

THE **Pharmaceutical** **Journal of Kenya**

PJK



Vol. 24 No. 4/2020

ISSN 2411-6386



FEATURE ARTICLE:
**Therapeutic Drug
Monitoring: A Golden
Opportunity for
Pharmacists**

OFFICIAL JOURNAL OF THE PHARMACEUTICAL SOCIETY OF KENYA



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The Pharmaceutical Society of Kenya (PSK) is a representative organization that was formed enabling Pharmacists' to employ their professional expertise in the care of patients.

Established in 1964, PSK has its roots in the Pharmaceutical Society of East Africa, which was registered in 1950. Since its formation, PSK continues to promote a common standard for professional conduct and code of ethics for its members, as well as advocate for the welfare of Pharmacists.

EDITORIAL

REPORTING OF ADVERSE DRUG REACTIONS

Prof. Apollo O. Maima, PhD
Editor-in-Chief, Pharmaceutical Journal of Kenya

Antimicrobial Resistance (AMR) can be defined as the ability of a microorganism to multiply or persist in the presence of an increased level of an antimicrobial agent relative to the susceptible counterpart of the same species. It bears the greatest potential risk in the current management of infectious diseases.

Exposure to antimicrobials is the major cause of the emergence and rise of AMR. Research on the consumption of antimicrobials, in outpatient settings of 26 European countries, showed that AMR rates were higher in countries which consumed more antimicrobials. The abuse and overuse of antimicrobials has been phenomenal for decades, exacerbating the development of AMR, and rendering some infections untreatable using existing antimicrobials. This escalation of AMR has led to ineffective treatment, prolonged epidemics, increased morbidity and mortality

It is estimated that without adequately effective interventions, especially policy changes, AMR associated human global mortality will increase from 700,000 in 2014 to over ten million by 2050. In the process, the global economy may lose more than USD 6 trillion dollars, almost 4% of Gross Domestic Product, annually by 2050 because of AMR if not controlled. By 2030, 24 million more people may be forced into extreme poverty, hunger and malnutrition because of AMR, and many will be from low income countries. Because of the burden of infectious diseases, low-income countries like Kenya are more vulnerable to hardships, hence most affected by AMR, putting the achievement of Sustainable Development Goals (SDG's) in peril. Resistant bacteria are a global problem that requires a holistic and multi-sectoral (Global One Health) solution. Changes in agricultural production practices can help keep present antimicrobials working. Antimicrobials used in animals are similar to those used in humans; bacteria in humans, animals or the environment may spread from one species to the other, and from one country to another.

The 2016 United Nations General Assembly resolution and the 2017 Berlin Declaration of the G20 Health Ministers are signs that AMR is being taken seriously. International governments and agencies through the World Health Organization (WHO) in 2015 also took steps towards containment of AMR and member states agreed to develop action plans by 2017. Many countries, Kenya included, largely met this deadline. However Kenya, like many other low and medium income countries (LMIC's), has not yet started implementing appropriate policies to contain amplification of AMR, and reduce overuse and misuse of antimicrobials. The World Health Organization (WHO), Food

and Agriculture Organization (FAO), and World Organization for Animal Health (OIE), the Tripartite Partnership, are jointly primed to minimize the emergence and spread of AMR. The partnership supports the Global Action Plan (GAP) on AMR with a strategic plan on AMR; to provide the international standards to guide prevention and containment. It has led the global campaign on AMR and initiated country self-assessments on AMR to monitor progress with implementing their National Action Plans (NAP) on AMR.

Challenges abound in addressing AMR through government policies due to limited political commitment, low awareness and weak stakeholder engagement. Most governments globally also suffer limited capacity to implement policies because of poor technical capacity and financial resources. Kenya has developed a number of multi-sectoral policies in its attempt to contain AMR. They provide for what appear to be clear roadmaps for coordinated efforts to set national standards for minimizing transmission of AMR and associated infections. They should culminate in the formulation and establishment of a national integrated surveillance system for antimicrobial resistance by the National Policy for the Prevention and Containment of Antimicrobial Resistance. However, there is no evidence of much activity on the ground towards the implementation. In fact, due to lack of systematic surveillance, the actual burden of AMR in Kenya is unknown.

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Medication Related Problems in Patients with Head and Neck Cancers at Kenyatta National Hospital

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Abstract

Background: Treatment of cancers is often associated with a wide range of medication-related problems (MRPs) due to the toxic nature of the regimens used. Studies have characterized the extent of these therapy problems in specific subsets of cancer, but no data is currently available for head and neck cancers. This group of patients faces unique challenges that have a significant impact on the administration, adherence, effectiveness, and safety of medications used.

Objective: The study assessed the medication-related problems among patients on treatment for head and neck cancer patients at Kenyatta National Hospital.

Methods: A cross-section design was used, and ninety participants were randomly sampled at Kenyatta National Hospital oncology clinic after voluntarily consenting to participate. Data was collected using a researcher administered questionnaire and data abstraction form from the hospital records and through a patient interview between February and April, 2019. The collected data were entered into Microsoft Excel 2016 workbook and exported to STATA version 14 for analysis.

Results: The study had 90 participants, and the majority (58, 64.4%) were male. The mean age was 49.4 ± 17.08 years. Participants with at least one MRP were 83 (92.2%). The three most prevalent MRPs were adverse drug reactions (71, 78.9%), the need for additional drug therapy (28, 31.1%), and unnecessary drug therapy (14, 15.6%). The majority (80, 88.9%) of the patients were appropriately managed and 43 (48%) were treated with chemoradiation. Moderate to severe drug-drug interactions and those requiring monitoring or therapy change were found in 40 (44.4%) participants. The reasons for non-adherence were adverse reactions to treatment (11, 12.1%), forgetting to take drugs (6, 6.7%), cost of drugs (3, 3.3%), unavailability of medications (3, 3.3%), and difficulty in using the medications (3, 3.3%).

Conclusion: Adverse drug reactions, the need for additional medication, and unnecessary drug therapy were identified as the most commonly occurring MRPs among the participants.

Keywords: Cancer, Medication related problems, Prevalence.

Introduction

Head and neck cancers (HNCs) are a heterogeneous group

of neoplasms that affect the anatomical structures, including the nasal cavities, skull base, oral cavity, and salivary glands. Other parts that are affected include paranasal sinuses, oropharynx, nasopharynx, hypopharynx, larynx, maxillofacial bones, odontogenic processes, ear, and neck lymph nodes. HNCs are of particular interest because of two reasons: First, they affect vital structures needed for essential life functions such as breathing, speech, swallowing, hearing, taste, and smell [1]. Interruption of these functions is associated with high morbidity and mortality. In Kenya, the incidence of head and neck cancers is increasing. According to Globocan 2018, nasopharyngeal carcinoma is the most prevalent HNC and is ranked eleventh among new cases [2].

Medication-related problems arise when a patient's drug needs are not adequately met in terms of efficacy, safety, indication, and patient compliance. Thus, desired patient outcomes such as cure of disease, prevention, and resolution of symptoms or slowing down of the disease process are not achieved [3]. Pain and functional impairment of the mouth and throat is experienced by most patients undergoing treatment for head and neck cancers [4]. These disorders often lead to problems when administering oral medication for managing important treatment-related adverse events such as nausea, vomiting, and pain. It also presents difficulties in maintaining the patient's nutrition needs leading to loss of weight and worsening of the condition. Generally, cancer patients have a higher risk of developing MRPs compared to other diseases because of the nature of the treatments, stage of disease burden, comorbidities and, polypharmacy [4,5]. Although studies on MRPs have been done for cancer patients, there is a glaring gap in research when it comes to MRPs experienced by patients suffering from head and neck cancers [6,7]. The objective of the study was to assess the medication-related problems among patients on treatment for head and neck cancers at Kenyatta National Hospital.

Materials and Methods

Study site and design

A prospective hospital-based descriptive cross-sectional study was used. It involved adult patients undergoing treatment for head and neck cancer at Kenyatta National Hospital (KNH) between February and April, 2019. The facility is the largest teaching and referral hospital in Kenya and the primary referral site for the diagnosis and treatment of cancers in Kenya.

Study Population

The study population was patients at least 18 years of age that were undergoing treatment for head and neck cancers, regardless of the treatment modality. Only those patients who consented to participate were included. Those with cognitive impairment or not on any treatment were excluded.

Sample size and sampling technique

The sampling frame consisted of patients being managed for head and neck cancers in the Cancer Treatment Centre of KNH. The sample selection was made using simple random sampling until the sample size was achieved. The sample size was determined using Cochran formula [7]:

$$n = z^2 * \frac{p(1-p)}{d^2}$$

Where: z – the standard normal deviate = 1.96 at 0.05 level of significance

p – the prevalence of MRPs in cancer patients=0.74

d – Precision estimate = 0.05

n – sample size

Taking into account that no previous studies on MRPs in HNC have been done in any setting, the prevalence of MRPs in this population was unknown. However, in a prospective cross-sectional study conducted in Ethiopia among cancer patients, the prevalence of MRPs was 74% [33].

$$n = 1.96^2 * \frac{0.74(1-0.36)}{0.05^2}$$

$$n = 409 \text{ patients}$$

By applying the correction formulae to account for the finite population, the minimum sample size (n) required was:

$$n = \frac{n_0}{1+n_0/N}$$

Where: n = Minimum sample size required

n₀ = Calculated sample size (409 patients)

N = Total number of patients that had HNC and attending the oncology clinic at KNH between May and August in 2018.

$$n = \frac{409}{1+409/103} = 82 \text{ patients}$$

Since there was a possibility that not all participants will respond, a 10% nonresponse rate was added, resulting in a sample size of 90 patients.

Data Collection

Data collection involved two sources. The first source was the patients where data was collected using a researcher administered structured questionnaire through an interview. The eligible patients were informed of the study and provided with the informed consent form to assent before

the interview. The second data source was the medical records of patients who had agreed to be interviewed.

Data Analysis

Data analysis involved data entry into Microsoft Excel 2016 worksheets. The appropriateness of medical therapy for the patients was compared to the recommendations of the National Comprehensive Cancer Network guidelines for HNC treatment. The degree of adherence was determined using patient self-reporting. Potential drug-drug interactions were assessed using the Micromedex drug interaction checker. Data on the appropriateness of therapy and drug interactions were coded and entered in MS Excel 2016 software. After data entry and cleaning, it was exported to STATA version 14 for analysis.

Ethical Considerations

Before beginning the study, ethical approval from the KNH and University of Nairobi Ethics and Research Committee was granted. Also, authorization from relevant authorities in the clinics and wards in KNH was granted. Participation in the study was open and voluntary, and only those who signed the informed consent were included in the study. Confidentiality of the data was maintained by removing participants' identifiers and all hard copy documents placed under lock and key. The Excel worksheets and soft copy documents were password-protected, and only the principal investigator had access to them. Data was not shared with anyone except those involved in the study.

Results

Sociodemographic Characteristics

The study involved ninety participants and majority (58, 64.4%) were males (Table 1). The mean age was 49.4 (SD 17.08) and the range was 18 to 89 years. The proportion of underweight participants was 28.9%. There were more males (31, 34.4%) with smoking history compared to females (30, 33.3%), and the same trend was observed with use of alcohol. 38 (42%) respondents were self employed and 75 (83.3%) were feeding normally. 67 (74.4%) participants were married, while 30 (33.3%) relied on their spouses and children for social support.

Table 1. Sociodemographic characteristics (n=90)

Variable	Frequency (n)	Percentage (%)
Sex		
Male	58	64.4
Female	32	35.6
Age in Years		
18-37	24	26.7
38-57	35	38.9
58-77	29	32.2
78-87	2	2.2
BMI Status		
Underweight	26	28.9
Normal	43	47.8
Overweight	15	16.6
Unknown	6	6.7

Marital Status		
Single	23	25.6
Married	67	74.4
Smoking Status		
Current Smoker	2	2.2
Previous Smoker	30	33.3
Never Smoked	58	64.4
Drinking Status		
Currently Drinking	3	3.4
Previously Drunk	29	32.2
Never Drunk	58	64.4
Level of Education		
Primary	33	36.7
Secondary	39	43.3
Tertiary	13	14.4
None Given	5	5.6
Employment Status		
Formally Employed	10	11.1
Not Employed	42	46.7
Self Employed	38	42.2
Home Care		
Spouse	19	21.1
Children	13	14.4
Spouse & Children	30	33.3
Extended Relatives	8	8.9
Parents	8	8.9
Others	12	13.4
Feeding Status		
Feeding Normally	75	83.3
Feeding Through Tubes	15	16.7

Prevalence of head and neck cancers

The prevalence of head and neck cancers among the participants are shown in Figure 1. Regarding the distribution of the cancers according to gender, males had more incidences of the nasopharyngeal, laryngeal, tongue, and oral cancers than female participants. Conversely, the latter had a higher incidences of hypopharyngeal and oropharyngeal cancer. The majority (73, 81.1%) of cases had primary tumours with recurrent and metastatic ones accounting for 14 (15.6%) of them. The remainder (3,3.3%) were due to residual and metastatic-recurrent cancers. The distribution of the various stages of these malignancies is shown in Figure 2.

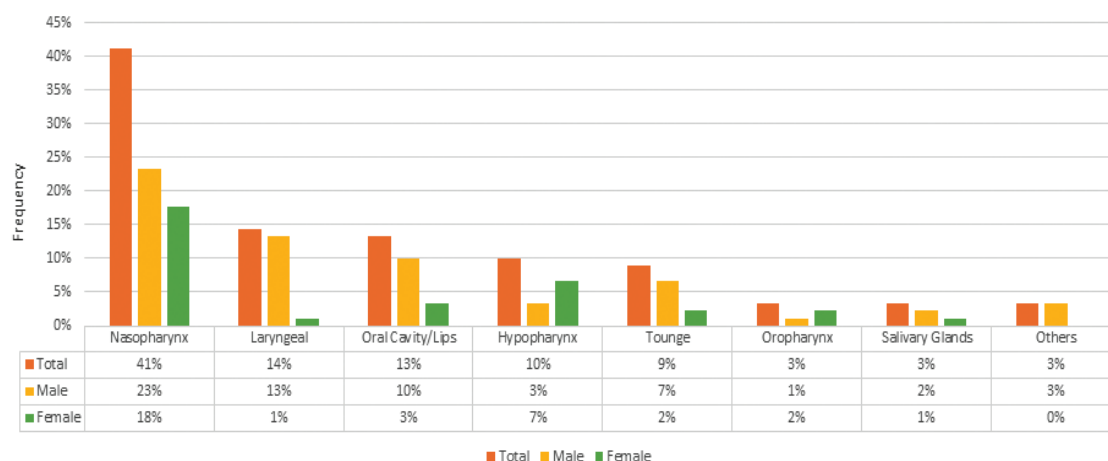


Figure 1. Prevalence of head and neck cancers (n=90)

Others: Invasive neoplasm of the neck (1), hypopharynx and tongue (1), oral cavity, and tongue (1). 48 (53%) cases were in stage four, and 25 (28%) were not clinically staged.

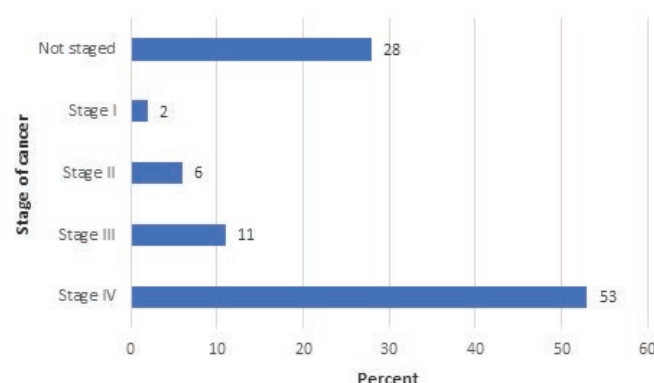


Figure 2. Stage of cancer at time of diagnosis (n=90)

Only 19 (21.1%) participants had concurrent illnesses. These were hypertension (8, 9%), HIV (4, 4%), diabetes and hypertension (3, 3%), and diabetes mellitus alone (2, 2%).

Management of head and neck cancers

The various treatment modalities for head and neck cancers utilized were chemotherapy (30, 34%), chemoradiation (43, 48%), radiation alone (12,13%), and others (5, 5%), which included a combination of chemoradiation and surgery or radiation and surgery. The chemotherapy regimens used mostly consisted of alkylating agents, taxanes and antimetabolites (Table 2).

Table 2. Chemotherapy regimens (n=90)

Chemotherapy Regimen	Frequency (n)	Percentage (%)
Weekly Cisplatin	35	38.89
High Dose Cisplatin (3-weekly regimen)	5	5.55
Carboplatin/Paclitaxel	3	3.33
Cisplatin/Docetaxel	3	3.33
Docetaxel/Cisplatin/5-Fluorouracil	17	18.9
Cisplatin/5-Fluorouracil	3	3.33
Vinorelbine/Gemcitabine	1	1.11
Cisplatin/Paclitaxel	7	7.78
Carboplatin	1	1.11
Capecitabine	1	1.11

Of these, cisplatin and docetaxel were the most commonly used. 42 (5 5 . 3 %) participants received chemotherapy as part of their chemoradiation treatment plan. The remainder of the regimens were used for induction, adjuvant and palliative purposes.

Docetaxel/Cisplatin/5-Fluorouracil regimen was extensively used during induction therapy, before surgery or

chemoradiation. Weekly cisplatin was frequently used in chemoradiation though high dose cisplatin, carboplatin, and capecitabine were also used.

Prevalence of adverse effects of treatment regimen

The majority (84, 93.3%) of participants experienced more than one adverse drug effect.

Table 3. Prevalence of adverse effects of treatment regimens

Side effects	Frequency (n)	Percentage (%)
Chemotherapy-related adverse effects (n=76)		
Nausea	54	71.6
Local site reactions	11	14.9
Anemia	14	18.9
Neutropenia	11	14.9
Fatigue	8	10.8
Pain	28	36.8
Nephrotoxicity	9	12.2
Loss of appetite	4	5.4
Alopecia	2	2.7
Paresthesia	2	2.7
Constipation	2	2.7
Bleeding	4	5.4
Radiotherapy- related side effects (n=59)		
Mucositis	26	44.1
Skin reactions	10	16.9
Dysphagia	15	25.4
Pain	24	40.7
Odynophagia	13	22
Dry mucous membrane	14	23.7
Skin desquamation	6	10.2
Mouth sores/ulcers	23	39.0

Of the 76 that were on chemotherapy treatment, 12 (14.9%) did not report any side effect, and 63 (82.9%) had several. Out of the 59 (65.6%) participants on radiotherapy treatment, 10 (16.9%) did not report any adverse effect. The most common side effects of drugs were nausea (54, 71.6%), mucositis (26, 44.1%), mouth sores (23, 39%), and anemia (14, 18.9%), as shown in Table 3.

Management of side effects

Medication used to manage the side-effects are shown in Table 4.

Table 4. Drugs used to manage adverse effects (n=90)

Medication	Frequency (n)	Percentage (%)
Anti-emetics		
Serotonin receptor (5HT-3) antagonists	54	60
Metoclopramide	8	8.9
Dexamethasone	51	56.7
Antihistamines		
Ranitidine	23	25.6
Chlorpheniramine	10	11.1
Anti-anemics		
Blood-transfusion	3	3.3
Iron Supplements	7	7.8
Anti-neutropenic		
Filgrastim	7	7.8
Analgesics		
NSAIDs	20	22.2
Paracetamol	23	25.6
Opioids	33	33.7
Others	4	4.4

Mucositis management		
Mouthwashes	22	24.4
Oral Lozenges	9	10
Sucralfil	2	2.2
Nystatin Oral Drops	14	15.6
Xylocaine Mouth Spray	16	17.8
Skin Related side-effects		
Antibiotic creams	10	11.1
Dry Mucous Membrane		
Pilocarpine	1	1.1
Anti-Fungal (Oral Candidiasis)		
Fluconazole	4	4.4

The serotonin receptor (5HT2A) antagonists used were ondansetron (36, 40%), granisetron (16, 17.8%) and palonosetron (2, 2.2%). Among the medicines used to manage pain were non-steroidal anti-inflammatory drugs and opioids. Pre-medications for cisplatin to limit toxicity involved furosemide, potassium chloride, and magnesium sulfate. 31 patients received taxanes, and of these, pre-medications were administered in 17 (54.8%) participants.

Characterization of medication-related problems

The seven medication-related problems were assessed, and the results are shown in Figure 3.

83 (92.2%) participants had at least one medication-related problem. The majority (71, 78.9%) were due to adverse reactions followed by the need for additional drug therapy (28, 31.1%) and unnecessary drug therapy (14, 15.6%).

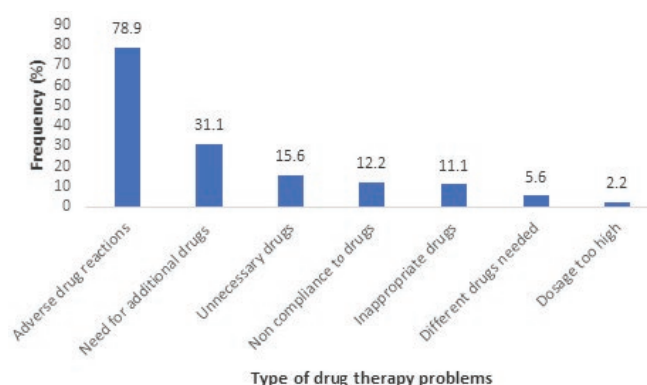


Figure 3. Prevalence of medication-related problems (n=90)

The prevalence of unnecessary drug therapy was 15.6%. Of the five sub-categories, the most reported MRP was lack of medical indication (8, 8.9%) among several drugs. Ranitidine was administered in four (4.4%) cases without any justification in addition to prednisolone and tranexamic acid each with one (1.1%) and two (2.2%) for omeprazole. Additionally, duplicate therapy was found for dexamethasone and prednisolone (1, 1.1%), aceclofenac and diclofenac (1, 1.1%) as well as the serotonin receptor antagonists ondansetron and granisetron (2, 2.2%).

The prevalence for the need for additional drug therapy was 31.1%. There were 15 (16.7%) cases of unmanaged radiation-based side-effects with mucositis being the most

unaddressed (9, 10.0%). Other untreated adverse reactions requiring pharmacological therapy included dry mucous membranes, skin reaction, pain, and odynophagia with 5 (5.5%), 3 (3.3%), and 1 (1.1%) case respectively. For chemotherapy-induced side effects, pain (5, 5.6%), anemia (2, 2.2%), nausea (2, 2.2%), neutropenia (1, 1.1%) and paresthesia (2, 2.2%) were left untreated in 13 (14.4%) participants.

Five (5.6%) respondents needed different drugs to be prescribed. A change in the dosage form was found necessary in 3 (3.3%) cases affecting the pain management medication and 1 patient was refractory to paclitaxel necessitating a change of therapy. In 1 (1.1%) case, more effective therapy for paresthesia was required.

Out of the seven possible causes for adverse drug reactions, undesirable effects were experienced by 65 (72.2%) respondents. In addition, the drug-drug interactions with the potential to cause moderate to severe harm were recorded. 40 (44.4%) patients had potentially harmful interactions with those involving cisplatin and furosemide being the most abundant (23, 25.6%). Other interactions included 5HT3 antagonists and opioids (12, 13.3%), NSAIDs and dexamethasone (4, 4.4%), ondansetron and dexamethasone (1, 1.1%), fluconazole and ondansetron (1, 1.1%), opioids and chlorpheniramine (3, 3.3%) paracetamol and metoclopramide (1, 1.1%), paracetamol and granisetron (1, 1.1%), metoclopramide/opioids (4, 4.4%) and opioids and furosemide (3, 3.3%).

Only 2 (2.2%) patients had potential interactions that could affect dose levels. These mainly involved fluconazole which can increase the effects of opioids and NSAIDs by increasing their availability in the body. None of the other sub-categories of this MRP were identified.

Eleven (12.2%) patients had problems adhering to their medication with three sub-categories cited. 7 (6.7%) just forgot to take their medicines while 3 (3.3%) had difficulty taking their drugs and 2 (2.2%) could not comply with treatment as the drugs were not available. In relation to this, 17 (17.8%) patients had treatment delays due to various reasons such as severe skin reactions (3, 3.3%), low hemoglobin levels (2, 2.2%), low creatine clearance/raised serum creatinine (6, 6.6%), cost of treatment (3, 3.3%), unavailability of drugs (1, 1.1%), and low bed capacity for inpatient chemotherapeutic regimens (1, 1.1%). Ten (11.1%) participants had inappropriate therapy in reference to National Comprehensive Cancer Network guidelines.

Discussion

The majority of the participants were male, as has been observed in other studies [8,9,10,11]. Males are more likely to engage in activities that are known to increase the risk of HNCs, such as use of tobacco and alcohol [10,12,13]. More than half of the respondents had no history of either alcohol and cigarette use which was contrary to previous studies [14]. A majority of the patients were appropriately managed in accordance with current NCCN Guidelines. These treatments are based on the type and stage of cancer.

Multimodal treatment strategies were widely utilized in the study group. Combining different treatment strategies improves survival rates and treatment outcomes [4,15,16,17]. Chemoradiation was the mainstay of treatment and platinum-based chemotherapy regimens were the most utilized [4,15]. Taxane-based induction chemotherapy was exclusively used in the study setting. These specific therapies involving platinum compounds and taxanes are extensively utilized in the management of HNCs [4,15,18].

In the management of chemotherapy-induced nausea and vomiting, 5-HT₃ receptor antagonists were preferred. They have demonstrated superior efficacy and better tolerability compared with other antiemetics [19]. Dexamethasone was often used together with the 5-HT₃ receptor antagonists [6]. Pain in HNC is widespread arising from both the disease process and treatments initiated, especially radiotherapy [20]. The widely used drugs for managing pain were opioids due to the duration and nature of the pain [21,20]. Non-steroidal anti-inflammatory drugs were also widely used singly or in combination. The use of xylocaine to manage pain due to mucositis is supported by its easy mode of application, as a mouth spray, and its rapid onset of action though it should not be applied when performing oral hygiene measures to prevent accidental trauma in the oral cavity [22].

The prevalence of MRP's was high and this observation concurred with similar studies done in Kenya [6] and Nigeria [33] but was much higher than Ethiopia [28]. Other studies in the Netherlands, Norway, and Portugal among cancer patients yielded similar results [24,25,26]. Adverse effects as the most common MRP was expected, given the proven toxicity of chemotherapeutic drugs [4]. Similar findings have been reported in Ethiopia and Thailand [23,34]. The ADRs recorded in these studies were mainly nausea and vomiting, which are associated with the highly emetogenic attribute of platinum-based compounds and fluorouracil. ADRs, for both chemotherapy and radiotherapy, were also responsible for most of the treatment delays with severe skin toxicities, low hemoglobin count and low creatinine clearance standing out.

The second most common MRP in this study was the need for additional drugs [5,23]. Closely tied to the adverse reactions caused by the two main treatment modalities used to manage HNCs, radiotherapy and chemotherapy, the need for additional drugs was manifested in the inadequacy of managing these side effects. Studies have shown that adverse reactions to treatment can affect the quality of life and cause treatment delays [27,28,29]. It is, therefore, important to ensure that adequate pharmacological therapies, where applicable, are utilized to promote patients' wellbeing. This is especially so for radiotherapy-related side effects, such as mucositis, pain, and skin toxicities, where more were left untreated compared to chemotherapy-induced side-effects, such as anemia, nausea, and pain.

The prevalence of unnecessary drug therapy was similar to a study done in Ethiopia [23]. The lack of indication was especially evident for a number of drugs standing at 8.9%.

This is comparable to a prevalence of 12.4% found in a study among cervical cancer patients in Kenya. Also, there was the duplication of therapy involving antiemetics, NSAIDs, and glucocorticoids.

Significant drug-drug interactions were present in 44.4% of the patients. The complexity of chemotherapeutic regimens, including pre-medications, increases the susceptibility of cancer patients to drug interactions. This has been consistently demonstrated in studies done in Kenya and Dutch though lower levels of DDI have been found in Ethiopia [6,23,30]. This disparity may be due to a large number of software and tools used to check for drug and food interactions. These tools are not standardized in their interaction checkers and categorize interactions severity differently.

The most significant interaction was between cisplatin and furosemide. Furosemide is used mainly as a premedication to promote diuresis in patients receiving cisplatin to minimize the risk of cisplatin-induced nephropathy. However, studies have shown this combination can increase the likelihood of ototoxicity, which is especially significant for these types of patients where treatment and disease processes can cause hearing deficits [31]. In other interactions, 5HT3 antagonists' efficacy could be reduced by dexamethasone. On the other hand, dexamethasone, in combination with NSAIDs enhances the risk of gastrointestinal irritation [32]. Fluconazole was more likely to deter the metabolism of opioids and NSAIDs, thus increasing their effect.

In prescribing for head and neck cancer patients, it is crucial to consider the appropriate dosage form as most patients will experience pain and difficulty when taking commonly used solid dosage forms, especially tablets. This consideration was evident in practice where liquid dosage forms, syrups and solutions, suppositories, and effervescent formulations were dispensed in several cases. Still, a small percentage needed dosage form adjustments to ease the administration of their medication. There was only one case of cancer being refractory to treatment necessitating a switch to second-line therapy for recurrent nasopharyngeal carcinoma. Only a few participants showed low adherence to medicines since most of them were administered in the hospital under supervision, whether parenterally or orally. Also, the confidence among the patients in the efficacy of the medication administered to them could help explain this scenario. However, some patients did experience problems with compliance as a result of forgetfulness, difficulty in taking drugs, unavailability, and the high cost of treatment [33].

Conclusion

The prevalence of medication related problems was high and the most prevalent were adverse drug reactions and the need for additional drug therapy.

Conflict of interests

No conflict of interest was declared by the authors.

Acknowledgements

The authors acknowledge the Department of Pharmaceutics and Pharmacy Practice of the University of Nairobi, the Kenyatta National Hospital administration. Also, the oncology unit for providing a favorable site for the research as well as the participants for being very cooperative.

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Prevalence and Antimicrobial Susceptibility of Urogenital Pathogens in a Kenyan Tertiary Health Facility

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Abstract

Background: Urogenital infections are among the most commonly reported infections in outpatient care and are caused by bacteria, protozoa, or fungi. They occur in both males and females, but the incidence is much higher in females. Most patients respond well to antimicrobial treatment, but there has been an increase in the incidence of recurrent infections due to the development of resistance.

Objective: The study aimed at evaluating the prevalence and antimicrobial sensitivity patterns of bacteria implicated in urogenital infections at Kenyatta National Hospital (KNH).

Methodology: A retrospective descriptive cross-sectional study design was adopted for the study. The study population comprised patients whose urine samples had undergone antimicrobial susceptibility testing at the KNH microbiology laboratory. Simple random sampling was used to select patient records between January 2019 and May 2019. The data was collected using predesigned forms. Data collected included biodata, type of organisms isolated and antimicrobial susceptibility. The data was analyzed using STATA version 14.

Results: Out of 330 participants, 204(61.8%) were females. The most affected age groups were between 18 and 25 years (25.7%) and those between 26 and 35 years (34.8%), respectively. Gram-negative uropathogens were the most common isolates. The most prevalent microorganism was *Escherichia coli* (50.6%), followed by *Staphylococcus aureus* (12.8%), *Klebsiella spp* (11.5%), *Proteus spp* (10.0%), *Coagulase negative staphylococci* (8.2%) and *Pseudomonas aeruginosa* (7.0%). *Escherichia coli* showed high sensitivity to Ceftriaxone (94.0%), Ciprofloxacin (91.0%) and Gentamicin (81.4%), while sensitivity to Ampicillin was low (15.0%). Other Gram-negative isolates including *Klebsiella spp*, *Proteus spp*, and *Pseudomonas aeruginosa* were generally sensitive to Ciprofloxacin at, 86.8%, 97.0%, and 82.6% respectively.

Conclusion: Gram-negative bacteria were the most common cause of urinary tract infection, and they were generally sensitive to ciprofloxacin.

Keywords: Prevalence, susceptibility, pathogens, urogenital.

Introduction

Urogenital infections are caused by bacteria, protozoa, and fungi. Clinical evidence has shown that these organisms have a significant role in maintaining the health of the genito-urinary tract. Non-pathogenic *Lactobacilli* is the most dominant species of healthy vaginal flora [1]. Both men and women are predisposed to urinary tract infection, which occurs more frequently in females, with approximately one billion women around the world suffering from non-sexually transmitted urogenital infections [2]. Most female patients respond well to antimicrobial treatment, although recurrence does occur, and treatment is associated with side effects.

This scenario may be explained in part by the fact that the pathogens migrate upwards from the rectum to the vagina and then the bladder, a process mediated by bacterial adherence that is not altered by the use of antibiotics [3]. Under the normal and healthy condition, the genito-urinary tract is sterile. This is ensured by the presence of various antibacterial and anti-adherence factors such as low pH, high osmolality, urea and salt concentration, secretory cytokines (IgA), and urinary oligosaccharides, among others. However, uropathogenic organisms can resist the host defence system, adhere to and colonize tissues of the urinary tract leading to infection [4].

The risk factors associated with the development of urogenital infections include female gender, sexual intercourse, pregnancy, use of diaphragm and spermicides, diabetes mellitus, urinary tract obstruction, catheterization, and prostatic enlargement in men [2]. The risk of acquiring these infections also increases with age due to factors such as lack of estrogen in post-menopausal females, loss of *lactobacilli* in vaginal flora, increased incidence of diabetes mellitus in the older population and urethral colonization by *Escherichia coli* [2].

There are six categories of urogenital infections [5]. Uncomplicated infection occurs when there's no

physiological or structural abnormality of the urinary tract, and no comorbidities impairing the host defence mechanisms. Complicated infection occurs when there is obstruction of the ureter, including renal calculi. Isolated infections refer to the first incidence of infection or when episodes occur six months apart. Unresolved infections occur when antimicrobial treatment fails due to infection by two different species of bacteria with limited susceptibility or bacterial resistance to agents being used.

Reinfection occurs when there is no bacterial growth after successful treatment, but the same organism regrows after two weeks. This accounts for >90% of recurrent infections in females. The sixth is a relapse, which refers to infection by the same microorganism within two weeks of therapy. The incidence of urogenital infections is more common in women due to the short distance between the anus and urethra since infection occurs by ascending route. The clinical manifestations include dysuria, frequency of micturition, pain in the back or lower abdomen, dark urine, occasionally haematuria, pyuria and fever or chills, which may indicate spread to the kidneys [5].

Management involves the use of antimicrobial agents. For recurrent infections, antimicrobial susceptibility testing is done when the patient has a history of the previous infection with antibiotic-resistant strains. These patients have a longer course of treatment, and fluoroquinolones such as ciprofloxacin may be used (6,7). However, their use is reserved due to the severe side effects associated with their use [8,9]. Recently, there has also been an observed increase in the incidence of antibiotic-resistant strains among uropathogens to fluoroquinolones, which has led to a corresponding increase in the incidence of recurrent infections due to ineffective and inadequate therapy. There has also been the development of multidrug-resistant strains [10]. This study assessed the prevalence of the bacteria implicated in urogenital infections and their antimicrobial susceptibility patterns at Kenyatta National Hospital.

Materials and methods

Study design and site

A retrospective descriptive cross-sectional study design was used, and the site was Kenyatta National Hospital, Microbiology Laboratory. The hospital is located in Nairobi and is the largest teaching and referral health facility in Kenya. This laboratory handles all samples collected for microbiological testing in the hospital.

Study population

The study population comprised patients whose urine samples underwent antimicrobial susceptibility testing at KNH. All laboratory records of patients above the age of 18 years diagnosed with urogenital infections between January 2019 and May 2019 were included in the study.

Sample

The sampling frame consisted of records of patients whose urine samples were analysed at the KNH Microbiology laboratory. The sample size was determined using the Fischer's formula [11].

$$n = Z^2 * \frac{p(1-p)}{d^2}$$

Where: n = Sample size, Z = Standard normal deviate (1.96), p= prevalence of organism implicated, d = Degree of precision (5%)

From a previous study carried out in India, the prevalence of *Escherichia coli* was found to be 68.8%. This pathogen was chosen because it is the main cause of urinary tract infection globally especially in developing countries like India and Kenya. Using this prevalence and a degree of precision of 5%, the sample size was

$$1.96^2 \times 0.688 (1-0.688)/0.05^2 = 330$$

Thus 330 records were selected, and the data abstracted accordingly.

Simple random sampling was used to select patients' records for this study. This was done using computer generated random numbers. The researcher accessed the records of patients whose urine samples were tested and apportioned the numbers accordingly. This approach was used to ensure that each record had an equal chance of being selected.

Data collection

Data were obtained from the laboratory records and entered into an abstraction form. This form contained sections for patient's biodata, type of infecting pathogens, and antimicrobial susceptibility testing results.

Data analysis

Data was entered into excel worksheets and exporting to STATA version 14. The variables analysed included the gender, age, prevalence of the pathogens and their antimicrobial susceptibility patterns. The results were summarized as proportions and presented in frequency tables.

Ethical and logistical considerations

Before beginning this study, ethical approval was granted by the KNH and University of Nairobi Ethics and Research committee. Authorization was also obtained from the research office and head of microbiology laboratory of KNH. Confidentiality of the data was ensured by coding. The worksheets and softcopy documents were password-protected and stored in a computer and flash disk. Only the principal investigator had access to the data.

Results

Sociodemographic characteristics

Majority (61.8%) of the participants were females (Table 1).

One hundred and fifteen participants (34.8%) were in the age group between 26 and 35 years.

Table 1. Sociodemographic characteristics of study participants

Characteristics	Frequency	Percentage
Gender		
Male	126	38.1
Female	204	61.8
Age (Years)		
18-25	85	25.7
26-35	115	34.8
36-45	62	18.8
46-55	49	14.8
56-65	10	3
Above 65	9	2.7

Prevalence of bacterial uropathogens

The most prevalent organism was *Escherichia coli* (50.6%), followed by *Staphylococcus aureus* (12.7%), *Klebsiella spp* (11.5%), *Proteus spp* (10%), *Coagulase negative staphylococci* (CONS)(8.2%) and *Pseudomonas aeruginosa* (7%).

Antimicrobial susceptibility patterns

The susceptibility patterns are shown in Table 2. The urine samples were collected from both hospitalized and ambulatory patients. The drugs tested were commonly used at KNH and therefore included in the institution's drug formulary. *Escherichia coli* showed the highest sensitivity to Ceftriaxone (94%), Ciprofloxacin (91%) and Gentamicin (81.4%) while sensitivity to Ampicillin was low (15%). Other Gram-negative isolates including *Klebsiella spp*, *Proteus spp* and *Pseudomonas aeruginosa* exhibited high sensitivity to Ciprofloxacin at, 86.8%, 97%, and 82.6% respectively.

Table 2. Antimicrobial sensitivity pattern of the uropathogens at KNH.

Drug	Type of organism					
	<i>Escherichia coli</i> (n=167)	<i>Staphylococcus aureus</i> (n=42)	<i>Klebsiella spp</i> (n=38)	<i>Proteus spp</i> (n=33)	CONS (n=27)	<i>Pseudomonas aeruginosa</i> (n=23)
Ampicillin	25 (15.0 %)	25(59.5%)	2 (5.3%)	8(24.2%)	19(70.4%)	0
Ceftriaxone	157(94.0 %)	29(69.0 %)	20(52.6%)	24(72.7%)	26(96.3%)	9(39.1%)
Gentamicin	136 (81.4%)	36(85.7%)	17(44.7%)	23(69.7%)	23(85.2%)	7(30.4%)
Ciprofloxacin	152(91.0 %)	31(73.8%)	33(86.8%)	32(97.0 %)	22(81.5%)	19(82.6%)
Cotrimoxazole	78 (46.7%)	19(45.2%)	8 (21.1%)	5(15.2%)	15 (55.6%)	3(13.0 %)
Tetracycline	33(19.8%)	17(40.5%)	0	33(100%)	17(63.0%)	1 (4.3%)

Discussion

The study aimed at evaluating the prevalence of urogenital infections and antimicrobial sensitivity patterns of organisms implicated in urogenital infections at Kenyatta National Hospital. The results depict that females were more infected compared to males, and *Escherichia coli* was the most prevalent pathogen [12,13]. However, a similar study carried out in Serbia, show that *Enterococcus spp.* predominated

[14]. High prevalence of UTIs in females is due to the inherent virulence of *Escherichia coli* for urinary tract colonization such as its abilities to adhere to the urinary tract and association with other microorganisms moving from the perineum areas contaminated with fecal microbes to the moist warm environment of the female genitalia [15]. *Staphylococcus aureus* was the second most prevalent bacteria. The high frequency of this pathogen in UTI is not unique to this study and had been observed in Uganda [16]. This organism is not a primary pathogen of urinary tract infection, but the use of instrumentation such as bladder catheters may explain this scenario [17].

The isolates exhibited low levels of sensitivity to commonly used antimicrobial agents such as Ampicillin and Trimethoprim-Sulfamethoxazole. These findings are consistent with previous studies carried out in Portugal [18] and Pakistan [19]. However, *Escherichia coli* was highly sensitive to Gentamicin and Ciprofloxacin, contrary to findings from Pakistan and Taiwan [19]. *Klebsiella spp* was highly sensitive to Ciprofloxacin but relatively resistant to other drugs [20]. *Proteus spp* was highly sensitive to Ciprofloxacin and resistant to Ampicillin and Cotrimoxazole due to plasmid-mediated resistant genes [20]. *Pseudomonas aeruginosa* demonstrated marked resistance against all the drugs except Ciprofloxacin [21]. The most significant contribution to this decrease in sensitivity to antimicrobial agents could be due to the increased irrational use of over the counter antibiotics [22].

Conclusion

Gram-negative bacteria were the most common cause of urinary tract infection. The isolates were highly sensitive to ciprofloxacin.

Conflict of interest

No conflict of interest was declared by the authors.

Acknowledgment

The authors acknowledge the Department of Pharmaceutics and Pharmacy Practice of the University of Nairobi, the Kenyatta National Hospital administration for providing a conducive environment during the study.

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Therapeutic Drug Monitoring: A Golden Opportunity for Pharmacists

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Abstract

Clinical outcomes following therapeutic intervention can be confounded by drug-related side effects and comorbidities. Therapeutic drug monitoring involves measuring and adjusting drug levels to maximize clinical benefits and reduce adverse effects. The aim of this opinion article is to revisit the principles and applications of therapeutic drug monitoring as well as the challenges and opportunities in the local context. The article argues for the role of pharmacists in lending their expertise in this specialty.

Key Words: Therapeutic drug monitoring, Drug levels, Toxicity, Pharmacist role.

Introduction

Therapeutic drug monitoring (TDM), also referred to as drug level monitoring, is a vital component of modern medical care [1]. The practice of TDM relies on measuring drug levels in body fluids and subsequent dose adjustments so as to optimize clinical outcomes while limiting drug-related side effects [2].

Over half of the patients receiving drug-related interventions for various illnesses experience suboptimal efficacy or suffer unwanted adverse effects [3]. There is limited patient follow-up after initial patient-clinician encounters, except for those suffering from chronic conditions [4]. In developing countries, where the quality of medicines has been questioned severally, there is a need to closely monitor the safety and efficacy of treatment interventions.

This opinion article revisits the principles and applications of TDM. The role of TDM in the clinical management of patients with diverse medical and physiological conditions is also discussed. The article goes on to analyse the challenges and opportunities of implementing TDM in the Kenyan health care set-up, emphasizing the dominant role that the pharmacist can, and should, play in this specialisation.

Prerequisites and criteria for TDM

Performing TDM requires appropriate infrastructure not only in terms of laboratory equipment but also with regards to human resource. An understanding of the basic principles of pharmacology and interpretation of laboratory test results, with the aim of optimising the clinical outcomes of the patient, is critical [5,6].

Drug-related characteristics that favour TDM include severe or irreversible toxicity and the existence of predictable dose-effect relationships. It should also be possible to perform dose titrations to attain an effective plasma drug concentration associated with desired clinical outcomes and minimal toxicity (Figure 1) [7].

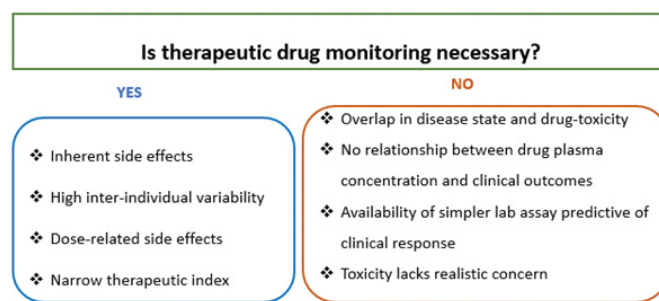


Figure 1. Drug characteristics that inform the need to therapeutic drug monitoring

Roles and indications of TDM in healthcare

A successful patient-clinician encounter must translate into good clinical prognosis with minimum intervention-related side effects. Inefficacious treatments are a waste of resources. Moreover, if the lack of efficacy arises due to subtherapeutic drug concentrations, this poses a risk for resistance against antimicrobial agents. Besides additional costs of care, drug-resistant infections are associated with poor prognosis, higher morbidity and mortality [8].

Applying TDM can also help to establish patient compliance to medications. This is important especially for the treatment of chronic diseases which often necessitate the use of multiple drug regimens for protracted periods of time. Using TDM, reasons for therapeutic failure, whether due to non-compliance to medication, unusual patient-specific pharmacokinetics or inefficacy of the medication in the patient or groups of patients, can be determined [9].

Pharmacogenetics and personalised medicine

Genetic variability impacts on drug safety and efficacy. Differential expression of receptors, transporters and drug metabolising enzymes can cause dissimilarities in therapeutic outcomes when the same drugs are administered to different patients even at the same doses [10]. The cytochrome P450 superfamily of enzymes mediate the biotransformation of over 75% of the drugs in clinical use

and clinically relevant genetic polymorphisms have been identified with CYP2D6, CYP2C9, CYP2B6 and CYP2C19 isoenzymes [11].

Personalised medicine involves adjusting the dose of a drug depending on the patient's genetic profile and other key determinants of drug action [4]. For example, the prescription of some anticancer drugs has already been restricted based on the genetic profile of patients [12].

Special populations: The elderly, pregnant women and paediatrics

Pharmacokinetic processes are dependent on divergent factors that affect body physiology. Increased physiological demands such as during pregnancy, changes in the body volumes and fluid compartments, as well as fluctuations in biochemical parameters, can impact on drug disposition [13]. Among the elderly, there is a general decline in the functional capacity of organs involved in the absorption, metabolism and excretion of drugs. On the other hand, neonates and the paediatric population have immature systems unable to efficiently metabolise drugs like normal healthy adults. These groups of patients may require close monitoring of drug levels to ensure optimal clinical outcomes [14].

Disease status, comorbidities and polypharmacy

Diseases, especially those affecting key organs involved in the biotransformation or excretion of drugs, often necessitate TDM. Moreover, changes in pharmacokinetic parameters such the volume of distribution due to circulatory changes, secondary to congestive heart failure, can considerably alter drug pharmacokinetics [15]. In liver disease, several functions, besides drug metabolism, are perturbed. As the major organ involved in protein synthesis, severe liver disease can alter levels of albumin, causing changes in plasma protein binding. For highly protein-bound drugs, this can cause drug toxicity due to supratherapeutic concentrations as the unbound fraction of the drug, which is responsible for pharmacological actions, increases above the minimum toxic concentration. Renal disease, on the other hand, can lead to decreased excretion and drug cumulation [16].

Comorbidities, which frequently lead to polypharmacy-the use of multiple drugs to manage one or more disease condition, present potential scenarios requiring TDM. Diseases can alter drug metabolism and excretion while polypharmacy is a precipitant of drug-drug interactions [17]. Drug-drug interactions can occur at any of the pharmacokinetic processes, as described earlier, or at the point of receptor interactions, also termed pharmacodynamic interactions. Severe drug-drug interactions may require staggering the administration of the drugs or adjusting dosages using TDM. In extreme cases, however, it may be necessary to consider replacing the offending drug or changing the drug combinations altogether.

Global practices, challenges and local potential for TDM

TDM has gained momentum across the spectrum of therapeutic areas ranging from infectious communicable, to non-infectious non-communicable diseases as summarised in Table 1 [5].

Table 1. Examples of drug candidates suitable for therapeutic drug monitoring

Drug	Therapeutic area	Comments and Toxicity profile
Digoxin	Cardiovascular	High protein-binding, interacts with other highly protein-bound drugs
Carbamazepine	Anticonvulsant	Ataxia, hallucinations, seizures
Sodium valproate	Anticonvulsant	Hepatotoxicity, arrhythmias, central nervous and respiratory systems depression
Phenytoin	Anticonvulsant	Stupor, coma, respiratory arrest, seizure
Lithium	Acute mania	Gross tremor, slurred speech, confusion and lethargy
Theophylline	Respiratory conditions (asthma, chronic obstructive pulmonary disease)	Central nervous system, cardiovascular, metabolic, gastrointestinal, musculoskeletal side effects
Ciclosporin	Immunosuppressant	High blood pressure, elevated blood urea nitrogen
Tacrolimus	Immunosuppressant	Tremors, neurologic toxicity
Gentamicin	Aminoglycoside antibiotic	Nephrotoxic, ototoxic
Vancomycin	Antibiotic	Nephrotoxic

Resource-endowed countries have exploited the use of TDM to a greater extent compared to low- and middle-income countries (Figure 2). As with many other developing countries in Africa, there is still potential for the uptake of TDM services in Kenya [4].

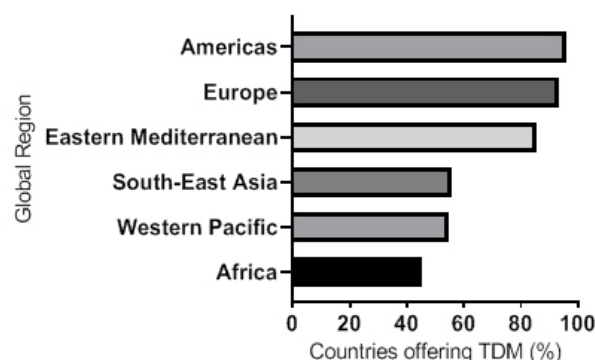


Figure 2. Uptake of therapeutic drug monitoring services across the world

Challenges in the implementation of TDM relate to, among others, infrastructure and human capital. Vibrant and robust TDM requires instruments and equipment critical in measuring and monitoring biomarkers or drug plasma levels. Availability of the inanimate infrastructure must then be coupled with knowledgeable human expertise, to interpret and undertake necessary drug dosage adjustments to maximize clinical benefits [6]. Extensive application of

TDM, therefore, requires a critical mass of competent personnel with sound understanding of the principles of pharmacology and the measurements of biochemical parameters.

The use of traditional herbal medicines and other forms of complementary and alternative therapies present an opportunity as well as a potential challenge in conducting TDM. Health care practitioners must become increasingly conscious of the possibility that patients could be using traditional and complementary medicine which can modify their response to conventional therapies. Adequate medication history and understanding the potential influence that these may have on drug levels is vital in interpreting lab results and implementing appropriate changes in TDM [18].

Progress and proposed way forward in expanding TDM services

A greater application and utilisation of TDM services needs more than furnishing our clinical laboratories with requisite instruments and equipment. Health care practitioners need to be sensitized on the utility of TDM towards achieving optimal patient outcomes.

There is a silver lining regarding the prospects of expanding TDM in Kenya. We have witnessed a steady increase in the pool of specialists in Clinical Pharmacy and toxicology over the years. As a result, there has been continued enlightenment of the role of Clinical Pharmacists in patient care both amongst health care professionals and the general public.

Equally, the concept of TDM has gained considerable attention not only in the corridors of health institutions but also in the social spaces such as in the main media outlets. This is attested to by articles penned by Clinical Pharmacists on patient health education on medicine use and associated dangers of their misuse. The Pharmaceutical Society of Kenya stands to be complemented for their constant effort in championing quality patient care and trumpeting the role of the pharmacist in the attainment of quality health care services in line with Universal Health Coverage and the current National Big Four Agenda.

The foregoing factors, coupled with improvements in technology to facilitate service delivery, present a golden opportunity for the Pharmacy profession. We expect the role and impact of Clinical Pharmacists and Toxicologists in patient care to be amplified further. If well supported by the various stakeholders, TDM stands to provide an additional and exciting specialisation for pharmacists.

Conclusion

Therapeutic drug monitoring provides an interesting and exciting field of specialisation that favours pharmacists due to their extensive knowledge in pharmacology and related preclinical disciplines. An interest and further training in this area should see many more pharmacists engaging in this

practice which, elsewhere in the developed world, is already taking shape in regular patient care towards offering personalised, evidence-based medicine. Sound knowledge on the prerequisites for TDM and priority drugs that qualify for the service are vital aspects in championing for this specialisation in Kenya.

Declaration of Conflict of Interest

There are no conflicts of interest to declare.

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Effects of UV, Red and Sun Light on the Stability of Phytochemicals, Antioxidant and Antimicrobial Activity in the Rhizomes of *Zingiber officinale* (Zingiberaceae)

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Abstract

Phytochemicals have been reported to be degraded by environmental factors such as heat, light and oxygen. *Zingiber officinale* (Rosc.) is widely consumed worldwide with remarkable medicinal properties due to its phytochemicals. This study investigates the effect of exposure to sun, red and ultraviolet light of *Z. officinale* for 168 hours on the stability of the phenols, flavonoids, saponins, antioxidant and antimicrobial activity of this plant. Total phenolic and flavonoids content was determined using Folin-Ciocalteu reagent with gallic acid (GA) as standard and Colorimetric aluminium chloride method with quercetin as standard respectively and total saponin was also determined. The antioxidant and antimicrobial analysis of the irradiated rhizomes extracts were carried out using 1,1-Diphenyl-2-picrylhydrazyl (DPPH) and agar diffusion methods. The total phenolic, flavonoid and saponin content before exposure were 1.30±0.019 mg/g GA, 1.27±0.351 mg/g and 28.4±7.35% respectively while after exposure the values ranged from 1.21-1.40 mg/g GA for phenols, 0.981-2.0 mg/g of quercetin for flavonoid and 22.4-33.2% for saponins content respectively. The IC₅₀ before exposure to the different light sources was 0.2025 mg/mL while after exposure the IC₅₀ ranged from 0.0024 - 0.9262 mg/mL. Exposure to sunlight caused changes in the phytochemicals present as well as its antioxidant activity. Upon irradiation with the different light sources, there was significant increase (P<0.05) of DPPH radical scavenging activity as well as decrease in activity against *Staphylococcus aureus* 25913, *Staphylococcus aureus* 41, *Escherichia coli* and *Candida albicans*. These changes may be due to degradation of the phytoconstituents. Appropriate storage of herbal materials is necessary to prevent phytodegradation.

Key words: *Zingiber officinale*, radiation, antioxidant assay, Antimicrobial assay, phytochemical assay.

Introduction

The characteristics and effects on human health of natural bioactive compounds especially from plant sources have been investigated extensively [1]. Light is one of the most important variables among various environmental factors affecting the concentrations of phytochemical in plants [2]. For example, blue light significantly enhance the contents of total phenolics and total flavonoids in buckwheat sprouts grown under blue light [3]; UV-A induction of anthocyanins accumulation was observed in lettuce [4] and ascorbic acid in Komatsuna and lettuce [5]. Sunlight, ultraviolet (UV) light and visible light are known to accelerate autoxidation processes by triggering the hydrogen abstraction that results in the formation of alkyl radicals [6].

Zingiber officinale is a flowering plant, known commonly as Ginger and belongs to the family Zingiberaceae. Its rhizome has been used worldwide as a spice and food flavoring agent. It grows annual stems about 1 metre tall bearing yellow flowers and narrow green leaves; it's also a herbaceous perennial. For centuries, it has been an important ingredient in Chinese, Ayurvedic and Tibb-Unani herbal medicines for the treatment of rheumatism, asthma, catarrh, gingivitis, nervous diseases, stroke, toothache, constipation and diabetes [7].

The important active constituents in Ginger rhizomes include: essential oils (zingiberole, citral, borneol, citronellol, zingiberene, camphene, cineole, bisabolene, phellandrene, geraniol, linalool, limonene and camphene), phenols (gingerol and zingerone), vitamins (vitamin C, vitamin B6), minerals (calcium, magnesium, phosphorus, potassium and

sulfur), oleoresins, proteolytic and enzymes [8]. In Nigeria, this plant is being exposed to sunlight directly by street hawkers, traditional health practitioners (in bottles) and in combination with other products at times for more than two weeks. This study aimed at evaluating the effect of prolonged irradiation of red light (RL), ultraviolet (UV) and sunlight (SL) on powdered rhizomes of *Zingiber officinale* (RZO) and the effect on phytochemicals, antioxidant and antimicrobial activities.

Materials and Methods

Chemicals and Equipment

All chemicals and solvents used in this experiment were of analytical grade. Water bath (Fisher Scientific Company, USA), analytical weighing balance (Ohaus, USA), Electro-Heating Standing Temperature Air Dry Oven, UV-visible Spectrophotometer (Hewlett Packard), UV lamp and Red bulb (60W), Incubator, Autoclave, Sterile petri dishes were used.

Methods

Collection and Treatment of Plant Materials

Fresh RZO were obtained from Oja-oba market, Ilorin, Kwara state in March, 2016 and was authenticated at the herbarium section of the Department of Plant Biology, University of Ilorin, Nigeria by a botanist. A voucher number: UILH/001/984 was deposited for future references. After identification, the rhizomes were dried in an oven at 35°C for 5 days, pulverized and stored in a polythene bag for further use.

Exposure to Light

The method of Bakare-Odunola et al. [9] was adopted for the exposure to the light sources. One hundred and seventy five grams (175 g) of each of the powdered rhizomes of the plant was weighed into three flat trays labelled UV, RL and SL. Two of the trays were each placed in two cartons affixed with a UV lamp in one and RL in the other, for the light exposure at room temperature. The third tray was exposed to sunlight. Seventeen grams (17g) of the powdered samples was weighed out from each of the light sources at time intervals of 1, 2, 3, 6, 12, 24, 48, 72, 144 and 168 hours for analysis.

Extraction

Extraction of the plant samples was done separately before exposure and after exposure at each of the time intervals for the three light sources. The exposed powdered rhizomes and the unexposed were extracted with 100 mL of 99.5% methanol by the maceration method and decanted after 48 hours. The solvent in the extract was allowed to evaporate over a water bath at 40°C. The percentage yield was calculated and thereafter preserved for further use.

Qualitative Phytochemical Analysis of RZO

The methanolic extracts were tested for the presence of alkaloids, flavonoids, saponin, steroid, terpenoids on the unexposed and exposed sample using the standard procedures [10].

Determination of total phenolics

Total phenolic contents were evaluated using Folin Ciocalteu colorimetric method [11] with some modifications. A solution of 0.028 mg of the extract was made up to 1 mL with methanol and then mixed with 1 mL Folin-Ciocalteu reagent previously diluted with water (1:9 v/v). After 5 minutes, 0.8 mL of 7% Na₂CO₃ solution was added with mixing. The tubes were shaken for 5 seconds and allowed to stand for 30 min at 40°C in an oven for colour development. Absorbance was then measured at 765 nm using UV-vis spectrophotometer. Samples of extract were evaluated at a final concentration of 0.01 mg/mL. Gallic acid at different concentrations of 0.01 to 0.07 mg/mL was used as standard. All tests were performed in triplicates. Total phenolic content was expressed as mg/g GA equivalent/1mg of extract using the following equation based on the calibration curve: $y = 1.99x$, $R^2 = 0.93$, where y was the absorbance and x was the concentration.

Determination of total flavonoids

Colorimetric aluminum chloride method was used for flavonoid determination of each extract [12]. Equivalent of 0.3mg from a stock solution of the extract was diluted to 1.4 mL with methanol. The solution was mixed with 1.5 mL of 2% aluminum chloride. After one hour at room temperature, the absorbance was measured at 420 nm. Extract samples were evaluated at a final concentration of 0.1 mg/mL. Quercetin at different concentrations of 0.06 to 0.18 mg/mL was used as standard. All tests were performed in triplicates. Total flavonoid contents were calculated as quercetin equivalents (mg/g) using the following equation based on the calibration curve: $y = 0.023x$, $R^2 = 0.9424$, where y was the absorbance and x was the concentration.

Saponin determination

The method by Ezeonu and Ejikeme [13] with some modifications was used for saponin determination. One hundred grams (100 mg) of the extract was dissolved in 4 ml of methanol and separated in two equal halves in two different separating funnels. In each separating funnel, 5 mL of distilled water was added into it, then 4 ml diethyl ether was also added and shaken vigorously. The ether layer was discarded, while the purification process was repeated. Four millilitres (4 mL) of n-butanol was added and shaken, then allowed to stand for separation after which the n-butanol layer was then collected. This process was repeated five times. The n-butanol extracts were washed twice with 2 mL of 5% aqueous sodium chloride after which it was dried over a water bath at 40°C and the % saponin content was calculated. The test was carried out in duplicate.

Assay of DPPH scavenging activity

The Assay of DPPH radical-scavenging activity of the test extracts was examined as described by Aryal *et al.* [12] with some modifications. Different concentrations (0.03- 0.1 µg/mL) of each extract were added, to an equal volume, to methanolic solution of DPPH (100 µM). The mixture was allowed to react at room temperature in the dark for 30 minutes. Vitamin C was used as standard control while a

mixture without the extract was taken as blank. Two replicates were made for each test sample. After 30 minutes, the absorbance was measured at 518 nm and converted into the percentage antioxidant activity using the following equation:

$$\frac{\text{Absorbance (DPPH)} - \text{Absorbance (Extract)}}{\text{Absorbance (DPPH)}} \times 100$$

IC₅₀ values denotes the half effective concentration of sample which is required to scavenge 50% of DPPH free radicals. The IC₅₀ values were calculated by nonlinear regression using graph pad prism. Where the abscissa represented the concentration of the tested plant extract and the ordinate represented the average percent of scavenging capacity from two replicates.

Antimicrobial assay

Staphylococcus aureus (clinical isolate 41 and Typed culture 25913), (*Escherichia coli*. Typed culture 35928) and the fungus *Candida albicans* were used in this study in the antimicrobial assay. These organisms were collected from the Pharmaceutical Microbiology Laboratory of the Department of Pharmaceutical Microbiology and Biotechnology University of Ilorin, Nigeria.

The antimicrobial assay of RZO extract was performed by deep-well agar diffusion method using Mueller-Hinton agar (bacteria) and Saboraud dextrose agar (fungi). Agar plates were prepared as specified by the manufacturer. The agar was inoculated separately with 10⁷ CFU of test microbe culture and evenly spread on the entire surface of each plate. The agar was carefully punched using a cork-borer No 6, 4 wells were bored at equal distance around the plates, and the extracts were dispensed into the well's agar wells seeded with bacterial culture. The plates were left at ambient temperature for 30 minutes and then incubated at 37°C for 18-24 hours and 25°C for 48-72 hours for bacteria and fungi respectively. The diameter of inhibition zones was measured using a ruler in millimeters. The 3rd and 4th wells served as positive and negative controls. The negative and positive control well was filled with sterile dimethyl sulfoxide and gentamycin respectively [14].

Statistical Analysis

Results were analysed using Graph Pad prism 7 (GraphPad prism 6 software. Inc, USA), and the results were expressed as mean ± standard error of mean, (n=3). Values carrying * are significantly different (p<0.05) from the zero hour for each parameter.

Results

Percentage yield of RZO

The percentage yield of the extract after exposure to UV light was the highest followed by that exposed to RL while that exposed to SL was the least as shown in Figure 1.

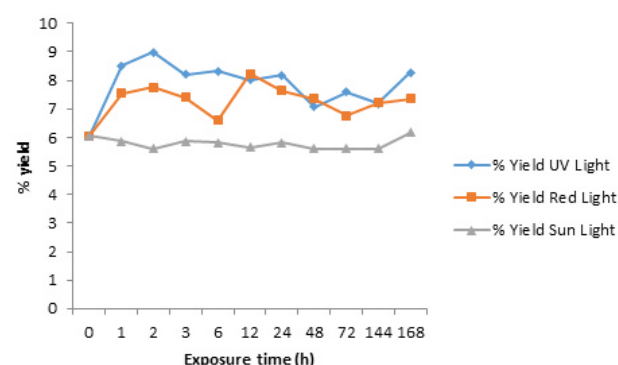


Figure 1. Percentage yield of the methanol extract of RZO before and after exposure to red light and ultraviolet and sun light from 0-168 hr.

Qualitative phytochemistry of RZO

The unexposed methanol extract of RZO was found to contain saponins, phenols, tannins, cardiac glycosides, flavonoids, alkaloids, steroids as shown in Table 1.

Table 1. Qualitative photochemistry of RZO leaves.

Phytochemical Constituent	Methanol
Alkaloids	+
Cardiac Glycosides	+
Flavonoids	+
Saponins	+
Steroids	-
Phenols and Tannins	+
Terpenoids	+

KEY: + = Presence; - = Absence.

Quantitative phytochemistry

The phenolic content of the RZO after exposure to UV was generally higher followed by that exposed to SL while that exposed to RL was the least (Figure 2). The highest flavonoid content was at the 24 hour exposure for UV, that for RL was at the second hour of exposure while that for SL was at the 168 hour of exposure as shown in Figure 2.

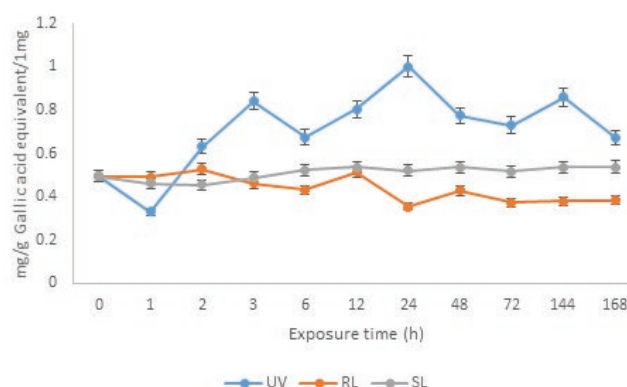


Figure 2. Phenolic Content of *Zingiber officinale* rhizome before and after exposure to UV, red and sun light.

The flavonoid content of the RZO after exposure to RL was decreasing as the exposure time increased while that for UV increased up to the 12 hour exposure and then started decreasing as shown in Figure 3. That for SL also decreased upon exposure up to the third hour of exposure and

generally increased after (Figure 3). Generally the flavonoid content for exposure to SL was higher than that exposed to UV then last with that of RL (Figure 3).

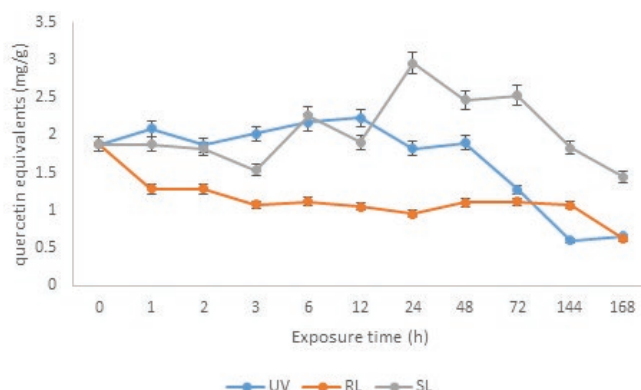


Figure 3. Flavonoid Content of *Zingiber officinale* rhizome before and after exposure to UV, red and sun light.

The highest and lowest percentage of saponin was at 2 h and 168 h of exposure respectively to RL and SL (Figure 4). A constant reduction was observed after 6 h and 72 h of exposure to RL and UV respectively.

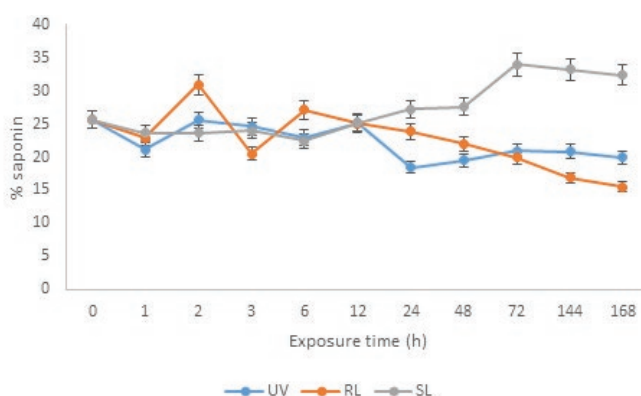


Figure 4. Saponin Content of *Zingiber officinale* rhizome before (0 hr.) and after exposure to UV, red and sun light.

Antioxidant Activity

The antioxidant activity of the RZO increased with increase in exposure to UV and RL while that exposed to SL decreased generally up to the 12 hour exposure time and then started increasing as the exposure time further increased shown in Figure 5.

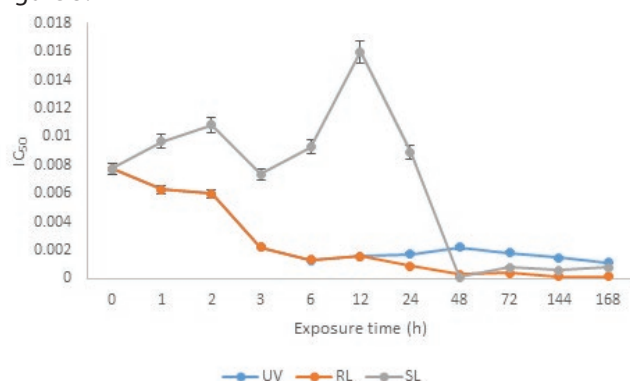


Figure 5. IC₅₀ of *Zingiber officinale* rhizome before and after

exposure to UV, Red and Sun light (UV = Ultraviolet light, RL= Red light, SL = Sun light; Data are mean $\pm$ SEM, (n=3).

Antibacterial Properties

The RZO extract before exposure showed antibacterial activity against *S. aureus* 25913. After exposure, the activity becomes inconsistent as shown in Figure 6. After the two hours exposure to RL, the activity against *S. aureus* 25913 was lost completely likewise upon exposure to UV light, there was no activity in the 1 hour exposure and later loss of activity from the 6 to 168 hour exposure time. Exposure to sunlight shown activity except at the 3, 12 and 24 hour exposure time (Figure 6).

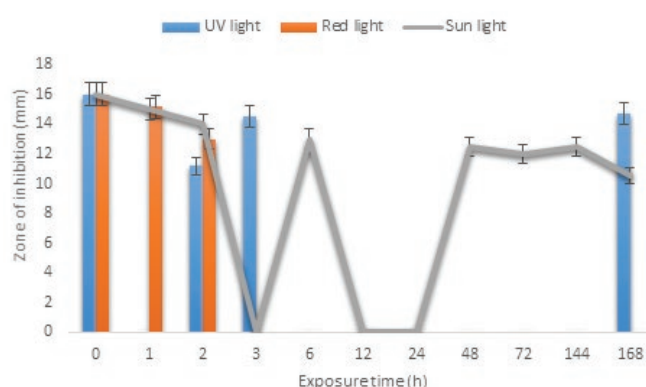


Figure 6. Effect irradiated RZO before and after exposure to UV, Red and Sun light on the susceptibility of *S. aureus* 25913(n=3)

The RZO extract before exposure showed antibacterial activity against *S. aureus* 41. After exposure to RL, the activity against *S. aureus* 41 was lost completely at the 1-2, 24-168 hours exposure time with activity only at the 3-6 hour exposure time. Exposure to UV and SL showed activity until 24 hour and thereafter, complete loss of activity (Figure 7).

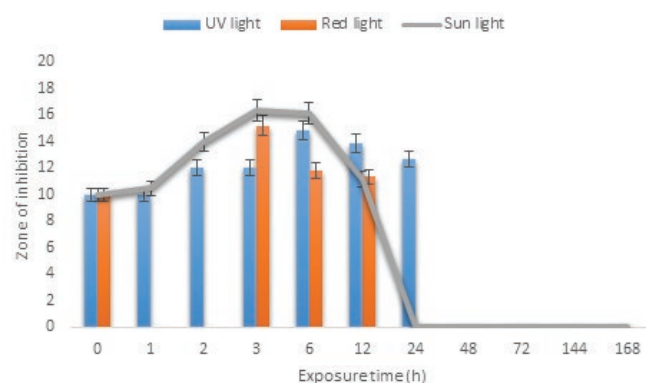


Figure 7. Effect irradiated RZO before and after exposure to UV, Red and Sun light on the susceptibility of *S. aureus* 41(n=3).

The activity against *E. coli* after exposure generally was less than that after exposure. Exposure to UV light showed activity up to the 48 hour exposure and loss of activity after 48 to 168 hour exposure. Likewise, exposure to SL showed activity up to the 24 hour and complete loss of activity after 24 hours onward. Exposure to RL showed activity only at the first and 24 hour exposure time (Figure 8).

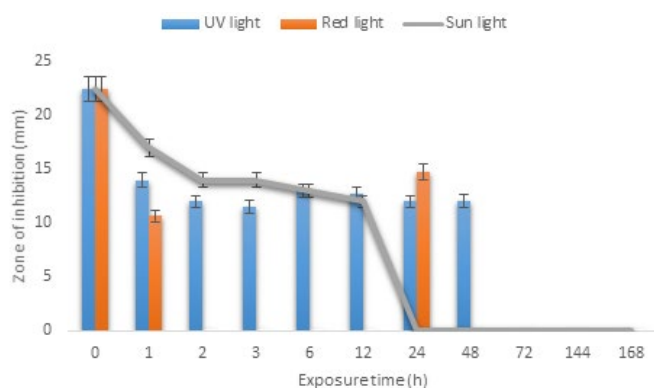


Figure 8. Effect irradiated RZO before and after exposure to UV, Red and Sun light on the susceptibility of *E. coli* (n=3).

Generally, the activity of RZO against *C. albicans* before exposure was higher than after exposure to all the different radiations. RL and SL showed activity throughout exposure while UV showed activity up to the 72 hour only (Figure 9).

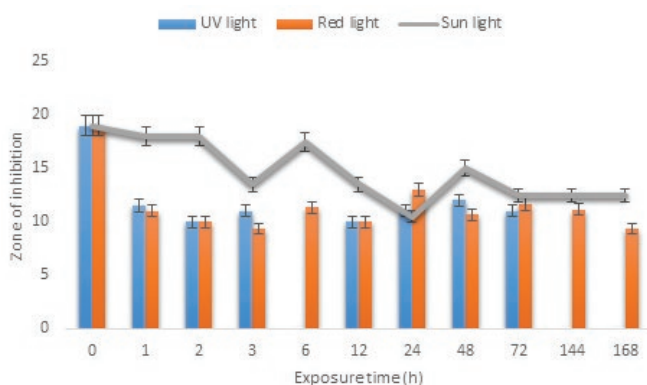


Figure 9. Effect irradiated RZO before and after exposure to UV, Red and Sun light on the susceptibility of *C. albicans* (n=3).

Discussion

The relative increase in extractive value after exposure to UV and RL but not SL was noted (Figure 1). The differences in the extraction yield could be caused by several factors such as differences in solubility and polarity [15]. Saponins, phenols, tannins, cardiac glycosides, flavonoids, alkaloids, steroids were present in the methanol extract (Table 1) which is similar to literature [16].

The decrease in flavonoid content upon exposure to RL (Figure 3) shows that RL requires a shorter time to reduce total flavonoids. There was a significant reduction in samples exposed to UV after 48 h exposure.

The reduction in the total flavonoids when exposed to UV light may be due to UV induced effect, while the slight increase between 6-12 h may be due to photochemical transformation [23]. In a similar study carried out by Zvezdanović et al. [17] where the degradation of flavonoids (quercetin) was dependent on UV-photon energy input on quercetin. The flavonoid content after exposure to SL was inconsistent as shown in figure 3. Variability in the level of flavonoids could be as a result of photochemical

transformation that flavonoids may undergo. A photochemical transformation requires excitation of an electron from a ground state orbital to an excited state orbital, this is usually achieved via the absorption of light by a chromophore [18].

There was a significant increase in phenolic content for UV, while that for RL and SL was nearly constant throughout exposure (Figure 2). Various chemical reactions may have occurred such as the formation of intermediate products of phenol to cause a significant rise and fall in total phenolics when exposed to UV and RL. The difference in the phenolic content of *Z. officinale* when compared to those exposed to the three light sources could be caused by a change or degrade in the structure of polyphenols, resulting in marked changes in their concentration [19].

RL showed a greater reducing effect on total saponins as compared to UV while SL showed a greater % saponin content. Abiotic stress factors such as light and temperature can influence both the quality and quantity of saponin content [20]. A similar result was observed for saponin content in a study carried out by Mechthild in 1981 on exposing *Avena sativa* seedlings to RL.

The antioxidant activity of the extract of RZO exposed to UV light correlated with the total phenolic content indicating that phenolic compounds are dominant contributors of antioxidant activity of the extracts. The finding (implies) that phenolic compounds have the ability to scavenge the reactive oxygen species and are commonly accepted as the most vital antioxidative plant component [3]. On exposure to RL, high antioxidant activity was observed when compared to the unexposed (Figure 5) while that of SL was inconsistent. This could be as a result of lower levels in the phenolic content on exposure to RL and SL. This is possibly due to reduction of bioactive phenolic antioxidants in the extracts. Overall, all the irradiated extract exhibited significant DPPH radical scavenging activity as compared to the standard ascorbic acid with IC₅₀ 41.25 µg/mL [24]. RL showed a greater reduction effect on antioxidant activity which is in line with a study carried out by Samuolienė et al. [21] where red light was observed to negatively affect the antioxidant activity in Lettuce.

There was a decrease in antibacterial activity of the exposed extract against *S. aureus* 25913, *S. aureus* 41, *E. coli* and *C. albicans* (Figures 6-9). There was no activity *S. aureus* 25913 after the 6h for both red and UV light (Figure 6). All the exposed rhizomes lost activity against *S. aureus* 41 after the 48 h exposure (Figure 7). Exposure to red light causes loss of activity against *E. coli* after the 2 h exposure (Figure 8). The decrease in activity on exposure to RL correlates with the reduction in flavonoids. For the UV and SL, it might have been due to photo deterioration and chemical decomposition resulting in reduced bioactivity [22].

In conclusion, saponins, flavonoids and phenolics present in RZO become unstable on irradiation with UV, red light and sunlight, which has a negative effect on its antimicrobial activities but a positive effect in antioxidant properties. The

study revealed the possibility of photodegradation of phytochemicals. Thus herbal hawkers and traditional health practitioners needs to preserve their plant material under shade to prevent degradation and to obtain maximum benefit

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A review on Psychological Impact of Disease Outbreaks and how to RESPOND to the IMPACTS of COVID-19

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Abstract

Disease outbreaks have been known to cause substantial devastation in the world. The impact of such outbreaks on mental health has been documented but unfortunately these haven't been mainstreamed into emergency response preparedness. Low-income countries are the most disadvantaged in this front especially considering mental health care hasn't been much developed with countries having limited capacity for psychological support. These are put to test at times of such crisis when far reaching mental distress is caused with need for remedy.

To correlate research findings, proposals and recommendations from different sources on mental health and the impact of disease outbreaks on mental health, we did desktop review of literature sources to establish some of the findings and align them with the current COVID-19 outbreak. These have then been used to propose feasible approaches that can be used to mitigate the immediate, sustained and long-term psychological impacts of this disease outbreak while at the same time cushioning the public from mental health problems.

Keywords: Mental health, Pandemic, Psychological support, Capacity Building and Advocacy.

Introduction

Mental health is a state of well-being in which every individual realizes his or her own potential, can cope with normal stresses of life, can work productively and fruitfully, and is able to contribute to his or her community [1]. An individuals' mental wellbeing is influenced by a myriad of factors such as social, psychological, and biological factors. Among the explicit contributors to poor mental health are rapid social change, stressful work conditions, gender discrimination, social exclusion, unhealthy lifestyle, physical ill-health and human rights violations.

With the coronavirus disease (COVID-19) outbreak there have been concerns of mental health impacts of this disease outbreak. Ranging from the anxiety and apprehension of the outbreak in different countries, media reporting, infection of a close relative, caring for the sick to disruption of lifestyles are piling pressure on the well-being of individuals. The first case was reported in Wuhan China on 28th December 2019, the National Health Commission of

China released guiding principles of the emergency psychological crisis interventions on 26th January 2020 [2]. These were meant to guide in provision of mental health services to the affected, provide psychological crisis intervention for people in need and to actively prevent, mitigate and try to control the psychosocial impact of the epidemic. This level of response is a clear pointer of the growing recognition of mental health as a critical aspect of human health and well-being. The World Health Organization (WHO) also as a follow up to this released "Mental health and psychosocial considerations during the COVID-19 outbreak" [3].

COVID-19 is causing great devastation to the global systems both in developed and developing economies. The difference is that for developed countries, certain structures which were already in place need slight augmentation to serve the current situation unlike for developing countries where these structures do not exist and at best as segregated. The mental health landscape in African countries is poorly developed. This is as accounted for by Prof. Ndeti et al. where there is an estimated treatment gap of 85% in low-income countries compared with 35% to 50% in high-income countries [4]. This current pandemic presents insurmountable psychological impacts to a wide range of individuals by attacking the core of their livelihoods. This is from loss of jobs, disruption of social networks, heightened anxiety and uncertainty among others.

Through this paper, we are keen to argue out the impact of disease outbreaks on mental health of different populations from the onset of an outbreak through to the end and residual consequences to be felt. We will share anecdotal recommendations on how better to drive advocacy and capacity building for mental health in low-income countries sustainably. This is cognizant of the fact that when disease outbreaks occur, the immediate and automatic response is to prevent spread of infection and to heal those who fall sick [5].

Fear, Anxiety and Panic associated with knowledge of the disease outbreaks: media reporting

With the outbreak of the disease first reported in Wuhan, China all over the world people got alarmed on the nature of the virus and the impact it was causing. With growing media coverage and rapid spread all over the world, anxiety levels

sparked. This led to irrational stockpiling of essential goods including hygiene products e.g. sanitizers, toilet papers, masks among others causing shortages in supermarkets [6,7]. These frantic responses have a clear pointer to the psychological impact of such disease outbreaks.

Individuals who cannot afford to purchase such supplies may feel disadvantaged and undergo pressure associated with feelings of heightened risk of exposure. These psychological impacts can lead to physical health consequences as these people present with depressive symptoms in certain circumstances. The devastation caused by such anxiety and panic have been reported in other disease outbreaks [8] and can outlive the outbreak. It's therefore imperative to invest in emergence response preparedness which would ideally span effective communication strategies to avert such occurrences and manage the situation as it unfolds. Media outlets should take responsibility and manage their reporting as well. When the media captures scary captions during an outbreak, this drives panic among the unaffected with negative impacts. Integrating media responsibility to the society as an integral component of media reporting as provided for under the ethical reporting guidelines [9] can help reduce anxiety levels, help in effective response coordination and address the consumer frenzy of stock-piling.

Psychological impact of infection of relatives and close associates

When an individual falls sick, close friends and relatives feel their pain. As Catherine et al. argues, the impact of disease to relatives and family was associated with the emotional, financial, relationships, livelihood and leisure time among others [10]. With a disease outbreak and compounded with the seriousness of the condition, sickness of an individual affects the family even more. There is an associated fear of being infected by the relative while out of care and love for the individual, the family has to look after them. When such information gets to the neighborhood this can elicit some form of fear and discrimination against the family which compounds to psychological discomfort. The impact is even severe when the infected individual dies. Grieving the abrupt loss of a loved one may traumatize the family with a risk of family members to develop Post-Traumatic Stress Disorder (PTSD). An example of such impact has been witnessed in Kenya following the recent death of a resident of Siaya County who died and was given rash burial at 2am in the night. This has had negative impacts on the relatives even to calls for exhumation of the body for a decent burial [11].

There is need to adopt measures to mitigate the impact of such adverse psychological impacts. This can be through adoption of decent burials with involvement of family members to ease their grieving process, provision of psychotherapy for the family which can leverage on local capacity i.e. social workers, traditional counsellors & elders and even religious leaders who can relate with the circumstances of the family [4]. Additionally, health workers

can be part of the support team to relay information between the sick patient and the family to ensure they are part of their lives. These can be done through the integration of technological solutions with either audio or video options especially where isolation and quarantine measures are put in place [3].

Restricted and monitored family visits can also be adopted where circumstances are suitable for such an arrangement e.g. visits as those for which prisoners are normally accorded where they can get to talk to their visitors. These can be structured to ensure there is no physical contact with the patient or relative in isolation.

Psychological impact on health workers

Health workers are always in the frontline of care looking after their patients. This comes with extra emotional demand on them to support patients and their families. In the case of an outbreak, the impact is ever higher as there is compounded risk of infection to the medical practitioner, extra strain to take care of the patients and their overwhelmed relatives. A study conducted by McAlonan et al. on the immediate and sustained psychological impact of an emerging infectious disease outbreak on health care workers during SARS outbreak in 2003 found out that health workers at high risk are more prone to suffer psychological impacts than those at low risk [12]. From the study they recommend adoption of stress management protocols as part of preparation for future outbreaks.

The extra pressure that is put on healthcare workers in times of such crisis can compromise on quality of care if not managed with higher risk of disease spread even among the health workers. Health workers are also exposed to discrimination or fear in their communities out of suspicion that they may spread the disease from the hospitals. This negates the value of social structures and sense of community that health workers normally rely on for support. In such situations, family support is encouraged whether in person or through technological solutions such as video calls with loved ones.

The WHO in its recommendations advocated for the adoption of a buddy system coupled with rotation between high stress and low stress stations among health workers that would help them establish coping mechanisms from among themselves [3]. The adoption of psychological support systems for health workers can safeguard the well-being of medical practitioners, improve treatment outcomes for patients and save our health systems if done right.

Stigma and discrimination associated with COVID-19: Chinese and Africans in China

Stigma and discrimination have been associated with various diseases for a long time [13]. This has been witnessed for different diseases especially with HIV/AIDS as accounted for by Brian Honneman; "My youngest sister loved to play with other kids in the neighbourhood. One day

she was playing with Chris, a ten month-old baby boy, and she was kissing Chris who was laughing. Suddenly Chris's mum, who was watching them through the window, came running and took Chris out of my sister's arms, saying: "Don't ever come back here, I don't want you to infect my baby with AIDS. Don't try to kill my baby. We all know that you are dying of AIDS."

– *Claire Gasamagera describing her experience with stigma in Rwanda*

With outbreaks, stigma and shaming can be directed to a particular race or ethnic group as was observed for Asian Americans during SARS, West Africans during Ebola, Haitians and gay men during early days of HIV/AIDS [5]. When coronavirus disease (COVID-19) was reported from China, there were initial attacks on Chinese nationals in the USA following profiling statements by Donald Trump identifying the virus as a "Chinese virus" or "Wuhan virus" [14,15]. On the backdrop of this, there is racial profiling of blacks in China as China opens up operations post-gaining control of the outbreak.

With racial profiling and stigma, the targeted groups are less likely to seek care which compromises response efforts to mitigate the impact of such an outbreak [5]. Other than the impact on response, such kind of mistreatment is directly linked to the psychological well-being of individuals. It breeds division, a feeling of not belonging and causes trauma to the afflicted [16,17].

Psychological impact as a consequence of economic downturn, job loss and associated financial hardships with uncertainty about the future

When disease outbreaks occur, governments institute restrictive measures to stop spread of the viruses. This has been witnessed all over the world with recommendation of work from home measures following a surge in COVID-19 cases. Lock downs and curfews have been imposed to different extents and with these, economies have suffered a big blow. It's projected that the world economy will experience a recession of up to 3% [18]. With this economic downturn, companies are expected to downsize with layoffs which will compound to financial hardships. With work from home measures, individuals in developing countries where unemployment rates are high and the majority of those employed are in informal employment, this presents an unprecedented threat to their livelihood [19,20]. This is putting to account the fact that majority of these people work on a daily basis to earn their meal at the end of the day. The impact of such measures in worsened where these persons, are the breadwinners, even for extended families down in the rural villages. It will compound to neglect of their responsibility to care for their people. Compounded on such, individuals would be more inclined to risk being infected but to look out for and provide for their families. In such situations, this presents a risk to the entire community in case they happen to be infected and spread infection. This

negates a critical aspect of good mental health which calls for contribution to society for which in this case there is a trade-off to be made on whether to provide for your people while at the same posing a threat to their wellbeing on one end.

In efforts to curb such harm, it's imperative to have national initiatives to cushion such populations from the devastation through social safety nets, alternate market days to ensure access to essentials, structure long-term job-creation interventions and provide business stimulus packages to ensure business continuity [21]. These will look out for the immediate impacts while at the same time secure the future of these people post the outbreak when normalcy sets in.

Psychological impact of social distancing measures, self-isolation, quarantine and treatment to individuals allied with disruption of social support networks

Following declaration of COVID-19 as a pandemic by the WHO, social distancing measures, self isolation and quarantine were recommended for individuals who were at risk and the general public to different degrees depending on their circumstances. According to research, social networks have been found to serve an important purpose in promoting the mental well-being of individuals [22]. In the midst of such a crisis, these support systems are disrupted with a critical impact on their mental wellbeing.

It's recommended that in such circumstances technological and digital solutions be adopted to help in maintaining relationships within individual social networks. In situations where these are not feasible, it would be ideal to have designated national psychotherapy call centers with capacity to offer psychosocial support.

Long-term psychological impact of the outbreak

Painful experiences have been found to lead to trauma which can affect individuals later in life. These are referred to as Post-Traumatic Stress Disorder (PTSD). With disease outbreaks, there are a myriad of stressful events that have taken place ranging from infection and death of loved ones, loss of jobs to stigma and discrimination from peers and communities. These experiences dent human relationships and unless addressed during and after such an experience, they can lead to long-standing psychological impacts. These can compromise on the quality of life the affected individuals live after this occurrence. From the study conducted on immediate and sustained psychological health of health care workers by McAlonan et al. they recommended stress management through the disease outbreak and even offer packs to the most at risk groups to continue accessing care beyond the outbreak [14].

There is no health without mental health. Unfortunately, this is a concept that has taken the world some time to realize. Kenya launched its mental health policy paper in 2019 following the frantic move by advocacy groups, academicians

and some politicians in the space. This was a move in the right direction but from experiences, a policy is just as good as it is implemented. At this point with total knowledge of the importance of mental healthcare, there has been little attention to mental health impacts of the disease in the local context except for isolated zoom meetings to discuss the same. Zoom meetings with experts doesn't address anything especially when they postulate the probable impacts of the pandemic without clear action plans to mitigate these impacts and improve the quality of human lives.

Conclusion

Mental health is an important aspect of human health and well-being. Disease outbreaks may not have a direct impact on the brain but their far-arching and wide-reaching effects on social, economic and political systems influence mental wellness. It's therefore imperative to discern emergency response and preparedness strategies with consideration of the mental health impacts of such outbreaks. With such a plan, psychotherapy support can be assured to those who need them, social support systems are established, health workers welfare is put to consideration, and the long term recuperation measures are in line. This is what guarantees a mentally healthy society and this is what we should all aspire to achieve.

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