherapy-induced neutropenia, or febrile neutropenia (FN) occurs in approximately one-third of neutropenic episodes in children with cancer or recipients of haematopoietic stem cell transplantation for chemotherapy, and at least half of all FN cases are due to an overt or occult infection.[1] Infection, and particularly bacterial infection, is the leading cause of morbidity and death in patients with FN.[2]

Between 10% and 40% of FN episodes are associated with clinical evidence of infection,[1 3 4] and specific microorganisms are isolated in 10–30% of cases.[5 6] The most common infection in FN is bacteraemia, followed by infection of the gastrointestinal or respiratory tract, and urinary tract infection (UTI).

Although algorithmic approaches and guidelines for FN call for blood analysis and culture,[7] there is debate as to whether other laboratory tests such as urine culture (UC) should be performed routinely.[8 9] UTI is identified in 4–30% of adult patients with cancer with FN,[10–13] while the only existing study in the paediatric population reported an estimated prevalence of less than 10%.[14]

The objective of this study is to evaluate the need for routine urine studies in children with FN with cancer. As a secondary objective, we compared urinalysis against UC, the gold standard.

MATERIAL AND METHODS

Study design and data collection

This multicentre, cross-sectional prospective registry was conducted between November 2019 and October 2022. The study, which was endorsed by the Spanish Pediatric Emergency Research Group, included two Spanish paediatric emergency

departments (PEDs). The attending paediatricians acted in accordance with their own and local protocols for the diagnosis and treatment of children with FN. In each participating PED, a collaborating physician researcher collected epidemiological and clinical data from the medical records of study patients.

Population

Children were eligible if they were patients with cancer with urinary continence (≈2–18 years old), and had FN.

Exclusion criteria were antibiotic treatment in the previous 48 hours and refusal to participate.

Variables

The primary outcome was the presence of positive UC. The variables recorded were as follows: age, sex, cancer diagnosis, history of urinary tract disease, immunosuppressive treatment, antimicrobial prophylaxis, colony-stimulating factor treatment, Pediatric Assessment Triangle (PAT) on arrival to the PED, duration and severity of fever, other associated symptoms, physical examination findings, results of laboratory tests and diagnosis. Medical records were reviewed for all patients.

Children were divided into three groups: group 1 (positive UC and negative blood culture (BC)); group 2 (negative UC and positive BC) and group 3 (both cultures negative).

Definitions

History of urinary tract disease: past nephrectomy, syndromes affecting the proper formation of the urinary tract, neurogenic bladder and kidney transplantation; carriers of a double-J ureteral stent.

Fever was defined as an axillary temperature ≥38°C on one measurement or ≥37.5°C on two or more occasions over a 1-hour period.

The PAT was used to assess the overall initial impression of the child.[15]

Neutropenia was defined as an absolute neutrophil count (ANC) of <500 cells/mm^3 or an ANC expected to decrease to <500 cells/mm^3 over the following 48 hours.

Pyuria was defined as >5 white blood cells/high-power field.

Positive UC: growth of ≥100 000 colony-forming units/mL of a single pathogen in a clean-catch urine specimen.

Positive BC: growth of a single pathogen in a BC.

A UTI was considered confirmed when associated with compatible signs and/or symptoms, pyuria and positive UC.

Episodes associated with compatible signs and/or symptoms and positive UC without pyuria were considered possible UTIs.

Asymptomatic bacteriuria was defined as bacteriuria not associated with compatible signs or symptoms—except presence of isolated microorganisms—or pyuria despite a positive UC.

All urine samples were collected before antibiotic administration using the clean-catch method.

Occult bacteraemia (OB): isolation of a single pathogen in the blood of a febrile child who appeared well and in the absence of an identifiable focus of infection.

Sepsis: we defined sepsis based on the criteria published by Goldstein *et al*.[16] Patients with persistent hypotension who required vasopressors despite adequate fluid resuscitation were diagnosed as having septic shock.

If a patient had multiple episodes but remained asymptomatic and received no antibiotic treatment for at least 4 weeks between each, the subsequent episode was considered a new occurrence of FN for the purposes of this study.

Statistical analysis

All analyses were conducted using STATA V.17. Numerical variables were described using median and IQR when the data were dispersed. Categorical variables were expressed as counts and percentages. Comparisons between groups were performed using the Fisher's exact test for categorical variables and the Mann-Whitney U test for numerical variables after it was determined by Kolmogorov-Smirnov goodness-of-fit test that the data did not follow a normal distribution. Statistical significance was set at a p value of <0.05. The sensitivity, specificity, the negative predictive value and area under the curve (AUC) for urinalysis were calculated with a positive UC as the gold standard. The sample size was too small to carry out a multivariate analysis.

The article was drafted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational research.

RESULTS

Between 2019 and 2021, the two institutions recorded a combined total of 242 FN episodes in patients with urinary continence; of these, 205 (96.2%) patients—8 refused to participate—with a median age of 7.6 years (IQR, 4.8–13.5) were included. Seven patients (3.4%; 95% CI 1.4% to 6.9%) had a positive UC (group 1), 22 (10.7%; 95% CI 6.8% to 15.8%) a positive BC (group 2) and 176 (85.9%; 95% CI 80.3% to 90.3%) had a negative UC and BC (group 3). Table 1 contains the epidemiological and clinical data of these 205 patients.

Ongoing non-chemotherapy treatments at the time of PED presentation (ie, other immunosuppressive therapies, antimicrobial prophylaxis, treatment with colony-stimulating factors) as well as fever characteristics appear in table 2 as stratified by study group.

Values of blood tests per study group are reported in table 3 and the characteristics of urinalysis testing are shown in table 4. Pyuria was negative in 85.7% (6 of 7) of children with a positive UC. Bacteria were detected in the urinalysis of 42.9% (3 of 7) and 14.6% (29 of 198) of children with a positive and negative UC, respectively.

Among the patients with a positive UC (group 1, n=7), two had urinary symptoms and five were diagnosed with asymptomatic bacteriuria (5 of 205, prevalence 2.4%; 95% CI 0.8% to 5.6%). Of the former, one had pyuria (diagnosed with confirmed UTI) and one did not, and thus was diagnosed with possible UTI (2 of 205, overall prevalence 1.0%; 95% CI 0.1% to 3.5%). In total, three patients had a history of urinary tract disease, including kidney transplantation in a child diagnosed with non-Hodgkin's lymphoma (asymptomatic without pyuria), neurogenic bladder secondary to spinal cord compression in a female diagnosed with Ewing sarcoma (asymptomatic without pyuria), and a third was a carrier of a double-J stent due to obstructive renal failure of tumour origin (pelvic desmoplastic tumour); the latter was the only child with confirmed UTI. All seven children had a stable PAT except one, who presented with compensated shock with tachycardia and normal blood pressure and was diagnosed with sepsis/septic shock. All other characteristics are reported in tables 2 and 3. All data on positive UCs appear in the online supplemental table. The bacteria isolated in urine included three specimens containing extended spectrum beta-lactamase (ESBL)-producing *Pseudomonas aeruginosa,* one ESBL-producing *Escherichia coli,* one ESBL-producing *Enterobacter cloacae*, one *Enterococcus faecalis* and one *Citrobacter freundii.* None of the three children with nitrite-producing Gram-negative bacteria isolated in the UC had nitrituria. Thus, the prevalence of positive

Table 1 Characteristics of the patients included in the registry

	Total (n=205)
Sex (male), n (%)	113 (55.1)
Age in years, median (IQR)	7.6 (4.8–13.5)
Cancer diagnosis, n (%)	
Acute lymphoblastic leukaemia	100 (48.8)
Bone tumour	42 (20.5)
Central nervous system tumour	22 (10.7)
Non-Hodgkin's lymphoma	18 (8.8)
Sarcoma	6 (2.9)
Hodgkin's lymphoma	5 (2.4)
Neuroblastoma (abdominal)	4 (2.0)
Wilms tumour	2 (1.0)
Hepatoblastoma	2 (1.0)
Germ cell tumour	2 (1.0)
Acute myeloid leukaemia	1 (0.5)
Desmoplastic tumour	1 (0.5)
Bone marrow transplant, n (%)	2 (1.0)
Personal history of kidney disease, n (%)	11 (5.4)
Renal transplant	3 (1.5)
Renal agenesis	2 (1.0)
Nephrectomy	2 (1.0)
Hypertension	1 (0.5)
Nephrolithiasis	1 (0.5)
Carrier of a double-J stent	1 (0.5)
Tubulopathy caused by drug toxicity	1 (0.5)
Normal PAT upon arrival, n (%)	192 (93.7)
Reported symptoms, n (%)	
Fever without a source	115 (56.1)
Fever with other symptoms	90 (43.9)
Respiratory	38 (18.5)
Digestive	23 (11.2)
Otorhinolaryngological	22 (10.7)
Neurological	6 (2.9)
Urinary	2 (1.0)
Others†	5 (2.4)
Normal PE, n (%)	158 (77.1)

*Two with renal origin.
†Ocular, cutaneous, local pain.
%, percentage; PAT, Pediatric Assessment Triangle; PE, physical examination.

Table 2 Non-chemotherapy treatment and fever characteristics of the study patients according to study group

	Group 1 N=7	Group 2 N=22	Group 3 N=176	P value
Other immunosuppressives*, n (%)	3 (42.9)	10 (45.5)	42 (23.9)	n.s.
Antimicrobial prophylaxis, n (%)	7 (100)	21 (95.5)	168 (95.5)	n.s.
Colony-stimulating factors, n (%)	5 (71.4)	6 (27.3)	67 (38.1)	n.s.
Time since fever onset (hours), median (IQR)	3 (2–3)	1 (1–2)	2 (1–4)	n.s.
Maximum temperature at home (°C), median (IQR)	38 (38–38.2)	38.1 (37.8–38.6)	38 (38–38.4)	n.s.
Temperature on arrival to emergency department (°C), median (IQR)	37.6 (37–38.3)	38.2 (37.4–38.6)	37.9 (37.4–38.3)	n.s.

Group 1: positive urine culture and negative blood culture; group 2: negative urine culture and positive blood culture; group 3: negative urine and blood cultures.
*Biological treatments, corticosteroids.
n, number; %, percentage; n.s., non-significant.

Table 3 Values for blood tests in all three study groups

	Group 1	Group 2	Group 3	P value
ANC (cells/mm^3)	200 (100–300)	250 (150–400)	150 (50–200)	n.s.
CRP (mg/L)	52.3 (23.1–107.0)	23.5 (15.0–67.0)	35.2 (19.9–67.5)	n.s.
Procalcitonin (ng/mL)	0.2 (0.1–0.6)	0.2 (0.1–0.3)	0.2 (0.1–0.3)	n.s.

Data are expressed as median (IQR).
Group 1: positive urine culture and negative blood culture; group 2: negative urine culture and positive blood culture; group 3: negative urine and blood cultures.
ANC, absolute neutrophil count; CRP, C-reactive protein; n.s., non-significant.

UC in patients with urinary symptoms and/or history of urinary tract disease was 23.8% (5 of 21) (95% CI 8.2% to 47.2%), and the prevalence among those without urinary symptoms or history was 1.1% (2 of 184) (95% CI 0.1% to 3.9%) (p<0.001).

Among the patients with positive BC (n=22; 10.7%), none had a positive UC: 16 were coagulase-negative staphylococci, 3 *E. coli*, and 1 each for *Staphylococcus epidermidis*, *Streptococcus viridans*, and *Klebsiella pneumoniae*.

A final diagnosis of FN with no microbiologically confirmed infection was determined in 159 patients (77.6%), OB in 10 (4.8%), viral upper respiratory tract infection in 9 (4.4%), sepsis/septic shock in 8 (3.8%), FN with positive UC in 4 (1.9%), bacterial diarrhoea in 3 (1.5%), pneumonia in 2 (1.0%), catheter-related bloodstream infection in 2 (1.0%), fungal infection in 2 (1.0%), dental abscess in 2 (1.0%), confirmed UTI in 1 (0.5%), possible UTI in 1 (0.5%), typhlitis in 1 (0.5%) and ventriculoperitoneal shunt infection in 1 (0.5%).

DISCUSSION

The results of this study of children with FN with urinary continence and cancer reveal that UTI was an infrequent cause of infection (1%), as only two children had urinary signs or symptoms and positive UC. If we take history of urinary tract disease into account regardless of the presence or absence of symptoms, the rate of positive UC increases to ~3.5% (7 of 205). However, doing so would likely include asymptomatic bacteriuria, which has no clinical significance and should not be treated unless the patient has recently undergone kidney transplantation or is scheduled to undergo urological surgery in the near future.[17] Children with urinary signs or symptoms and/or history of urinary tract disease had a significantly higher rate of positive UC than those who had neither (20% vs ~1%). Furthermore, although the prevalence of UTI among individuals in the general population with urinary symptoms and/or fever between the ages of 2 and 18 years is 7.8% (95% CI 6.6% to 8.9%), this and other studies reveal a much lower rate in children with cancer presenting with fever and neutropenia.[18] Due to this low prevalence, a urine study should not be performed routinely in children with neutropenic cancer and fever. Rather, this test should be performed if urinary signs/symptoms are present, if the patient has a history of urinary tract disease or where the

Table 4 Characteristics of urinalysis

Sensitivity	16.7 (3.0 to 56.4)
Specificity	98.4 (95.3 to 99.4)
Negative predictive value	97.3 (93.9 to 98.9)
Area under the curve	0.65 (0.51 to 0.79)

Data are expressed as percentage and 95% CI.

history is unknown; doing so would avoid underdiagnosing patients who may have a previously undetected urinary tract abnormality. As shown in this study, urinalysis is of scarce value in asymptomatic children with no previous urinary tract disease. Especially in symptomatic children, UC should be performed at the time of urine sample collection regardless of the result of the urinalysis, as urinalysis has a low sensitivity and AUC.

This registry contains a comparable percentage of boys and girls with positive UC (4:3) and UTI (1:1), which differs from the general population, where most positive results are found in females.[18]

A cancer diagnosis does not seem to be related to a higher risk of UTI. Of the nine children with a tumour related to the urinary tract, the one male with a UTI was a symptomatic carrier of a double-J stent. The rest had no urinary symptoms. In our sample, ongoing treatment with other immunosuppressive therapies or a colony-stimulating factor did not change the risk of having a UTI. In addition, risk of UTI did not decrease when a patient was receiving antibiotic prophylaxis. All children with UTIs were receiving prophylactic trimethoprim–sulfamethoxazole (TMP-SMX) to prevent pneumocystis. TMP-SMX is commonly used in the prophylaxis of children without cancer who develop a UTI. Prophylactic antibiotics modestly reduce the risk of recurrent symptomatic UTI compared with placebo or no treatment.[19] In our registry, the bacteria isolated in UC are common urinary pathogens, but it is important to note that most were multiresistant. In four out of seven positive UCs studied here, the microorganisms were resistant to TMP-SMX. This may be due to the use of this antibiotic as a prophylaxis, possibly increasing the risk of bacterial resistance in subsequent infections.[19] A study of cancer-free paediatric patients with vesicoureteral reflux and a first recurrence of UTI caused by *E. coli* reported a higher proportion of isolates resistant to TMP-SMX in the prophylaxis group than in the placebo group.[20]

The pattern of fever in children with a positive UC was not different from that of the rest of the children included in this study. According to other research, UTI is not related to temperature in children older than 2 years old, unlike in infants.[18]

All children with a positive UC except one were well appearing, as were most of the other patients in our sample. Of all the children included, only two had urinary symptoms, both with a positive UC. This finding reinforces the fact that these symptoms should be taken into consideration when evaluating individuals with neutropenia in the PED, and all patients with urinary symptoms should be screened for UTI.

None of the results of blood testing showed significant differences in any of the three groups. ANC was similar in all groups, and neutropenia was severe in a majority of cases, most of whom appeared well independently of a positive microbiological isolate or not. C-reactive protein and procalcitonin were of little use in identifying children with FN with a positive UC or BC.

Only one of the patients with a positive UC and urinalysis had pyuria, thus suggesting that it is not possible to determine whether these children really have a UTI as there is no inflammatory reaction. The lack of association between UC, urinalysis and pyuria may not be because they have a neutropenia—the vast majority with severe one—and do not generate a sufficient inflammatory reaction to excrete leucocytes in the urine—a higher ANC is significantly associated with the presence of pyuria[21]—or they really have an asymptomatic bacteriuria because most of these children with FN (five of six) do not have urinary signs or symptoms. However, two of these children had a history of urinary tract disease (ie, neurogenic bladder, kidney transplantation) and UTI. Furthermore, as nitrites were not found in any of the specimens tested, this value also contributes little to the diagnosis.

The most frequent abnormality in urine was bacteriuria (15.6%, 32 of 205), as in previous reports.[14 22] Consequently, significant bacteriuria in the absence of pyuria may indicate contamination, particularly in patients where urine was not collected by catheterisation, as in our study.[21]

Limitations

This study has several limitations. First, UTI prevalence may be underestimated in this population. We cannot ensure that the asymptomatic children without pyuria and with positive UC did not present true UTI, as no additional urinary testing was performed after the acute febrile episode. However, the prevalence of UTI in this sample remains very low even with the addition of these five doubtful cases, and the rate is much lower than in the general population. Second, as we included only continent children, we cannot give recommendations for non-continent infants, who have the highest UTI prevalence. A similar study should be carried out in infants.

In conclusion, UTI is an infrequent cause of infection in children with FN with cancer and urinary continence. A urine study should be performed only in febrile patients with urinary signs/symptoms and in asymptomatic patients with a history of urinary tract disease or in cases in which the history of disease is unknown. When a urine sample is collected, UC should be requested regardless of the result of the urinalysis, particularly in the presence of symptoms.

Contributors JAAC contributed to the study conception and design, material preparation and analysis, wrote the first draft of the manuscript and act as the guarantor. BH, AL and MdlT conceptualised and designed the study, coordinated and supervised the data collection, and critically reviewed the manuscript. The following doctors revised the data collection form, collected data and critically reviewed the manuscript—MSR, ELC and RR.

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Patient consent for publication Parental/guardian consent obtained.

Ethics approval This study involves human participants and was approved by the Hospital Infantil Universitario Niño Jesús (number R-0003/19). Informed consent was obtained from the parents or guardians of all patients.

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ORCID iD

Jose Antonio Alonso-Cadenas http://orcid.org/0000-0002-7648-1336

REFERENCES

1 Castagnola E, Fontana V, Caviglia I, *et al*. A prospective study on the epidemiology of febrile episodes during chemotherapy-induced neutropenia in children with Cáncer or after hemopoietic stem cell transplantation. *Clin Infect Dis* 2007;45:1296–304.
2 Perrone J, Hollander JE, Datner EM. Emergency Department evaluation of patients with fever and chemotherapy-induced neutropenia. *J Emerg Med* 2004;27:115–9.
3 Lucas KG, Brown AE, Armstrong D, *et al*. The identification of febrile, neutropenic children with neoplastic disease at low risk for bacteremia and complications of sepsis. *Cancer* 1996;77:791–8.

4 Rackoff WR, Gonin R, Robinson C, *et al*. Predicting the risk of bacteremia in children with fever and neutropenia. *J Clin Oncol* 1996;14:919–24.
5 Haeusler GM, De Abreu Lourenco R, Clark H, *et al*. Diagnostic yield of initial and consecutive blood cultures in children with cancer and febrile neutropenia. *Journal of the Pediatric Infectious Diseases Society* 2021;10:125–30.
6 Stergiotis M, Ammann RA, Droz S, *et al*. Pediatric fever in neutropenia with bacteremia-pathogen distribution and in vitro antibiotic susceptibility patterns over time in a retrospective single-center cohort study. *PLoS One* 2021;16:e0246654.
7 Lehrnbecher T, Robinson PD, Ammann RA, *et al*. Guideline for the management of fever and neutropenia in pediatric patients with cancer and hematopoietic cell transplantation recipients: 2023 update. *JCO* 2023;41:1774–85.
8 Klastersky J, de Naurois J, Rolston K, *et al*. Management of febrile Neutropaenia: ESMO clinical practice guidelines. *Ann Oncol* 2016;27(suppl 5):v111–8.
9 National Institute for Health and Care Excellence. Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients. 2012. Available: https://www.nice.org.uk/guidance/cg151 [Accessed 8 Apr 2023].
10 Al-Bahar S, Pandita R, Dhabhar BN, *et al*. Febrile neutropenia in cancer patients in Kuwait: microbial spectrum and outcome. *Support Care Cancer* 1994;2:400–2.
11 Engelhart S, Glasmacher A, Exner M, *et al*. Surveillance for Nosocomial infections and fever of unknown origin among adult hematology-oncology patients. *Infect Control Hosp Epidemiol* 2002;23:244–8.
12 Hamzeh F, Kanj SS, Uwaydah M. Febrile neutropenia in cancer patients in a tertiary care medical center in Lebanon: microbial spectrum and outcome. *J Med Liban* 2000;48:136–42.
13 Sandoval C, Sinaki B, Weiss R, *et al*. Urinary tract infections in pediatric oncology patients with fever and neutropenia. *Pediatr Hematol Oncol* 2012;29:68–72.
14 Steinrücken J, Pabst T, Zimmerli S, *et al*. Low impact of urine cultures as a diagnostic tool in patients with neutropenic fever. *Infect Dis (Lond)* 2016;48:872–4.
15 Dieckmann RA, Brownstein D, Gausche-Hill M. The pediatric assessment triangle: a novel approach for the rapid evaluation of children. *Pediatr Emerg Care* 2010;26:312–5.
16 Goldstein B, Giroir B, Randolph A. International consensus conference on pediatric sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005;6:2–8.
17 Nicolle LE, Gupta K, Bradley SF, *et al*. Clinical practice guideline for the management of asymptomatic Bacteriuria: 2019 update by the infectious diseases society of America. *Clin Infect Dis* 2019;68:1611–5.
18 Shaikh N, Morone NE, Bost JE, *et al*. Prevalence of urinary tract infection in childhood: a meta-analysis. *Pediatr Infect Dis J* 2008;27:302–8.
19 Williams G, Craig JC. Long-term antibiotics for preventing recurrent urinary tract infection in children. *Cochrane Database Syst Rev* 2019;4:CD001534.
20 Hoberman A, Chesney RW, RIVUR Trial Investigators. Antimicrobial prophylaxis for children with Vesicoureteral reflux. *N Engl J Med* 2014;371:1072–3.
21 Klaassen ILM, de Haas V, van Wijk JAE, *et al*. Pyuria is absent during urinary tract infections in neutropenic patients. *Pediatr Blood Cancer* 2011;56:868–70.
22 Zgheib H, Zakhem AE, Wakil C, *et al*. Role of urine studies in asymptomatic febrile neutropenic patients presenting to the emergency Department. *World J Emerg Med* 2021;12:99–104.