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The frequency and antimicrobial resistance patterns of nosocomial pathogens recovered from cancer patients and hospital environments

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ABSTRACT

Objective: To determine the prevalence and antimicrobial resistance rates of nosocomial pathogens isolated from cancer patients and hospital environments.

Methods: A descriptive cross-sectional study was conducted between December 2010 to May 2013 at Radiation and Isotopes Centre of Khartoum, Sudan. A total of 1 503 samples (505 clinical and 998 environmental) were examined. Isolates were identified, and their antimicrobial susceptibility was determined using standard laboratory procedures.

Results: Out of 505 clinical samples, nosocomial pathogens were found as 48.1%. Among hospital environment samples, bacterial contaminants were detected in 29.7% of samples. The main microorganisms recovered from cancer patients were *Proteus* spp. (23.5%), *Escherichia coli* (22.2%), *Pseudomonas aeruginosa* (*P. aeruginosa*) (21.0%) and *Staphylococcus aureus* (20.2%). The most frequent isolates from hospital environments were *Bacillus* spp. (50.0%), *Staphylococcus aureus* (14.2%) and *P. aeruginosa* (11.5%). The proportions of resistance among Gram-negative pathogens from cancer patients were high for ampicillin, cefotaxime, ceftazidime and ceftriaxone. Moderate resistance rates were recorded to ciprofloxacin, such as 51.0% for *P. aeruginosa*, 21.7% for *Klebsiella pneumoniae* and 55.5% for *Escherichia coli*. Except *Klebsiella,* there were no significant differences ($P \geq 0.05$) of resistance rates between Gram-negative isolates from cancer patients to those from the hospital environments. The proportions of extended-spectrum β-lactamase producing isolates from cancer patients were not differ significantly ($P = 0.763$) from those collected from the hospital environments (49.2%; 91/185 *vs.* 47%; 32/68).

Conclusions: The prevalence of nosocomial infection among cancer patients was high (48.1%) with the increasing of antimicrobial resistance rates. Hospital environments are potential reservoirs for nosocomial infections, which calls for intervention program to reduce environmental transmission of pathogens.

1. Introduction

Nosocomial infection is one of the most common life-threatening complications of immunocompromised hospitalized patients [1,2]. Cancer patients are more susceptible to hospital acquired infections due to their compromised immune system, the use of invasive technologies and they being subjected to surgical operations and chemotherapy [3,4]. Bacterial infection among cancer patients is continuing to emerge as particularly destructive complications of cancer treatment [2,5]. This infection among cancer patients could happen either as endogenously from normal flora on the skin or on the operative site or exogenously from the air, hospital staff, inanimate environment and medical equipments [6,7]. Patients with cancer are highly susceptible to almost any type of bacterial infection [3]. The colonization of the potentially pathogenic microorganisms on the various inanimate surfaces presents in a clinical setup has been reported as a potential vehicle for the transmission of nosocomial pathogens [6,7].

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The emergence of bacterial strains that are resistant to commonly used antibacterial agents, has created a potential public health problem, particularly among cancer patients [2,5]. The increasing of antimicrobial resistance rates among bacterial pathogens isolated from cancer patients and hospital environments are posing new challenges [5]. Many studies have been conducted to determine the prevalence of nosocomial infections among cancer patients in developed countries and developing countries [8–10]. In Sudan, no current data available documented nosocomial infections among cancer patients. Therefore, the aim of the present study was to determine the incidence and antimicrobial resistance of nosocomial pathogens isolated from cancer patients who admitted to the Radiation and Isotopes Centre of Khartoum in Sudan. In addition, the study also analyzed the distribution of pathogens that isolated from hospital environments.

2. Materials and methods

2.1. Study design and population

This descriptive cross-sectional hospital based study was conducted during the period from December 2010 to May 2013 in Radiation and Isotopes Centre of Khartoum, Khartoum state, Sudan. The Radiation and Isotopes Centre of Khartoum is one of the main oncology centers in Sudan, providing treatment for cancer patients with radiotherapy, chemotherapy and hormonal therapy [11]. All cancer patients who attended Radiation and Isotopes Centre of Khartoum were enrolled in the study. Each patient with no proven evidence of infection at the time of admission, but developed signs of infection after at least two days of hospitalization was included in the study. Patients with proven evidence of infection at the time of admission to the hospital were excluded from the study. The study was approved by the Research Committee of the Faculty of Medical Laboratory Sciences, University of Khartoum. All patients included in this study were consented verbally before collection of samples.

2.2. Collection of samples

Clinical samples of urine (n = 325), wound pus (n = 130), blood (n = 20) and sputum (n = 30) were collected from cancer patients for the investigations of pathogenic microorganism following standard laboratory procedures [12]. Hospital specimens were collected from different moist environments, including infrastructures (n = 551), furniture (n = 232), surgical equipments (n = 123), laboratories (n = 68), kitchens (n = 24) using sterile moist cotton swabs. All the collected specimens were properly labeled and the data were collected via a questionnaire form.

2.3. Isolation and identification of bacterial species

For possible isolation of bacterial pathogens, each specimen (clinical or environmental) were inoculated onto blood agar (HiMedia, India) and MacConkey agar (HiMedia, India) plates. Then all cultured plates were incubated aerobically at 37 °C for 24 h. Blood samples were inoculated onto brain heart infusion broth and incubated at 37 °C for a period of 7–14 days. Each bacterial isolate was identified on the bases colonial morphology, Gram staining and required biochemical tests following standard laboratory methods [12].

2.4. Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed using Kirby–Bauer disc diffusion technique on Mueller-Hinton agar medium (HiMedia, India) as recommended by the Clinical and Laboratory Standards Institute [13]. Isolates were tested for their susceptibility against different antimicrobial agents, including: amikacin (30 μg), ampicillin (10 μg), cefotaxime (30 μg), ceftazidime (30 μg), ceftriaxone (30 μg), ciprofloxacin (5 μg), gentamicin (10 μg), meropenem (10 μg) (HiMedia, India). The strain of *Escherichia coli* ATCC 25922 (*E. coli*) was used as control, and was examined each time when susceptibility testing was carried out. The test result was only validated in cases where inhibition zone diameters of the control strain within the performance range in accordance to the Clinical and Laboratory Standards Institute criteria [13].

2.5. Screening of extended-spectrum β-lactamase (ESBL) production

Gram-negative isolates recovered from cancer patients and hospital environments were screened for ESBL production by the double disc synergy test as described by Jarlier *et al*. [14]. All the isolates showed the resistance to third generation cephalosporin were examined for ESBL production. A disc containing amoxicillin/clavulanic acid (30 μg) was placed in the centre of the Mueller-Hinton agar plate, and discs containing ceftriaxone (30 μg), cefotaxime (30 μg) and ceftazidime (30 μg) were placed 30 mm distance from the disc of amoxicillin/clavulanic acid. A clear extension of the edge of the inhibition zone of third generation cephalosporin towards amoxicillin/clavulanic acid disc is interpreted as positive for ESBL production. Control strains of *Staphylococcus aureus* ATCC 25923 (*S. aureus*), *E. coli* and *Pseudomonas aeruginosa* ATCC 27853 (*P. aeruginosa*) were run at the same time on separate plates using the same turbidity as in the test organism to evaluate the conditions of the test and the potency of the discs.

2.6. Statistical analysis

The data obtained was coded and entered into the SPSS, version 16.0. The *Chi*-square test was used to test for the significant differences between the variables. $P < 0.05$ was considered as statistically significant.

3. Results

A total of 505 clinical samples collected from cancer patients (443 adults and 62 children) and 998 swab samples obtained from hospital environments were screened for the presence of bacterial pathogens. Out of the 505 clinical samples, pathogenic bacteria were detected in 48.1% (243). Of the 243 clinical isolates, 203 were recovered from adult patients and 40 from children. The majority of the isolates were from urine (n = 117), and wound pus (n = 113), with low frequency of the isolates from sputum (n = 12) and blood (n = 1) samples.

Overall the 998 swab specimens collected from hospital environments, 296 (29.7%) were yielded different bacterial species. As shown in Table 1, the most frequent microorganisms among cancer patients were *Proteus* spp. (23.5%), *E. coli*

Table 1
Frequency of different bacterial species isolated from cancer patients and hospital environments.

Bacterial isolate	Cancer patients			Hospital environment (%)
	Adult	Child	Total (%)	
E. coli	46	8	54 (22.2)	2 (0.7)
P. aeruginosa	46	5	51 (21.0)	34 (11.5)
Proteus species	48	9	57 (23.5)	10 (3.4)
S. aureus	38	11	49 (20.2)	42 (14.2)
K. pneumoniae	18	5	23 (9.4)	22 (7.4)
Streptococcus pneumonia	7	2	9 (3.7)	–
Bacillus species	–	–	–	148 (50.0)
Coagulase negative *Staphylococcus*	–	–	–	32 (10.8)
Micrococcus	–	–	–	6 (2.0)
Total	203	40	243	296

K. pneumoniae: *Klebsiella pneumoniae*.

(22.2%), *P. aeruginosa* (21%) and *S. aureus* (20.2%). Gram-negative bacteria were more frequently isolates from cancer patients than Gram-positive bacteria (76.1%; 185/243 *vs.* 23.9%; 58/243). Of the hospital environment isolates, *Bacillus* spp. were the common isolates (50%; 148/296) followed by *S. aureus* (14.2%; 42/296) and *P. aeruginosa* (11.5%; 34/296) (Table 1).

3.1. Antimicrobial susceptibility testing of the isolates

Table 2 summarizes the antimicrobial resistance patterns of Gram-negative bacilli isolated from cancer patients in comparison to the hospital environment isolates. There were no significant differences ($P \geq 0.05$) of resistance rates to the most tested antimicrobial agents between isolates (*Proteus* and *Pseudomonas*) from cancer patients to those from the hospital environments. On the other hand, both clinical and environmental isolates showed significant difference of resistance rates to four antimicrobials, including, ampicillin ($P = 0.020$ for *Proteus*), ciprofloxacin ($P = 0.001$ for *Proteus*), gentamicin ($P = 0.002$ for *Proteus*; $P = 0.018$ for *Pseudomonas*), ceftazidime ($P = 0.024$ for *Pseudomonas*). Among *K. pneumoniae* isolates, significant differences of resistance rates were recorded as follow (cancer patients isolates *vs.* hospital environment isolates) to: amikacin (0.0% *vs.* 27.3%; $P = 0.007$), ampicillin (82.6% *vs.* 100.0%; $P = 0.04$), ceftazidime (69.6% *vs.* 100%, $P = 0.004$), ciprofloxacin (21.7% *vs.* 54.5%; $P = 0.023$), gentamicin (0.0% *vs.* 45.4%; $P < 0.001$). In general, *K. pneumoniae* isolated from hospital environment were found to be more resistant than that isolated from cancer patients to the most commonly selected antimicrobial agents.

The proportions of resistance rates among Gram-negative isolates from cancer patients were high for ampicillin such as 63.1% for *Proteus* spp., 82.8% for *K. pneumoniae*, 88.9% for *E. coli* and 100.0% for *P. aerugenosa*. In addition, high resistance rates to ceftriaxone among isolates were recorded, such as 92.6% for *E. coli*, 96.1% for *P. aeruginosa*, 96.5% for *Proteus* spp., and 100.0% for *K. pneumoniae*. Similar high resistance rates among Gram-negatives isolates were observed for cefotaxime and ceftazidime. On the other hand, moderate resistance rates were recorded to ciprofloxacin, such as 51.0% for *P. aeruginosa*, 21.7% for *K. pneumoniae*, 55.5% for *E. coli*. Furthermore, moderate resistance rates were also recorded for amikacin, gentamicin and meropenem (Table 2).

3.2. Detection of ESBLs production

Table 3 summarizes the proportions of ESBL producing Gram-negative microorganisms recovered from cancer patients and hospital environments. Overall the isolates, the proportions of ESBL producing isolates from cancer patients did not differ significantly ($P = 0.763$) from those collected from the hospital environment (49.2%; 91/185 *vs.* 47.0%; 32/68).

Table 3
Comparison of the proportion of ESBL producing Gram-negative rods recovered from cancer patients to that collected from hospital environments. *n* (%).

Bacterial isolate	Cancer patients isolates ($n = 185$)	Hospital environment isolates ($n = 68$)
K. pneumoniae	30 (32.9)	12 (37.5)
E. coli	23 (25.3)*	0 (0.0)*
P. aeruginosa	21 (23.1)*	17 (53.1)*
Proteus mirabilis	14 (15.4)	2 (6.3)
Proteus vulgaris	3 (3.3)	1 (3.1)
Total	91 (49.2)	32 (47.0)

*: Indicate significant differences ($P < 0.05$) in the proportion of ESBL producing isolates from cancer patients and hospital environments.

Table 2
Comparison of antimicrobial resistance rates of Gram-negative nosocomial pathogens recovered from cancer patients and hospital environment. %.

Antimicrobial agent	*Proteus* spp.		*P. aerugenosa*		*K. pneumoniae*		*E. coli*	
	Patient ($n = 57$)	Hospital environment ($n = 10$)	Patient ($n = 51$)	Hospital environment ($n = 34$)	Patient ($n = 23$)	Hospital environment ($n = 22$)	Patient ($n = 54$)	Hospital environment ($n = 2$)
Amikacin	43.8	30.0	13.7	23.5	0.0*	27.3*	27.8	0.0
Ampicillin	63.1*	100.0*	100.0	100.0	82.6*	100.0*	88.9	50.0
Cefotaxime	100.0	100.0	94.1	100.0	91.3	100.0	100.0	100.0
Ceftazidime	86.0	100.0	86.3*	100.0*	69.6*	100.0*	81.5	100.0
Ceftriaxone	96.5	100.0	96.1	100.0	100.0	100.0	92.6	100.0
Ciprofloxacin	96.5*	0.0*	51.0	70.1	21.7*	54.5*	55.5	0.0
Gentamicin	52.6*	0.0*	49.0*	23.5*	0.0*	45.4*	0.0	0.0
Meropenem	45.6	33.3	23.5*	70.1*	56.5	68.2	24.1	0.0

*: Indicate significant differences ($P < 0.05$) in antimicrobial resistance rates between hospital and clinical isolates.

4. Discussion

Cancer patients are known to be susceptible to various nosocomial infections due to the negative effect of therapeutic practices on their immune system [1,15]. In the present study, we have analyzed the distribution and antimicrobial resistance of nosocomial pathogens isolated from cancer patients admitted to the Radiation and Isotopes Centre in Khartoum, Sudan. In addition, we estimated the frequency of bacterial pathogens isolated from hospital environments. We found that the incidence of nosocomial infections among cancer patients was 48.1%. In a study carried out in an oncology center, 12.0% of the patients developed nosocomial infections [16]. Another study found that 27.6% of adult cancer patients had bacterial bloodstream infections [17]. In this report, the predominant microorganisms causing nosocomial infections among cancer patients were *Proteus* spp. (23.5%), *E. coli* (22.2%), *P. aeruginosa* (21%) and *S. aureus* (20.2%). In Egypt, as a neighboring country, the most frequent isolates among patients with leukemia and solid tumors were *K. pneumoniae* (31.2%) followed by *E. coli* (22.2%) [1]. Our findings revealed that Gram-negative bacteria were significantly more predominant isolates from cancer patients than Gram-positive bacteria (76.1% *vs.* 23.9%; $P < 0.001$). Similar findings have been documented by others [18]. Recently, Trecarichi and Tumbarello [9] reported that the rate of Gram-negative bacteria recovery ranged from 24.7% to 75.8% in cancer patient cohorts. *E. coli* represented the most common species (mean frequency of isolation 32.1%) among the Gram-negatives, followed by *P. aeruginosa* (mean frequency of isolation 20.1%) [9]. Saghir *et al.* [10] noticed that Gram-negative bacteria were found associated with bloodstream infections in cancer patients. *P. aeruginosa* (38%) had been the most frequent bacterial isolates, followed by *E. coli* (25%), *K. pneumoniae* (20%), *Proteus vulgaris* (10%) and *Shigella* (8%) [10]. The epidemiology of bacterial infections among cancer patients showing a shift in the prevalence from Gram-positive to Gram-negative bacteria have been documented [9,19]. In contrary, current data indicate that Gram-positive microorganisms are predominant in patients with fever, neutropenia and hematological neoplasias followed by Gram-negatives like *E. coli* [20]. These findings indicated needs for evaluation of the local distribution of nosocomial pathogens and their susceptibility patterns and prompt initiation of effective antimicrobial treatment for severe bacterial infection in cancer patients [9].

The increasing rates of drug resistance among Gram-negative and Gram-positive pathogens are being documented in many hospitals, including cancer treatment centers [9]. In this study, Gram-negative bacterium revealed high resistance rates to β-lactams and cephalosporins groups. On the other hand, moderate resistance rates were recorded to ciprofloxacin, such as 51.0% for *P. aeruginosa*, 21.7% for *K. pneumonia* and 55.5% for *E. coli*. Moreover, moderate resistance rates also were recorded for aminoglycoside agent. Likewise, high resistant rates among Gram-negative rods to most of the commonly used antimicrobial groups have been determined by others [21,22]. Worldwide studies have been attributed to the increasing rates of cephalosporins among Enterobacteriaceae member due to β-lactamase activity [10,21,23].

In the hospital situations, the threat of contamination with potential pathogens is a great concern [7]. Our study showed that about 30% of the hospital environment samples were contaminated with different bacterial species. Furthermore, we found that the leading nosocomial isolates were *S. aureus* followed by *P. aeruginosa*, and *K. pneuomoneae*. In comparison of Gram-negative isolates from cancer patients to those from hospital environments in terms of resistance rates and ESBL production, there were almost no significant differences ($P \geq 0.05$) of resistance rates between both isolates. Exceptionally, *K. pneumoniae* isolated from cancer patients revealed a significant difference to those from the hospital environments of a resistance rate from amikacin, ampicillin, ceftazidime, ciprofloxacin and gentamicin. Our data suggested that hospital contaminant environments could be a mediator of cross transmission of nosocomial pathogens. Many of the nosocomial infections are acquired during the medical procedures, particularly with cancer patients [2]. In addition, other studies have reported the possibility of cross transmission of nosocomial bacterium from hospital devices and instruments [24,25]. Furthermore, hands and instruments used by health care workers have been recognized as vectors for the nosocomial transmission of microorganisms [24]. The inanimate objects and medical tools such as stethoscopes, ear thermometers, bronchoscopes, bedrails and bedside tables, bath basins or plumbing components in the patient's environment can harbor microorganisms [6,7,25]. The transmissions of nosocomial pathogens by electronic devices such as personal digital assistants, cell phone, handheld computers have been previously reported [26]. Therefore, the daily infection management that includes maintenance of hand hygiene, disinfection and sterilization of objects in the patients' environments to eliminate and reduce nosocomial pathogens should be implemented [6,25,27].

In conclusion, we found that the prevalence of nosocomial pathogens with cancer patients was high (48.1%). Gram-negative bacteria were the common cause of nosocomial infection among cancer patients. Antimicrobial resistance rates of nosocomial pathogens among this high-risk group were elevated and are becoming a clinical challenge. Hospital environment is a potential reservoir of different bacterial species which could be a source of transmission of nosocomial infection. Our findings highlight the need of intervention program to develop the cleaning methods as a way of reducing environmental transmission of pathogenic microorganisms. In addition, molecular epidemiological investigations of the clonal spread of specific pathogens should be included in infection control practices.

Conflict of interest statement

We declare that we have no conflict of interest.

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