Original article

Nosocomial infections and fever of unknown origin in pediatric hematology/oncology unit: a retrospective annual study

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Background: **Pediatric hematology/oncology patients are faced with an increased risk of nosocomial infections (NIs) that vary in different populations and different institutions with considerable morbidity and mortality. This study was undertaken to assess the frequency and patterns of NIs in 1564 pediatric patients and to determine the prevalence of causative organisms and their antimicrobial sensitivity.**

Methods: **A retrospective analysis was made in the patients admitted between January 2007 and January 2008 to the pediatric hematoloy/oncology unit of Mansoura University, Egypt. The 1564 patients showed 2084 admissions and 27 092 inpatient days. The Centers for Disease Control and Prevention criteria were used as a standard definition for NI.**

Results: **The overall rate of NIs in all patients and neutropenic patients was 8.6 and 25.3 per 1000 patient-days respectively. The frequent sites of NIs were blood stream (42.7%), the respiratory system (25.3%), the urinary system (22.2%) and the central nervous system (9.8%), whereas nosocomial fever of unknown origin constituted 52.9% of cases. The incidence of NIs was significantly higher during neutropenic days (P<0.001). Gram-positive organisms represented 64.5% of pathogens (*Staphylococci* 71.5%, *Streptococci* 16%, and *pneumococci* 7%), and Gram-negative organisms represented 30% (*E. coli* 48.6%, *Klebsiella* 15.7%, *Pseudomonas* 35.7%, and *C. albicans* 5.5%). Positive cultures were more frequent in summer (July to September). Susceptibility of isolated organisms was relatively low (cefoperazone/sulbactam 49.9%, amikacin 35.9%, imipenem/cilastin 34.4%, cefoperazone 33.6%, and vancomycin 36.5%). *Methicillin-resistant S. aureus*, *extended spectrum beta lactamase* and *vancomycin resistant enterococci* represented 30%, 45% and 75% of isolated *S. aureus*, Gram-negative organisms and *Enterococci*, respectively.**

Conclusions: **Blood stream infection and fever of unknown origin are the most common nosocomial infections in pediatric hematology/oncology patients with a higher risk during neutropenic days. Isolated organisms are multi-drug resistant, predominantly Gram-positive pathogens with a high incidence of methicillin-resistant *S. aureus*, extended spectrum beta lactamase and vancomycin resistant enterococci organisms.**

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Key words: **fever of unknown origin; hematology/oncology; nosocomial infections; pediatric**

Introduction

Nosocomial infections (NIs) are an important clinical complication in patients at different hospital wards leading to considerable morbidity and mortality. They are usually associated with prolonged hospital stay and increased healthcare costs.[1] Immunocompromised patients in pediatric hematology/oncology units are faced with an increased risk of nosocomial infections.[2,3] Severe and prolonged immunosuppression in hematology/oncology patients has multifactorial etiologies. The increasingly aggressive management in diagnostic and therapeutic procedures have contributed to a growing number of immunocompromised patients with life-threatening NI.[4,5]

The occurrence of NIs differs in different patient populations and different hospitals. However, there are few studies on the incidence of nosocomial infections in pediatric patients and comparative data from pediatric

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hematology/oncology units are rarely reported.[1,6,7]

This study was designed to evaluate the frequency of NIs in pediatric hematology/oncolgy patients in relation to different risks and to determine the main sites of infections, common microorganisms and their antimicrobial susceptibilities.

Methods

A retrospective study was carried out in pediatric hematology/oncology unit, Mansoura University, Egypt from January 2007 to January 2008. The hematology/oncology unit has 4 high efficiency particulate absorbing filtered rooms with single beds in addition to other 10 naturally-ventilated rooms each having 2 beds. The unit has 6 staff members, 3 registrars and one nurse for every 3 patients. The unit follows the standard recommendations of infection control measures.

During the surveillance period, 1564 patients (256 oncology patients, 1293 beta thalassemia patients and 15 patients with other hematologic disorders) were included. The beta thalassemia patients were included because they were maintained on the oral chelating agent, deferiprone, which may be complicated by neutropenia or agranulocytosis in addition to leukopenia that may be caused also by hypersplenism. These patients were also managed in the same unit and expected to be exposed to the same environmental risks.

The criteria of Centers for Disease Control and Prevention (CDC) were used as the standard definition for NI. Infections were regarded as NI if they appeared 48 hours after admission or within 48 hours of discharge.[8-11]

Demographic and clinical data including discharge diagnosis, date of onset, site of infections, results of microbiologic cultures from peripheral blood, body fluids and any suspected focus of infection and the antibiotics used were recorded. Cultures were done using Dade Behring automated Microscan (Sacramento, California, USA). Antimicrobial sensitivity was recorded for organisms isolated from sterile sites. The number of days during which patients were at increased risk as a result of leukopenia (leukocytic count $<1\times10^3$/μL) or severe neutropenia (neutrophil count $<0.5\times10^3$/μL) were calculated.[7,10]

Nosocomial fever of unknown origin (nFUO) was defined as fever of at least 38ºC for more than 4 hours occurring on several occasions in a hospitalized patient in whom neither fever nor infection was present on admission and for which a cause cannot be determined after 3 days of investigation, including 2 days of cultures.[7,12,13]

As to antibiotic prophylaxis, all of our oncologic patients were subjected to pneumocystis jiroveci prophylaxis with trimethoprim/sulfamethoxazole three times weekly. Prophylaxis with colistin and itraconazole was given to those patients with expected prolonged neutropenia (>10 days).[14]

Statistical analysis

Infection rates were calculated as overall infection rate (per 100 admissions) and incidence density rate (per 1000 patient-days and per 1000 patient-days at risk). The Chi-square test was used to compare the frequency of infections between neutropenic and non-neutropenic days. Data were analyzed using SPSS version 16 for windows.

Results

During 27 092 days of inpatient surveillance, 497 NIs and nFUO were registered in 1564 patients (2084 admissions with a mean length of hospital stay of 13 days) (Table 1). Of these, 234 (47.1%) were documented NIs, and 263 (52.9%) nFUO. The overall rates for NIs and nFUO were 8.6 and 9.7 per 1000 patient-days (25.3 and 15.4 per 1000 patient-days at risk), respectively.

A total of 497 cultures were collected (160 blood samples, 151 urine, 109 respiratory secretions, and 77 cerebrospinal fluid); 234 of the 497 cultures were positive (47.1%). Blood stream infection was detected

Table 1. Diagnosis and distribution of patients at risk and with nosocomial infections

Diseases	*n* (%)	Patients at risk (%)	Nosocomial infections (*n*)
Leukemias			
ALL	150 (9.6)	90 (51.4)	122
AML	20 (1.3)	15 (8.6)	18
CML	3 (0.2)	1 (0.6)	2
Lymphomas			
HD	15 (0.96)	4 (2.4)	4
NHL	24 (1.5)	9 (5.1)	12
Solid tumors			
Bone tumors			
Osteosarcoma	2 (0.13)	1 (0.6)	1
Ewing's sarcoma	5 (0.32)	3 (0.18)	5
Rhabdomyosarcoma	4 (0.25)	3 (0.18)	3
CNS tumors	5 (0.32)	1 (0.6)	2
Neuroblastoma	13 (0.08)	8 (4.6)	13
Wilms tumor	15 (0.96)	7 (4.0)	5
Other hematological disorders			
Beta thalassemia	1293 (82.7)	21 (12.0)	34
Aplastic anemia	10 (0.64)	10 (5.7)	10
LCH	5 (0.32)	2 (0.12)	3
Total	1564 (100)	175 (100)	234
Inpatient days	27 092	10 865	

ALL: acute lymphoblastic leukemia; AML: acute myeloid leukemia; CML: chronic myeloid leukemia; HD: Hodgkin's disease; NHL: non Hodgkin's lymphoma; LCH: Langerhan cell histiocytosis.

Table 2. Distribution of isolated organisms and frequency of microorganisms isolated from sterile sites

Types of organism	Total number of organisms (%)	Blood stream (*N*=100) (%)	Urinary tract (*N*=52) (%)	Central nervous system (*N*=23) (%)
Gram-positive (*n*=151)				
Coagulase +ve Staph	78 (51.5)	32 (32)	7 (13.4)	2 (8.7)
Coagulase –ve Staph	30 (20)	26 (26)	-	5 (21.7)
B hemolytic streptococci	24 (16)	7 (7)	-	-
Streptococcus peumoniae	11 (7)	8 (8)	-	3 (13.2)
Enterococcus faecium	8 (5.5)	4 (4)	-	-
Gram-negative (*n*=70)				
E. coli	34 (48.6)	7 (7)	27 (52)	7 (30.3)
Klebsiella spp	11 (15.7)	5 (5)	5 (9.6)	-
Pseudomonas aeuroginosa	25 (35.7)	6 (6)	11 (21.2)	4 (17.4)
Candida albicans	13 (5.5)	5 (5)	2 (3.8)	2 (8.7)
Total	234 (100)			

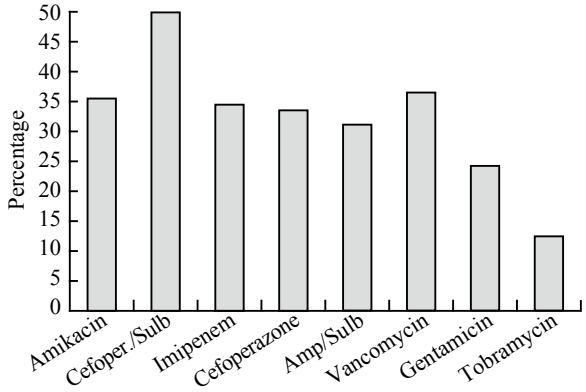

Fig. Sensitivity of isolated organisms to commonly used antibiotics.

Table 3. Comparison of the frequency of NIs and nFUO during neutropenic and non-neutropenic days

	Neutropenic days (*n*=10 865)	Non-neutropenic days (*n*=2657)	*P* value	Risk ratio
NIs	184/234 (78.6%)	50/234 (21.4%)	<0.001	6.6
nFUO	198/263 (75.3%)	65/263 (24.7%)	<0.001	3.9

NIs: nosocomial infections; nFUO: nosocomial fever of unknown origin.

in 100 of 234 positive cultures (42.7%), followed by respiratory tract infections (25.3%), urinary tract infections (22.2%), and lastly central nervous system infections (9.8%). nFUO accounted for 263 episodes (52.9% of defined patients).

Gram-positive cocci represented 64.5% of isolated organisms (151/234), followed by Gram-negative bacilli that were isolated in 30% of the organisms (70/234). *Staphylococci* were the most common Gram-positive bacterial isolates (71.5%), of which coagulase negative *Staphylococci* constituted 20%. *E. coli* were responsible for 48.6% of isolated Gram-negative bacilli (34/70). Fungal infections caused by candida albicans were detected in 13 patients (5.5%) (Table 2).

The highest sensitivity of isolated organisms was recorded for cefoperazone/sulbactam with a percent sensitivity of 49.9%, followed by amikacin, imipenem/cilastin, and cefoperazone with percent sensitivities of 35.9%, 34.4%, and 33.6% respectively. Vancomycin had a sensitivity of 36.5%, and the lowest sensitivities were recorded for erytheromycin (24.5%), gentamicin (24.1%), and tobramycin (12.5%) (Fig.). Methicillin-resistant *S. aureus* (*MRSA*), extended spectrum beta lactamase (ESBL) and vancomycin resistant *Enterococci* (*VRE*) represented 30%, 45% and 75% of isolated *Staphylococcus aureus*, Gram-negative organisms and *Enterococci* respectively.

The risks for NIs and nFUO were significantly higher during neutropenic days compared to non-neutropenic days, with 184 of 234 NIs (78.6%) and 198 of 263 nFUO (75.3%) occurring during 10 865 patient-days at risk ($P<0.001$) (Table 3).

Discussion

In this study, the overall incidence rate of NIs was 8.6 per 1000 patient-days (11.2 per 100 admissions). A similar incidence was reported by Wang et al.[6] However, higher incidences were found in other studies.[1,10,15] The sample size, the length of study, and the inclusion criteria together with the epidemiological data in different institutions may affect the rate of NIs in different studies. In our study, the inclusion of thalassemic patients who were at lower risk than oncologic patients (incidence rate 2.5 per 1000 patient-days) affected the overall NI incidence. The multi-center European study of Raymond and Aujard[5] supports this explanation with an overall incidence of 2.5%, ranging from 1% in general pediatric wards to 23.6% in pediatric intensive care units.

The rate of NIs was significantly higher in neutropenic patients (patients at-risk) than in non-neutropenic patients. This finding is consistent with that reported by Engelhart et al[10] who reported a significant risk of NI during neutropenic days with a rate of 25 per 1000 patient-days. Other studies have shown a higher incidence of NIs among cancer patients with neutropenia.

[4,16,17] This supports the role of neutropenia as a risk factor predisposing to NI and necessitates more careful management with strict application of infection control measures for this group of patients.[1]

nFUO represented 52.9% of defined nosocomial infection cases. It is in agreement with several other studies which reported a high incidence of FUO reaching up to 50% in hematology/oncology and neutropenic patients.[1,10,18,19] Viral infections may be among the pathogens responsible for FUO in these patients, but we did not screen for viruses because of lack of resources. However, viruses accounted for 6%-22% of NIs in different studies.[5,16] Fungal as well as bacterial infections may also underlie this problem as evidenced by response to empiric antifungal agents and antibiotics.[20,21]

With regard to the frequency of clinically or microbiologically documented sites of infections in our study, blood stream infection was responsible for the majority of cases, which is similar to the findings in other studies.[1,7,15,22] Interestingly, bacteremia was even observed in asymptomatic neutropenic patients.[23] This finding may raise the argument about the benefit of prophylactic antibiotics to prevent bacteremia in oncologic patients especially during neutropenia. Although this approach may reduce the incidence of fever, probable infection and the rate of hospitalization, it may interfere with culture results and may predispose to microbial resistance.[24]

Infections of the central nervous system and urinary tract represented 9.8% and 22.2% of documented infections respectively, which are relatively high. However, the reported incidence of central nervous system infections in immunocompromised patients ranged from 0.6% to 14% with an expected mortality of 42%-77%.[25] Similarly the incidence of urinary tract infections in oncologic patients was also reported to be as high as 25.6%.[4] Environmental and non-environmental factors could explain this wide variation of incidence in different localities. In addition to the immunocompromised state in studied patients, other factors such as intrathecal therapy, catheters placement, overcrowding and unhealthy hygienic habits of some patients may underlie this problem in our series as well as in those of other developing countries. However we could not document any predictors in such patients.

Most of the isolated organisms in this study were Gram-positive (64.5%), a finding that support the reported trend of Gram-positive predominance since the 1980s.[1,7,19] Several reasons were postulated to explain this predominance of Gram-positive pathogens in hematology/oncology patients. Generally, treatment of cancer has been intensified and it is associated with severe mucositis predisposing to *Strept viridans* bacteremia. In addition, partially or totally implantable intravenous catheters form a risk of *Staphylococcal* infection. The selection pressure of antibiotics that are more sensitive against Gram-negative organisms may play a role.[26,27]

In the present study, the highest sensitivity of isolated organisms was recorded for cefoperazone/sulbactam (49.9%) followed by amikacin, imipenem/cilastin, and cefoperazone. This finding confirmed the growing antimicrobial resistance, especially induced by *Staphylococci*, *Enterococci* and *Klebsiella*.[5,7,28,29] Unfortunately, vancomycin had a low *in vitro* sensitivity of only 36.5% against Gram-positive organisms in our study. Despite numerous reports of vancomycin resistance, the frequency of this resistance was found to be low.[30] Froggatt et al[31] however, observed that 42% of cases of *Staphylococcal haemolyticus* were intermediately resistant to vancomycin. This low susceptibility to vancomycin may be due to the frequent use of the agent leading to the appearance of resistant strains. The sensitive technique used to detect drug resistance that adds intermediate sensitivity to resistant organisms may be an additional factor. Anyhow, this should represent a serious problem of emerging or increasing resistance of Gram-positive bacteria to this antibiotic.

MRSA constitutes 30% of *S. aureus* isolates and 45% of Gram-negative bacteria showed an *ESBL* phenotype. These findings are in agreement with previous studies that the incidence of *MRSA* was 30%-38.5% from *Staphylococcus species* and that 30%-44% of enterobacteria were *ESBL*.[32-34] *VRE* represented 75% of the few enterococcus faceum isolates. Our results indicated the increased *VRE* colonization of patients. Colonization with *VRE* was recorded in 38%-50% of pediatric hematology/oncology patients.[35,36] This high frequency of resistant pathogens necessitates meticulous implementation of infection control measures with targeted *MRSA* control programs together with restrictive use of gylcopeptide antibiotics.

In conclusion, NIs and FUO are common problems in pediatric hematology/oncology patients especially with neutropenia. Infections, predominantly via blood stream, caused by Gram-positive organisms show significant multi-drug resistance with a high incidence of *MRSA*, *ESBL* and *VRE* organisms.

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References

1 Urrea M, Rives S, Cruz O, Navarro A, Garcia JJ, Estella J. Nosocomial infections among pediatric hematology/oncology patients: results of a prospective incidence study. Am J Infect Control 2004;32:205-208.
2 Tabone MD, Vu Thien H, Moissenet D, Leverger G. Nosocomial infections in immunocompromised children. Pathol Biol (Paris) 2000;48:893-900.
3 Simon A, Fleischhack G. Surveillance for nosocomial infections in pediatric hematology/oncology patients. Klin Padiatr 2001;213 Suppl 1:A106-113.
4 Velasco E, Thuler LC, Martins CA, Dias LM, Gonçalves VM. Nosocomial infections in an oncology intensive care unit. Am J Infect Control 1997;25:458-462.
5 Raymond J, Aujard Y. Nosocomial infections in pediatric patients: a European, multicenter prospective study. European Study Group. Infect Control Hosp Epidemiol 2000;21:260-263.
6 Wang A, Fan S, Yang Y, Shen X. Nosocomial infections among pediatric hematology patients: results of a retrospective incidence study at a Pediatric hospital in China. J Pediatr Hematol Oncol 2008;30:674-678.
7 Simon A, Ammann RA, Bode U, Fleischhack G, Wenchel HM, Schwamborn D, et al. Healthcare-associated infections in pediatric cancer patients: results of a prospective surveillance study from university hospitals in Germany and Switzerland. BMC Infect Dis 2008;8:70.
8 Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. Am J Infect Control 1988; 16:128-140.
9 National Nosocomial Infections Surveillance (NNIS) System report, data summary from October 1986-April 1998, issued June 1998. Am J Infect Control 1998;26:522-533.
10 Engelhart S, Glasmacher A, Exner M, Kramer MH. Surveillance for nosocomial infections and fever of unknown origin among adult hematology-oncology patients. Infect Control Hosp Epidemiol 2002;23:244-248.
11 Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36:309-332.
12 Durack DT, Street AC. Fever of unknown origin—reexamined and redefined. Curr Clin Top Infect Dis 1991;11:35-51.
13 Hughes WT, Armstrong D, Bodey GP, Brown AE, Edwards JE, Feld R, et al. 1997 guidelines for the use of antimicrobial agents in neutropenic patients with unexplained fever. Infectious Diseases Society of America. Clin Infect Dis 1997;25:551-573.
14 Simon A, Besuden M, Vezmar S, Hasan C, Lampe D, Kreutzberg S, et al. Itraconazole prophylaxis in pediatric cancer patients receiving conventional chemptherapy or autologous stem cell transplants. Support Care Cancer 2007;15:213-220.
15 Simon A, Fleischhack G, Hasan C, Bode U, Engelhart S, Kramer MH. Surveillance for nosocomial and central line-related infections among pediatric hematology-oncology patients. Infect Control Hosp Epidemiol 2000;21:592-596.
16 Carlisle PS, Gucalp R, Wiernik PH. Nosocomial infections in neutropenic cancer patients. Infect Control Hosp Epidemiol 1993;14:320-324.
17 Laws HJ, Kobbe G, Dilloo D, Dettenkofer M, Meisel R, Geisel R, et al. Surveillance of nosocomial infections in paediatric recipients of bone marrow or peripheral blood stem cell transplantation during neutropenia, compared with adult recipients. J Hosp Infect 2006;62:80-88.
18 Laws HJ, Amann RA, Lehrnbecher T. Diagnostic procedures and management of fever in pediatric cancer patients. Klin Padiatr 2005;217 Suppl 1:S9-16.
19 Laws HJ, Schneider DT, Janssen G, Wessalowski R, Dilloo D, Meisel R, et al. Trends in infections in children with malignant disease in 2000: comparison of data of 1980/81. Pediatr Hematol Oncol 2007;24:343-354.
20 Blau IW, Fauser AA. Review of comparative studies between conventional and liposomal amphotericin B (Ambisome) in neutropenic patients with fever of unknown origin and patients with systemic mycosis. Mycoses 2000;43:325-332.
21 Lehrnbecher T, Stanescu A, Kuhl J. Short courses of intravenous empirical antibiotic treatment in selected febrile neutropenic children with cancer. Infection 2002;30:17-21.
22 Rotstein C, Cummings KM, Nicolaou AL, Lucey J, Fitzpatrick J. Nosocomial infection rates at an oncology center. Infect Control Hosp Epidemiol 1988;9:13-19.
23 Penack O, Keilholz U, Thiel E, Blau IW. Value of surveillance of blood cultures in neutropenic patients-A pilot study. Jpn J Infect Dis 2005;58:171-173.
24 Cullen M, Steven N, Billingham L, Gaunt C, Hastings M, Simmonds P, et al. Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. N Engl J Med 2005;353:988-998.
25 Sahu RN, Kumar R, Mahapatra AK. Central nervous system infection in the pediatric population. J Pediatr Neurosci 2009; 4:20-24.
26 Elting LS, Bodey GP, Keefe BH. Septicemia and shock syndrome due to viridans Streptococci: a case-control study of predisposing factors. Clin Infect Dis 1992;14:1201-1207.
27 Viscoli C, Castagnola E. Factors predisposing cancer patients to infections. Cancer Treat Res 1995;79:1-30.
28 Kirby JT, Fritsche TR, Jones RN. Influence of patient age on the frequency of occurrence and antimicrobial resistance patterns of isolates from hematology/oncology patients: report from the Chemotherapy Alliance for Neutropenics and the Control of Emerging Resistance Program (North America). Diagn Microbiol Infect Dis 2006;56:75-82.
29 Mkaouar D, Mahjoubi F, Mezghani S, Znazen A, Ktari S, Hammami A. Resistance to third generation cephalosporins in Sfax hospitals, Tunisia (1999-2005). Med Mal Infect 2008;38:293-298.
30 Srinivasan A, Dick JD, Perl TM. Vancomycin resistance in Staphylococci. Clin Microbiol Rev 2002;15:430-438.
31 Froggatt JW, Johnston JL, Galetto DW, Archer GL. Antimicrobial resistance in nosocomial isolates of Staphylococcus haemolyticus. Antimicrob Agents Chemother 1989;33:460-466.
32 Cheguirian ML, Carvajal LR, Ledesma EM, Enrico MC, Reale AL, Culasso C, et al. Prevalence and antimicrobial susceptibility patterns of microorganisms causing bacteremia and fungemia in pediatric oncology patients. Rev Argent Microbiol 2008;40:111-115.
33 Grisaru-Soen G, Sweed Y, Lerner-Geva L, Hirsh-Yechezkel G, Boyko V, Vardi A, et al. Nosocomial bloodstream infections in a pediatric intensive care unit: 3-year survey. Med Sci Monit 2007; 13:CR251-257.
34 Zaki ME. Extended Spectrum β-Lactamases among Gram-negative bacteria from an Egyptian pediatric hospital: a two-year experience J Infect Developing Countries 2007;1:269-274.
35 Gray JW, George RH. Experience of vancomycin-resistant enterococci in a children's hospital. J Hosp Infect 2000;45:11-18.
36 Schuster F, Graubner UB, Schmid I, Weiss M, Belohradsky BH. Vancomycin-resistant-enterococci-colonization of 24 patients on pediatric oncology unit. Klin Padiatr 1998;210:261-263.

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