Identification and characterization of bacteria isolated from patients with cancer at Enugu State Teaching Hospital Parklane, Enugu, Nigeria

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Abstract

Cancer affects millions of people worldwide and contributes to the highest percentage of global deaths compared to other ailments. Most cancer sites are vulnerable to infection by a vast number of opportunistic pathogens. Data from several surveillance reports have revealed several opportunistic pathogens responsible for infections in cancer patients. The present study investigated the spectrum of bacteria isolated from acute cancer patients. Samples were recovered from urine, vaginal swab, and breast swab. Identification and characterization of the isolates were performed using standard microbiological methods. A total of 130 bacteria comprising 78(60%) gram-positive and 52(40%) gram-negative were recovered. A statistically significant difference (P<0.05) was observed between the two groups. The most prevalent organism was *Staphylococcus* spp. (42.3%) followed by *Escherichia coli* (36.2%), *Lactobacillus* spp. (8.5%), *Micrococcus* spp. (6.2%), *Streptococcus* spp. (3.1%), *Klebsiella* spp. (1.5%), *Proteus* spp. (1.5%) and *Pseudomonas* spp. (0.8%). Our findings showed the predominance of gram-positive bacteria in infections among cancer patients. However, *Enterobacteriaceae* (*E. coli*) was the most frequently isolated among the gram-negative. This study indicates that cancer patients may be infected by several opportunistic pathogens, highlighting an ongoing trend toward gram-positive organisms causing infection in cancer patients. Therefore, it underscores the importance of constant monitoring at regional levels as surveillance efforts are important to provide the clinicians with the appropriate information in choosing treatment regimens and implement a proper policy for infection control guidelines.

INTRODUCTION

Cancer is a lethal disease that is non-communicable but can spread within the organs of the affected patients (Bernstein *et al.*, 2013). Cancer is currently a major global public health threat and contributes to the highest percentage of global deaths compared to other ailments (Mofid *et al.*, 2016). Currently, cancer is one of the highest causes of morbidity and mortality worldwide. It accounts for the deaths of millions of people each year. As of 2018, the reported new cases and deaths as a result of cancer were 18.1 and 9.6 million, respectively (Bray *et al.*, 2018). The most common cancers are those affecting the breast, lung, bronchus, prostate, rectum, melanoma, liver, cervical, and prostate (Jemal *et al.*, 2011; Magalaes, 2013).

During aggressive therapy, infections due to bacteria and fungi are very common. Currently, gram-negative and gram-positive bacteria are found to be opportunistic in cancer cells. This is broadly due to the use of immunosuppressive agents (chemotherapy and radiotherapy) that increase cancer patients' susceptibility to opportunistic infection (Rezaei-Tavirani *et al.*, 2018). The current therapeutic strategies have helped increase survival rates (Sedighi *et al*, 2019). However, despite the availability of several antimicrobial agents (Kramer *et al.*, 2018; Sedighi *et al.*, 2019), bacterial infections in cancer patients persist as a critical challenge in medicine. In fact, infection due to multi-drug resistant bacteria (MDR) is currently a serious threat to global health (Cornejo-Juarez *et al.*, 2015; Russell *et al.*, 2018).

Generally, infection occurs in cancerous cells when there is a change in the microbiota of the cells. It can also occur when pathogens are introduced to the site. In addition, toxins and other damaging substances are often released into the sites. The release of these materials can enhance the growth of cancerous cells and further lead to a slow response to cancer treatment. Most infections in cancer patients are due to the invasion and proliferation of fungi (especially *Candida*) and bacteria (*Staphylococcus* species, *Escherichia coli*, *Klebsiella*, *Salmonella*, *Clostridium difficile*, *Streptococcus viridians*, *Pneumococcus*, *Pseudomonas*, and *Enterococcus*) (Zembower 2014; Kruger *et al.*, 2019). Infections due to opportunistic pathogens can complicate the pathophysiology of cancerous cells with several devastating effects, as microbial metabolites might lead to metastasis of cancer or other severe health complications.

In the present study, we sought to identify and characterize the bacteria isolated from cancer patients. The goal was to understand the distribution and frequency of occurrence of different bacteria implicated in infection in cancer patients.

MATERIALS AND METHODS

Ethical statement

This study was approved and carried out following the recommendations by the oncology unit of Enugu State University Teaching Hospital Parklane, Enugu, and the Faculty of Biological Science Ethical Review Board Committee, University of Nigeria, Nsukka. There was written informed consent from all subjects.

Recruitment of cancer patients and sample collection

This study recruited different cancer patients (≥18 years old) prospectively. The patients consisted of those with the following cancer types: breast cancer, cervical cancer, placenta cancer, prostate cancer, uterine cancer, and vaginal cancer). Before the commencement of the study, informed consent was obtained from all patients. Clinical vaginal swab, breast swab, cervical swab, and urine samples were collected from all patients at the acute stage of cancer at the Oncology Unit of Enugu State University Teaching Hospital Parklane, Enugu. These samples were collected by the hospital' laboratory technician and properly distinguished using standard operating procedures. Before the sample collection, the vagina, vulva, and cervix of the uterus were thoroughly sterilized. Then, decidual tissue samples were collected by curettage with vacuum aspiration. Thereafter, blood clots were removed. The vagina isolates were collected by swabbing the vagina of the cancer patients. All the collected samples were immediately transported to the laboratory for further analysis.

Identification and characterization

The isolates were identified via microscopic examination, cultural characteristics, and biochemical features. The appearance, microscopic and chemical evaluation of the urine were specifically carried out. The isolates were cultivated on nutrient agar, blood agar (Oxoid, Basingstoke, UK), MacConkey agar (Biozyme Laboratories Ltd, San Diego, USA), chocolate agar (Oxoid, Hampshire, UK), and potato dextrose agar (PDA) (HiMedia, Mumbai, India) and incubated at 37^OC for 24 h. The morphology (color, elevation, edge, and density) of the colonies was thoroughly evaluated. The isolates were further differentiated into gram-positive and gram-negative through gram staining. Standard biochemical characterization (citrate utilization test, catalase test, urease test, and sugar fermentation test) as described in the manual of clinical microbiology (Cheesbrough 2005; Ezeonu et al., 2011) was used in the final identification of the bacteria.

Statistical analysis

Chi-square test was used to determine whether there was a statistically significant difference in the distribution of the isolated bacterial species. Results with $P < 0.05$ were considered significant. The statistical analysis was done using the SPSS software version 23.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

All our samples were collected from patients who had cancer (breast cancer, cervical cancer, placenta cancer, prostate cancer, uterine cancer, and vaginal cancer) and admitted in the hospital during the time of the study. The presence of a high number of pus cells in the urine was indicative of bacterial infection. Budding yeast cells (small oval budding cells) were also observed. A total of 130 bacteria species comprising 78(60%) gram-positive and 52(40%) gram-negative were recovered. We observed a statistically significant difference ($P < 0.05$) in the distribution of the gram-positive and gram-negative isolates. The recovered groups of organisms include *Streptococcus* spp, *Staphylococcus* spp., *Klebsiella* spp., *Proteus* spp*, Escherichia coli, Pseudomonas* spp*, Lactobacillus* spp*, and Micrococcus* spp. *Staphylococcus* spp (42%) was the most

predominant bacteria in our study, followed by *Escherichia coli* (36%) (Table 1). Table 2 shows the distribution of gram-positive and gram-negative bacteria.

DISCUSSION

Opportunistic bacterial infections remain one of the common complications in cancer patients. It is important to recognize these pathogens as they are responsible for most morbidity and mortality in cancer patients (van Elsland and Neefjes 2018). The results from this study showed the predominance of gram-positive bacteria (55%), and the main isolated organism was *Staphylococcus* spp 55(42.3%), followed by *E. coli* 47(36.2%). In terms of predominance, our results are comparable with recent findings by Khatri et al. (2019), who isolated gram-positive, 42(48.8%), and gram-negative bacteria, 44(51.2%) from cancer patients in India. Our results further corroborate the findings by Singh et al. (2014), who reported *S. aureus* and *E. coli* as the most predominant gram-positive and gram-negative bacteria, respectively. Furthermore, our findings were also in agreement with results from Raja et al. (2017) where 51% gram-positive and 49% gram-negative bacteria were reported, and the most predominant organism in the study was *Staphylococcus* (22%), followed by *Klebsiella* spp (14%), *E. coli* (13%), *Streptococcus* spp (10%) and *Pseudomonas* spp (10%). Similar incidences of gram-positive isolates, *Staphylococcus* spp., have been reported in other studies (Karanwal et al., 2013; Lakshmaiah et al., 2014).

Our results further highlight a dominance of Enterobacteriaceae among the gram-negative bacteria, and *E. coli* was the most predominant isolate. This is similar to the study by Lubwama et al. (2019), who reported the predominance of Enterobacteriaceae among gram-negative bacteria in Uganda. In a recent investigation, Mahmoud et al. (2020) reported *E. coli* (72.4%) as the most predominant organism in the urine of cancer patients. In a similar study, Khapartkuntikar et al. (2017) reported *E. coli* 16 (38.09%) as the predominant pathogen, followed by *P. aeruginosa* 8 (19.04%) and other organisms. The slight differences in the distributions of bacteria in infections among cancer patients might be attributed to variations in the geographical region.

Table 1: **Distribution of the isolated bacteria in different cancer types**

Bacteria	Cancer types						Total (%)
	Vaginal cancer	Placenta cancer	Cervical cancer	Breast cancer	Prostate cancer	Uterine cancer	
Staphylococcus spp (n=55)	12 (21.8%)	7 (12.7%)	20 (36.4%)	7 (12.7%)	6 (10.9%)	3 (5.5%)	42.3
Streptococcus spp (n=4)	3 (75%)	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (0%)	3.1
E. coli (n=47)	6 (12.8%)	5 (10.6%)	23 (48.9%)	5 (10.6%)	7 (14.9%)	1 (2.1%)	36.2
Proteus spp (n=2)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1.5
Lactobacillus spp (n=11)	2 (18.2%)	0 (0%)	3 (27.3%)	0 (0%)	0 (0%)	6 (54.5%)	8.5
Micrococcus spp (n=8)	0 (0%)	2 (25%)	0 (0%)	3 (37.5%)	3 (37.5%)	0 (0.0%)	6.2
Klebsiella spp (n=2)	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0.0%)	1.5
Pseudomonas spp (n=1)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.8
	26 (20%)	16 (12.3%)	47 (36.2%)	15 (11.5%)	16 (12.3%)	10 (7.7%)	

Table 2: **The distribution of gram-positive bacteria (GPB) versus gram-negative bacteria (GNB)**

	Vaginal cancer	Placenta cancer	Cervical cancer	Breast cancer	Prostate cancer	Uterine cancer	Total (%)
GPB	17(21.8%)	9(11.5%)	24(30.8%)	10(12.8%)	9(11.5%)	9(11.5%)	78(60%)
GNB	9(17.3%)	7(13.5%)	23(44.2%)	5(9.62%)	7(13.5%)	1(1.9%)	52(40%)

E. coli (30%) was the most predominant pathogen in cancer patients, followed by *Pseudomonas aeruginosa* (24.5%) and *Acinetobacter baumannii* (18.7%) in a study Eldomany and Abdelaziz (2011). Among cancer patients in Ethiopia, Arega *et al* (2017), reported the emergence of MDR saprophytic bacteria. In Ghana, Obeng-Nkrumah *et al.* (2013), reported the presence of MDR bacteria in the bloodstream of cancer patients. In another recent investigation by Tigabu *et al.* (2020), *E. coli*, 9(32%), *Klebsiella* spp, 7(25%), *S. aureus*, 6(21.40%), *Enterococcus* spp, 3(10.70%), *Serratia* spp, 2(7.24%) and *Enterobacter aerogenes*, 1(3.57%) were isolated from cancer patients. Ashreen *et al.* in another study that investigated the prevalence of bacteria in oral cancer patients, showed that *Klebsiella* spp (37, 45%) was the most prevalent, followed by *Pseudomonas* spp. (29, 34.5%), *Proteus* spp. (8,9.5%) and *E.coli (*5,6%) (Ashreen *et al.*, 2020). Furthermore, Lyaddorai *et al.* (2020) showed that *E. coli* plays a role in the initiation and promotion of cancer. In a similar investigation, Guerrero-Del-cueto *et al.* (2018) isolated and characterized viridans group of Streptococci in patients with cancer. The study reported *Streptococcus* spp as an emerging pathogen with high mortality and morbidity in oncologic patients. Pasquerean-kotula *et al.* (2018), in a review, also reported that *Streptococcus* spp. is a promoter of cancer.

It is important to emphasize that microbes can produce toxigenic substances and even carcinogenic metabolites. These substances can trigger cancer-promoting inflammation. They can also enhance the resistance of tumors to chemotherapeutic drugs and decreases the immune cells responsible for fighting against cancer. Aymeric *et al.* (2017) showed that bacteria could produce a specific bacteriocin. This toxin-like substance creates a suitable environment that promotes cancer. Thus, most bacteria associated with cancer are not necessarily the principal cause of cancer, but they are, however, auxiliary factors enhancing the development of cancer. Thus, bacteria may be one of the key factors responsible for the development of cancer. The development of methods for the detection of cancer-associated bacteria will be of help to oncologists (Bullman *et al.*, 2017; Yu *et al.*, 2017). Studies comparing healthy individuals and cancer patients are needed to conclude that these bacteria are involved in the initiation and development of cancer.

The inability to identify the bacteria to their species level and the small sample size are major limitations in our study. This drawback makes our method likely unsuitable for comparison of our results with those obtained from other researchers working on the association between bacteria and cancer. However, the reliability of our study is supported by the fact that our findings are consistent with previous investigations reporting the characterization of bacteria isolated from cancer patients (Raad 2017; Fan *et al.*, 2017; Seifu and Gubissa 2018; MergaDuffa *et al.*, 2018).

Conclusion

Infection due to bacteria is a common problem and one of the contributing factors in deaths among cancer patients. These infections are caused by a variety of bacteria (gram-positive and gram-negative). The gram negatives in our study were mainly *Enterobacteriaceae*. It is possible these organisms are contributing to diseases seen in cancer patients. Therefore, the significance of these organisms emphasizes the need to reduce bacterial infection and improve the health of cancer patients. Future work can look at comparing healthy individuals and cancer patients using larger sample size and also comparing the results with patients' demographic information. Finally, molecular characterization of the bacterial isolates from cancer patients is also needed for a more accurate definition of bacterial burden in cancer patients.

Authors contribution

OPO and M-EUD conceived the study. IEM, OPO, and JCU wrote the manuscript. OPO, EAO, and VN participated in the collection of data and performed the analysis. IEM prepared the final version of the manuscript. IEM and M-EUD edited and proofread the final version of the manuscript. All authors approved the final manuscript.

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