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Microbial spectrum and susceptibility profile of opportunistic pathogens isolated from cancer patients attending a tertiary healthcare centre in Akure, Nigeria

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Abstract

Introduction. Cancer constitutes a formidable global public health challenge, infection complicates effective treatment regimen and detrimentally impacts survival in cancer-patients. This predicament is exacerbated by the rising specter of antimicrobial resistance. **Methods**. The study was conducted amongst clinically diagnosed cancer patients attending University of Medical Sciences Teaching Hospital, Akure. Characterization of bacterial and fungal isolates from blood samples of the patients was performed using standard microbiological procedures. Antimicrobial susceptibility assessment was performed using disk diffusion and microdilution methods. **Results**. Overall, 40.3% of cancer cases manifested in individuals aged above 60 years, with breast cancer emerging as the predominant malignancy, accounting for 68.1% of cases. Moreover, retirees constituted the demographic with the highest representation among the cancer patients, encompassing 36.8% of the study population. The prevailing bacterial isolates comprised *Klebsiella pneumoniae* (25%) and *Klebsiella aerogenes* (18.75%), while *Aspergillus fumigatus* (30.12%) and *Candida albicans* (24.09%) constituted the predominant fungal isolates. Remarkably, the antimicrobial agents Cefuroxime, Cotrimoxazole, and Amphotericin-B exhibited suboptimal efficacy against these isolates. **Conclusion**. This study shows the increased vulnerability of cancer patients to opportunistic bacterial and fungal pathogens, many of which show resistance to conventional antimicrobial agents. Strict infection prevention and antimicrobial stewardship measures are advocated to reduce infections in this susceptible population.

Key word: cancer, infection, antimicrobial-agents, antimicrobial-resistance.

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Introduction

Cancer is the outcome of genetic modifications leading to the malfunction of genes controlling normal cellular functions (1). In cancer cells, the regulatory systems preventing excessive cell proliferation and tissue invasion are disabled (2). Thriving on characteristic fitness hallmarks, cancer cells exhibit insensitivity to growth-inhibitory signals, evasion of apoptosis, self-sufficiency in growth signals, unbridled replicative potential, sustained angiogenesis, and metastasis (3). Globally, cancer stands as a leading cause of death and a significant public health burden (4,5). By 2040, an estimated 28.4 million new cancer cases may arise, marking a 47% increase from 2020 projections. If current incidence patterns persist, the global incidence of all cancers combined is projected to double by 2070, with lower-resource settings witnessing notable increases (6).

It is well-established that cancer patients are susceptible to infections (7). Cancer and its treatments predispose patients to infections, leading to a poor prognosis (8,9). Infections elevate the risk of morbidity and mortality in cancer patients, directly due to their immunocompromised state and indirectly by delaying treatment and impacting long-term outcomes (10). Risk factors for infections in cancer patients can be categorized into those related to treatments and those related to the underlying tumor. Patients often have multiple risk factors during infection exposure (10).

Antineoplastic therapy can result in prolonged and profound neutropenia and immune suppression (11). These treatments significantly influence host defense mechanisms, affecting antigen uptake and processing by phagocytes and altering immune reactions, rendering patients susceptible to various infectious agents (12). Moreover, these drugs may impede primary and secondary immune responses, leading to impaired antibody production or cell-mediated reactions (13). Cancer can directly disrupt skin and mucosal surfaces through invasion or as a result of treatments like catheter placement, radiation therapy, and chemotherapy. Mucosal barrier injury

is more common in hematologic malignancies, especially after bone marrow transplant (14). Additionally, obstruction often complicates advanced tumors, serving as a predisposing factor for infections, leading to post-obstructive infectious processes, perforation, and abscess formation (15). Sepsis after surgical intervention in cancer remains a significant challenge.

Infections, particularly involving bacteria and fungi, are a primary or associated cause of death in cancer patients (16,17). The challenge is exacerbated by antimicrobial resistance, making infections difficult to treat (17). Effective infection management necessitates a deep understanding of the changing spectrum of etiological agents and their antimicrobial susceptibility patterns, driving the need for this study. This research aims to investigate the spectrum of bacterial and fungal pathogens associated with infection in cancer patients and determine their antimicrobial susceptibility profile.

Methods

Patient Population and Sampling

The sample size for this study was determined following Sullivan's methodology (18) using the formula $N = p(1-p)(Z/E)^2$. Here, N represents the sample size, Z is the value from the standard normal distribution corresponding to the confidence level used (Z = 1.96 for 95%), E is the desired margin of error (0.05), and p is the cancer prevalence in Nigeria (19). A total of 144 clinically diagnosed cancer patients, including 32 males and 112 females across all age groups, participated in the study at the Oncology Clinic and from the wards of University of Medical Sciences Teaching Hospital Akure (UMTHA) from August 2019 to August 2020. Additionally, a control group comprising 30 apparently healthy non-cancer individuals (10 males and 20 females) was recruited.

Collection of Blood Samples

Blood sample collection adhered to the method outlined by the Clinical and Laboratory Standards Institute (CLSI) (20). Aliquots from each blood sample were dispensed into sterile Brain Heart Infusion broth and Thioglycollate broth bottles, while the remaining volume was preserved in the vacutainer tube. The samples were stored in an ice-packed cooler for subsequent transfer to the Microbiology Laboratory for further analysis.

Isolation of Microorganisms from Blood Samples

Incubation of all blood culture broth bottles was conducted at appropriate temperatures and examined daily for growth up to 7 days. Sub-culturing on suitable culture media was performed upon visible signs of growth. For bacterial isolation, subculturing involved inoculating cultures on different sterile bacteriological media such as Brain-Heart Infusion agar (BHA), Eosine methylene blue agar, Blood agar, MacConkey agar, Salmonella-Shigella agar, Mannitol salt agar, and Chocolate agar. Incubation conditions varied, with plates sub-cultured from Brain-Heart Infusion broth bottles under aerobic conditions at 37°C, while those from Thioglycollate broth bottles were incubated under anaerobic conditions in an anaerobic jar. All cultures were checked daily for growth, and distinct isolates from each plate were sub-cultured for pure colonies, then stored on agar-slant in the refrigerator for identification. Blood from vacutainer tubes was used for microbial enumeration by pour plating on BHA, followed by incubation for 24 to 72 hours, after which colonies were counted.

Biochemical Characterization of Bacterial Isolates

Bacterial isolates underwent sugar fermentation (glucose, sucrose, lactose, mannose, arabinose, raffinose, maltose, sorbitol, mellobiose, xylose, dulcitol, cellibiose, manitol) and biochemical tests such as Gram-reaction, Catalase, Oxidase, Coagulase, Citrate-utilization, Indole, Motility, Methyl-red, Vosges-proskauer, Hydrogen sulphide (H_2S) production, and Urease tests (21).

Antimicrobial Assays

Standardization of Inoculum: A McFarland standard (0.5) was prepared by combining 0.05 ml of 1% barium chloride dihydrate ($BaCl_2.2H_2O$) with 9.95 ml of 1% Sulfuric acid (H_2SO_4) to yield a 1.0%w/v barium sulfate suspension. For bacterial isolates, the 18 hours old bacterial colonies were transferred to a tube of sterile saline, and the bacterial suspension was compared to the 0.5 McFarland standards. The bacterial suspension was adjusted to the proper density as the 0.5 McFarland by adding sterile saline or more bacterial cultures. Then, the bacterial suspension was diluted to obtain 10^6 cfu/ml.

Isolation of Fungi from Blood Samples

For fungal isolation, subculturing from the broth bottles showing positive signs of growth involved inoculating cultures on Sabauraud Dextrose Agar (SDA). The SDA plates were incubated at 35±2°C for 5 to 7 days. Daily checks for growth were performed, and distinct isolates from each plate were sub-cultured for pure colonies, followed by storage on agar-slant in the refrigerator for identification. Blood from vacutainer tubes was used for microbial enumeration by pour plating on SDA, followed by incubation for 24 to 72 hours, after which colonies were counted.

Morphological and Biochemical Characterization of Fungal Isolates

Culture plates showing mycelial growth were identified by their colonial characteristics and microscopic appearance, employing a teased Lactophenol Cotton Blue (LPCB) stained mount. Colonies showing yeast-like growth were Gram-stained. Observation of Gram-positive budding cells identified them as Candida spp. Further speciation involved germ-tube tests, sugar-assimilation tests, sugar-fermentation tests, chlamydospore formation on Corn Meal Agar (CMA), Growth at 45° C, and the color of colonies on

CHROMagar (22).

Antimicrobial Assays

Inoculum standardization used McFarland standard, and antibiotic susceptibility testing employed disc-diffusion and microbroth dilution methods. Antifungal susceptibility testing utilized the broth microdilution method with Amphotericin-B, Voriconazole, and Caspofungin.

Data Analysis

Data were analyzed using the Statistical Package for Social Sciences (IBM-SPSS) version 22.0.

Ethical Consideration and Approval

Ethical approval (OSHREC/23/05/19/127) was obtained from the Ministry of Health, Ondo State. Consent was obtained from clinically diagnosed cancer patients at UMTHA, and a well-structured questionnaire was administered to investigate major socio-demographic parameters relevant to infection risk and disease progression.

Results

Socio-demographic Information of Cancer Patients at UMTHA

The distribution of cancer types among the patients enrolled in this study is summarized in Table 1. Notably, breast cancer was the most prevalent, accounting for 68.1% (98 cases), followed by lung cancer at 11.1% (16 cases), prostate cancer at 7.6% (11 cases), and endometrial cancer at 7.6% (11 cases). Regarding gender distribution, a majority of the patients were female (77.8%), with males constituting 22.2%. A detailed breakdown of these results is presented in Table 1.

Age Distribution

Figure 1 illustrates the age distribution of the patients. The highest number of cancer cases (40.3%) was observed in patients aged above 60 years, while the lowest (2.1%) occurred in the 21-30 age group. In the context of specific cancer types, breast cancer cases peaked in the 41-50 age group (46.9%) and were lowest in the 31-40 age group (6.1%). For lung cancer patients, the highest incidence (68.8%) was in the 31-40 age group, and the lowest (12.5%) occurred in those above 60 years. Leukemia, prostate, cervical, endometrial, and laryngeal cancers were exclusively recorded in patients aged above 60 years.

Family History and Treatment

Among the patients, 8.3% had a family history of cancer, and chemotherapy was the most frequently administered treatment (53.5%). Regarding lifestyle, 5.6% of patients reported alcohol use, while 6.9% engaged in both alcohol and tobacco use. These results are presented in Table 1.

Table 1

Socio-demographic Information of Cancer Patients Attending UMTHA

Socio-Demographic Information	Frequency	Percentage
Gender		
Male	32	22.2
Female	112	77.8
Type of Cancer		
Breast cancer	98	68.1
Prostate cancer	11	7.6
Cervical cancer	4	2.8
Endometrial cancer	11	7.6
Laryngeal cancer	2	1.4
Lung	16	11.1
Leukaemia	2	1.4
Type of Residence		
Urban	103	71.5
Peri-Urban	11	7.6
Rural	30	20.8
Family History of Cancer		
With family history	12	8.3
No family history	106	73.3
Not sure of family history	26	18.3
Type of treatment Received		
Chemotherapy	77	53.5
Radiotherapy	10	6.9
Surgery	64	44.4
Herbal	20	13.8
Type of Cancer patient	**Alcohol and Tobacco Use**	
	Alcohol only	Alcohol and Tobacco
Breast cancer	4	0
Prostate cancer	4	0
Cervical cancer	0	0
Endometrial cancer	0	0
Laryngeal cancer	0	0
Lung cancer	0	10
Leukaemia	0	0

Occupation and Duration of Diagnosis

Figure 2 depicts the distribution of cancer patients based on occupation, revealing retirees as the largest group (36.8%). In terms of the duration of diagnosis, 43% of patients had been diagnosed within 1-3 years, while only 1.4% were diagnosed within 7-9 years. Notably, breast cancer, cervical cancer, and leukemia cases were predominantly diagnosed within the first 1-3 years, as outlined in Table 2.

Figure 1

Age Distribution of Cancer Patients Attending UMTHA

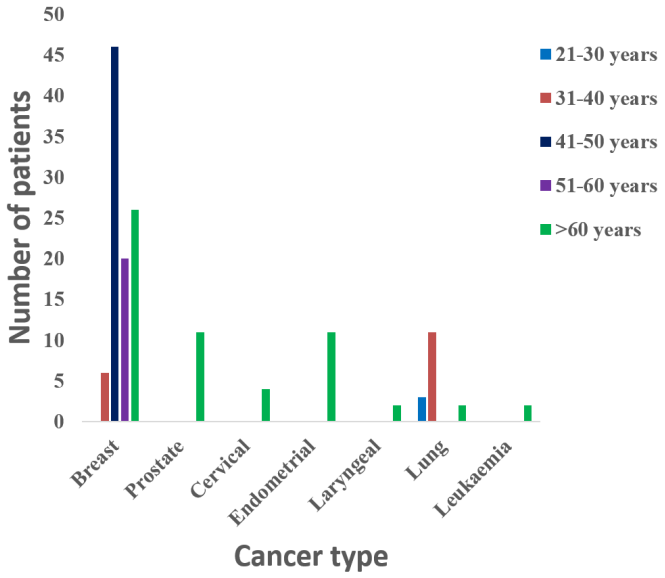
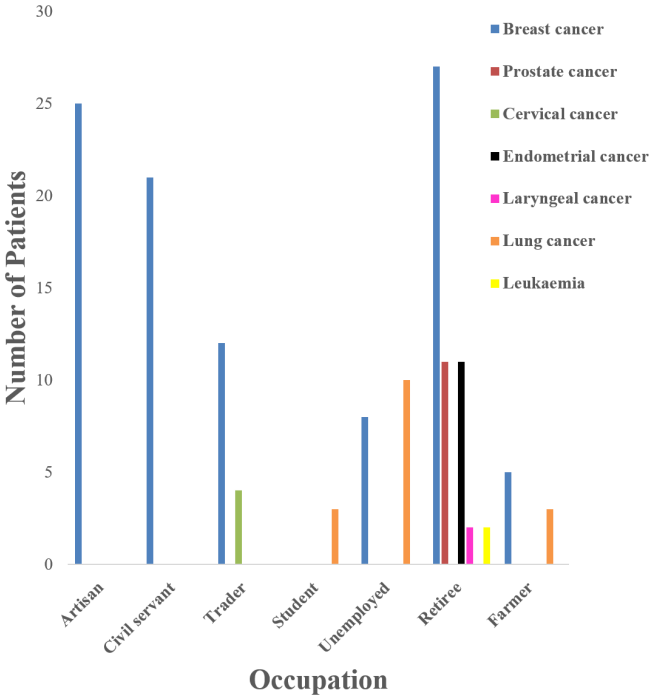


Figure 2

Occupational Distribution of Cancer Patients Attending UMTHA



Microbial Load of Cancer Patients at UMTHA

The mean bacterial and fungal loads in cancer patients were assessed, revealing noteworthy findings. Patients aged above 60 years exhibited the highest mean bacterial load (29.3 ± 3.7 cfu/ml), while those in the 51-60 age range had the highest mean fungal load (20.4 ± 3.7 sfu/ml). Conversely, the lowest mean bacterial load (4.4 ± 1.33 cfu/ml) and fungal load (10.0 ± 1.53 sfu/ml) were observed in patients aged 21-30 years. For a visual representation, refer to Figure 3.

Frequency of Bacterial Isolates and Antibiotic Susceptibility Patterns

The prevalent bacterial pathogens among the subjects were identified, with *Klebsiella pneumoniae* (25%) and *Klebsiella aerogenes* (18.75%) leading the list. Other significant isolates included *Staphylococcus aureus* (12.5%), *Shigella dysenteriae* (12.5%), and *Streptococcus pneumoniae* (12.5%). Notably, these bacterial isolates displayed resistance to several antibiotics, including Ceftazidime (45%), Erythromycin (49%), Ceftriazone (49%), Cefuroxime (65%), and Cotrimoxazole (69%). Further details are available in Table 3.

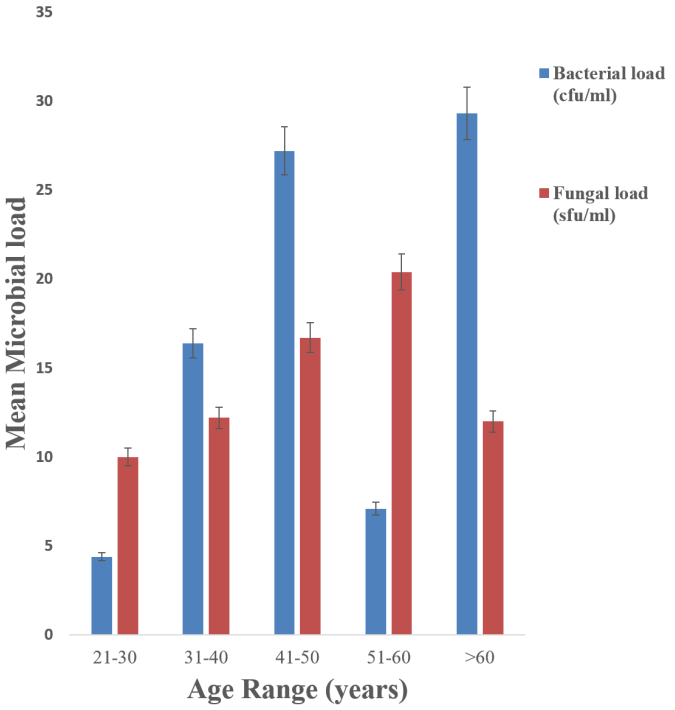
Table 2

Duration of Cancer Diagnosis in Patients Attending UMTHA

Duration of Diagnosis (years)	Type of Cancer							Total n(%)
	Breast cancer	Prostate cancer	Cervical cancer	Endometrial cancer	Laryngeal cancer	Lung cancer	Leukaemia	
< 1	30	5	0	7	2	16	0	60 (41.7)
1 – 3	52	2	4	2	0	0	2	62 (43)
4 – 6	12	0	0	2	0	0	0	14 (9.7)
7 – 9	2	0	0	0	0	0	0	2 (1.4)
10 >	2	4	0	0	0	0	0	6 (4.2)
Total n (%)	98	11	4	11	2	16	2	144 (100)

Figure 3

Microbial loads of Blood Samples Collected from Cancer Patients Attending UMTHA



Frequency of Fungal Isolates and Antifungal Susceptibility Patterns

Fungal pathogens isolated from cancer patients comprised *Aspergillus fumigatus* (30.12%), *Aspergillus flavus* (15.66%), and *Candida albicans* (24.09%). The minimum inhibitory concentration (MIC) values for antifungal agents varied across isolates. *Candida parapsilosis* exhibited the lowest mean MIC, while *Aspergillus flavus* and *Aspergillus fumigatus* displayed higher MIC values. Specific values are outlined in Table 4.

Table 3

Antibiotic Resistance Patterns of Bacterial Isolates from Cancer Patients Attending UMTHA

Organism	Ceftazidime	Cefuroxime	Gentamycin	Augmentin	Ofloxacin	Cotrimoxazole	Cefixime	Nitrofurantoin	Ciprofloxacin	Erythromycin	Cloxacillin	Ceftriazone
K. aerogenes n (9)	3 (33)	5 (56)	4 (44)	5 (56)	2 (22)	7 (78)	3 (33)	2 (22)	1 (11)	4 (44)	3 (33)	4 (44)
K. pneumoniae n (12)	5 (42)	7 (58)	4 (33)	1 (8)	2 (17)	10(83)	3 (25)	2 (17)	3 (25)	4 (33)	4 (33)	4 (33)
E. coli n (6)	1 (17)	5 (83)	1 (20)	4 (80)	1 (17)	3 (60)	1 (20)	0 (0)	0 (0)	4 (40)	3 (50)	3 (50)
S. dysenteriae n (6)	2 (33)	3 (50)	1 (17)	3 (50)	1 (17)	5 (83)	1 (17)	0 (0)	1 (17)	3 (50)	2 (33)	3 (50)
S. typhi n (2)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	0 (0)	1 (50)	0 (0)	1 (50)	0 (0)	1 (50)
P. mirabilis n (2)	1 (50)	1 (50)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	1 (50)
S. pneumoniae n (6)	5 (83)	5 (83)	3 (50)	1 (17)	1 (17)	4 (67)	3 (50)	1 (17)	1 (17)	4 (67)	2 (33)	4 (67)
S. aureus n (6)	4 (67)	5 (83)	2 (33)	3 (50)	3 (50)	4 (67)	3 (50)	3 (50)	3 (50)	3 (50)	1 (17)	4 (67)
Total 49 (%)	22(45)	32(65)	16(49)	18(37)	11(22)	34(69)	14(29)	9 (18)	9 (18)	24(49)	16(33)	24(49)
P value	0.399	0.877	0.826	0.269	0.293	0.918	0.388	0.625	0.078	0.553	0.779	0.559

Legend: values in parenthesis represent percentage resistance, Cft = Ceftazidime, Cfu = Cefuroxime, Gen = Gentamycin, Aug = Augmentin, Ofx = Ofloxacin, Cot = Cotrimoxazole, Cfx = Cefixime, Nit = Nitrofurantoin, Cpx = Ciprofloxacin, Ery = Erythromycin, Clx = Cloxacillin, Cfr = Ceftriazone.

Table 4

Susceptibility Profile of Fungal Isolates from Cancer Patients Attending UMTHA

Organism	Amphotericin-B (µg/mL)	Voriconazole (µg/mL)	Caspofungin (µg/mL)
Candida albicans (n=20)	1.306 ± 0.165^{b}	0.221 ± 0.034^{ab}	0.300 ± 0.022^{b}
Candida glabrata (n=8)	1.266 ± 0.241^{b}	0.313 ± 0.023^{b}	0.184 ± 0.026^{a}
Candida tropicalis (n=6)	0.792 ± 0.142^{ab}	0.467 ± 0.070^{c}	0.198 ± 0.018^{a}
Candida parapsilosis (n=4)	0.281 ± 0.041^{a}	0.109 ± 0.008^{a}	0.141 ± 0.021^{a}
Aspergillus fumigatus (n=25)	2.035 ± 0.205^{ab}	1.195 ± 0.146^{ab}	0.720 ± 0.077^{b}
Aspergillus flavus (n=13)	4.885 ± 0.491^{c}	2.000 ± 0.227^{b}	0.577 ± 0.074^{b}
Aspergillus terreus (n=4)	2.875 ± 0.907^{b}	0.500 ± 0.092^{a}	0.188 ± 0.019^{a}
Aspergillus niger (n=3)	0.521 ± 0.135^{a}	0.542 ± 0.127^{a}	0.146 ± 0.028^{a}

Discussion

Cancer, a formidable global health challenge, stands as a leading cause of mortality worldwide (26). This study encompassed various cancer patients, including leukaemia, breast, prostate, cervical, endometrial, laryngeal, and lung cancer patients. Notably, breast cancer emerged as the predominant cancer type, constituting 68.1% of cases, aligning with global patterns highlighting its prevalence among women (27,28).

Breast cancer's prominence resonates with broader literature, emphasizing its status as the most common malignancy and a leading cause of cancer-related deaths among women globally (26). Hereditary factors, lifestyle choices, and prolonged estrogen exposure contribute to the elevated risk in women (29,30,31). The significant role played by breast cancer genes BRCA1 and BRCA2, integral to DNA repair mechanisms, underscores the hereditary component, with pathogenic variants conferring substantial lifetime risks (27).

Cervical and endometrial cancers, accounting for 2.8% and 7.6%, respectively, manifested exclusively in women above 60 years. These cancers predominantly affect post-menopausal women, correlating with the observed age distribution (32,33,34). Associated risk factors encompass age, genetic predisposition, dietary habits, sedentary lifestyle, obesity, diabetes, hypertension, and hormone replacement therapy (35). The prognosis for cervical cancer, particularly in advanced stages, underscores a challenging clinical landscape (36).

Constituting 11.1% of cases, lung cancer emerged with a formidable impact, reflecting its global status as one of the deadliest cancers (37,38). Tobacco smoking, a pivotal risk factor documented among patients, contributes significantly to lung cancer incidence (37). Metabolic activation of tobacco carcinogens induces DNA mutations, initiating tumorigenesis, while non-tobacco factors also contribute (39,40).

Prostate cancer, exclusive to males above 60 years and comprising 7.6% of cases, aligns with its recognition as the most prevalent urologic cancer in men (42). Survival rates

hinge on disease stage, with localized cases exhibiting high 5-year survival, contrasting with metastatic scenarios (38). Leukaemia, representing 1.4% of cases in patients above 60 years, follows established trends of higher diagnoses in adults (43,44). Environmental and genetic factors, along with chemotherapy exposure, elevate leukaemia risk (43). Survival rates vary by age and leukaemia subtype (44,45). Laryngeal cancer, contributing 1.4% to cases, manifested exclusively in patients above 60 years. Risk factors, including smoking, alcohol abuse, and occupational exposures to carcinogens, underscore the complexity of laryngeal cancer etiology. Timely diagnosis remains pivotal for improved survival outcomes (46).

The study underscores a substantial gender disparity, with 78% of cancer cases occurring among females. This skew is predominantly attributed to the heightened incidence of breast cancer (68.1%) in females. The age-related distribution reveals a striking concentration among patients above 60 years, constituting 40.3% of cases. Combining the 41-60 years and above 60 years age groups escalates the proportion to 86.1%, emphasizing the correlation between cancer and ageing. This aligns with the concept of cancer as a disease primarily associated with advancing age, influenced by cumulative risk factors and diminishing cellular repair mechanisms (47).

Urban dwellers exhibited a higher prevalence of cancer (71.5%), potentially linked to disparate lifestyle and dietary choices, augmented exposure to environmental carcinogens due to technological advancements, and pervasive industrial pollution. The study delineates occupational trends, with retirees comprising the majority (36.8%), including patients with leukaemia, prostate, endometrial, and laryngeal cancers. The amalgamation of artisans, civil servants, traders, and farmers accounted for 48.6% of the occupational spectrum. Retirees' susceptibility may stem from past occupational exposures to carcinogens and sedentary lifestyles during retirement, impacting cancer manifestation. Occupational cancers, characterized by prolonged latency periods, may manifest post-retirement, emphasizing the importance of recognizing these risks (49). Sedentary lifestyles post-retirement contribute to cancer vulnerability, highlighting the protective role of physical activity against several cancer types (50).

Regarding the duration of diagnosis, a notable proportion (43%) was diagnosed within 1-3 years, primarily prevalent in breast cancer, cervical cancer, and leukaemia patients. Conversely, patients with prostate, endometrial, laryngeal, and lung cancers exhibited a more frequent diagnosis within <1 year. Few patients (5.6%) surpassed 6 years in their cancer diagnosis duration. While cancer-specific survival rates are increasing, challenges persist in managing aged patients, marked by comorbidities, functional decline, frailty, and reduced life expectancy, translating into lower cancer-specific survival compared to other age groups (51).

Family history indicated a fraction (8.3%) with hereditary cancer predisposition, emphasizing genetic susceptibilities and shared environmental factors within lineages. Alcohol and tobacco usage varied among cancer types, with lung cancer patients showing the highest prevalence (62.5%). Noteworthy alcohol consumption was evident in prostate (36.4%) and breast cancer (4.1%) patients. Sociocultural factors, traumatic history, and peer influence are attributed to alcohol and tobacco indulgence, aligning with documented associations between these habits and specific cancer types (53).

Chemotherapy emerged as the predominant cancer treatment modality, followed by surgery, herbal therapy, and radiotherapy. The prevalence of chemotherapy aligns with its systemic impact, addressing metastatic cancers and averting tumor recurrence. Despite advancements in cancer management, challenges persist, reflecting the multifaceted nature of effective cancer treatment (54-55).

Infection remains a significant complication in cancer patients, attributed to both prolonged chemotherapy effects and compromised immune systems with aging (7,56). The observed higher microbial load in older patients underscores increased susceptibility to infections (57,58). Gram-negative bacteria predominated (75% of bacterial isolates), consistent with global findings associating Gram-negative bacteria with infections in cancer patients (59). These bacteria are implicated in diverse infections, emphasizing the need for targeted preventive strategies (11,60,61).

The microbial profile aligns with previous studies identifying coagulase-negative *Staphylococcus spp., E. coli, Klebsiella spp., S. aureus*, and *Pseudomonas spp*. as major contributors to infections in cancer patients (7,9,17,56,59). *Aspergillus* and *Candida* species, prevalent in this study, concur with established roles of these organisms in infections among cancer patients, often originating from biofilms in medical devices and environmental exposures (62-66).

Globally recognized for invasive infections, *Candida spp* hold specific ties to healthcare-worker transmission and intravascular-catheter usage (67). Their entry into the bloodstream may stem from direct epithelial penetration post-tissue damage or biofilm propagation on medical devices. Imbalances between host immunity and opportunistic fungal species, influenced by host immunodeficiency and fungal adaptation, contribute to candidiasis (69,70). Prolonged treatments with antineoplastics and broad-spectrum antibacterials, coupled with exposure to resistant environmental pathogens, elevate the prevalence of these opportunistic pathogens (71,72).

In this study, *K. pneumoniae, C. albicans*, and *A. fumigatus* formed a predominant trio, often coexisting with other agents in polymicrobial infections. Their potency lies in efficient invasion and survival within the host. *K. pneumoniae* employs virulence factors such as hypermucoviscous phenotype, mucoviscosity-related genes, iron uptake genes, and hydrolytic enzymes. Similarly, *C. albicans* deploys high-affinity iron acquisition systems and hydrolytic enzymes. *A. fumigatus* produces adhesins, pigments, and various

hydrolytic enzymes, enhancing its resilience in host tissues (73,61,74).

Multidrug-resistant (MDR) infections, associated with elevated mortality and treatment costs, are increasingly prevalent in high-risk patients. Sensitivity to Ofloxacin, Nitrofurantoin, and Ciprofloxacin was notable, contrasting with resistance to Ceftazidime, Cefuroxime, Cotrimoxazole, Erythromycin, and Ceftriazone. *S. aureus, S. pneumoniae, E. coli, K. aerogenes, K. pneumoniae*, and *S. dysenteriae* exhibited notable resistance to specific antibiotics, reflecting the complex interplay between antibiotic exposure, resistance acquisition, and environmental factors.

The study aligns with previous reports on antibiotic resistance in cancer patients, emphasizing the impact of prolonged exposure, sub-therapeutic doses, and broad-spectrum antibiotic use. Genetic acquisition of resistance traits further compounds the issue, necessitating continuous surveillance and antimicrobial stewardship (75).

The antifungal agents employed in this study demonstrated substantial efficacy, with Caspofungin and Voriconazole outperforming Amphotericin-B. Resistance to Amphotericin-B, a long-standing antifungal, underscores the need for alternative treatment strategies. Voriconazole's improved pharmacological profile contributes to its enhanced efficacy, while Caspofungin's status as an echinocandin, characterized by potency, spectrum, and safety, positions it favorably in treating invasive fungal infections.

Conclusion

The study at the University of Medical Sciences Teaching Hospital Akure underscores the vulnerability of cancer patients to opportunistic bacterial and fungal pathogens. Notably, *Klebsiella pneumoniae, Aspergillus fumigatus*, and *Candida albicans* emerge as frequent threats. Resistance patterns to conventional antimicrobials, specifically Cefuroxime, Cotrimoxazole, and Amphotericin-B, call for stringent infection prevention measures and antimicrobial stewardship. Routine antimicrobial susceptibility testing is crucial to monitoring resistance trends, especially against prophylactically administered drugs. Exploring alternatives to conventional antimicrobials is essential to enhance survival outcomes for cancer patients.

Author Contribution Statement

The authors confirm their contribution to the paper as follows: Study conception and design: **O. Oluyele, M.K. Oladunmoye**; data collection: **O. Oluyele, N.A. Okunnuga**; analysis and interpretation of results: **O. Oluyele, M.K. Oladunmoye, A.K. Onifade, A.O. Ogundare**; draft manuscript preparation: **O. Oluyele, M.K. Oladunmoye, A.K. Onifade, A.O. Ogundare**. All authors reviewed the results and approved the final version of the manuscript. All authors agreed to be responsible for all aspects of the work to ensure the accuracy and integrity of the published manuscript.

Ethics Statement

The authors declare that the published work reflects an investigation and analysis carried out truthfully and completely.

Conflict of interest

The authors have no conflict of interest to declare.

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Data availability statement

Upon a reasonable request, the corresponding author can provide the study's data.

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