

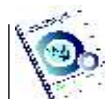
Covid-19 Lockdown and Cancer Drugs Shortage: Experience from an Oncology Center in Northern Nigeria

Adewuyi SA, Sani M, Liman AB, Mbanusi AA,* Shittu MT.¹

Department of Radiotherapy and Oncology and ¹Oncology Pharmacy Unit, Ahmadu Bello University Teaching Hospital, Zaria, P.M.B 06, Shika, Zaria Nigeria

Article Metrics

Date submitted: 28/03/2021
Date Accepted: 04/06/2021
Date Published: 30/07/2021



ABSTRACT

Background: The advent of COVID-19 in December, 2019 and its rapid progression to a pandemic has caused diverse health and economic challenges around the world. In order to mitigate this fast-spreading virus, the government of Nigeria imposed lockdown which further exacerbated the challenges already caused by the pandemic such as exhaustion of cancer drugs, difficulties in cancer drug production and distribution. This study aimed at identifying the presence of cancer drugs shortage due to COVID-19 lockdown, affected cancer drugs and the solutions proffered.

Methodology: This was a descriptive cross-sectional study carried out at an oncology center in northern Nigeria. Between March and June 2020, all patients receiving chemotherapy during the lockdown due to COVID-19 and were affected by cancer drug shortages were interviewed with a structured proforma when present for chemotherapy. Information on patient's personal data, clinicopathological characteristics, chemotherapy regimen, cancer drugs shortage experienced and solution proffered were obtained and data analyzed using Microsoft Excel sheet and result presented using simple tables.

Results: Sixteen of the 170 patients who had chemotherapy during the study period experienced drug shortages. Out of these patients, 4 had ovarian cancer followed by 3 patients each with cervical and lower limb cancer respectively. Cisplatin, Cyclophosphamide and Bevacizumab are the commonest drugs affected (5 each). Exhaustion of cancer drugs in the hospital oncology pharmacy as the reason for the drug shortage affected all the patients, while exhaustion of cancer drugs from neighboring facility and break in the supply chain further affected 3 and 4 patients respectively. Outsourcing of cancer drugs was the solution for all patients (16) ab initio. The unavailable drug was substituted in 2 patients and the regimen continued without the unavailable drug in another 5 patients.

Conclusion: The COVID-19 lockdown in the study environment resulted in cancer drugs shortage and Cisplatin, Cyclophosphamide and Bevacizumab were most affected. The causes for these shortages were

*Correspondence: Arinze Anthony Mbanusi, Department of Radiotherapy and Oncology, ABUTH.


Email: arinzeoj@gmail.com Tel: +234 803 368 9721

Find our articles on Google Scholar, fully indexed

Access to the article



website: <http://www.jmbsr.com.ng>

 : <https://doi.org/10.46912/jmbsr.45>

How to cite this article:

Adewuyi SA, Sani M, Liman AB, Mbanusi AA, Shittu MT. Covid-19 Lockdown and Cancer Drugs Shortage: Experience from an Oncology Center in Northern Nigeria. J Med Bas Sci Res 2021;2(1):107-116.

multifactorial with exhaustion of hospital stocks being the most significant causative factor. Delaying the administration of chemotherapy for a few days while the unavailable drug was sourced from neighboring facility were the main approach to resolving this problem.

Keywords: COVID-19, Lockdown, Cancer drugs, Drugs shortage

INTRODUCTION

The emergence of the new corona viral disease in Wuhan China late 2019 led to the nomenclature Corona virus disease 19 (COVID-19) by the world Health Organization, (WHO).¹ Few months later, the Director General of the WHO declared COVID-19 as a pandemic with about 83, 179, 814 reported cases across over 110 countries and territories as at 31st December, 2020.¹ The first confirmed case of COVID-19 in Nigeria was on the 27th February, 2020.² Subsequently number of cases rose majorly in Lagos and Abuja most probably due to international travels, which led to the declaration of lockdown of non-essential services and movements in the cities of Lagos, Ogun and Abuja by the Federal Government of Nigeria on 30th march, 2020.^{2,3} In an attempt to prevent the spread of the virus, the Kaduna state Government, had earlier on the 25th march, 2020 declared lockdown in the state with closing of its borders, an action that caused major activities and supplies in and out of the state to be on stand still.⁴

According to the United States Food and Drugs Administration (FDA), Drug Shortages can be defined as 'The period of Time when the demand exceeds the supply of the drug'.⁵ Drug shortages may be triggered by many reasons, such as inadequate quantities of raw materials, legislative, manufacturing, or procurement issues and drug discontinuation from the market.^{6,7}

There is paucity of literatures addressing cancer drugs shortage during the COVID-19 pandemic lockdown. However, with the lockdown at both the federal and

state levels, grounding of local and international flights, the supply chain of various commodities and drugs was interrupted. As a result, patients faced series of challenges in accessing care, including treatment delays, drugs and other supplies shortages. According to Hishman A.B et al, in this new landscape, the cancer community is steering a difficult course amid several challenges: revisiting optimal standards of cancer care, facing persistently evolving shortages and acknowledging the paradoxical need to keep patients away from health care facilities.⁸ The article further suggested that drug shortages during COVID-19 lockdown could lead to the use of alternatives that may be less effective or may place patients at risk of developing more adverse effects.⁸ A drug shortage could also result in an increased risk of a drug overdose as a result of changing of drug brand with different concentrations and strengths.⁹ According to a study by the World Health Organization to assess the impact of COVID-19 pandemic on Non-Communicable Disease (NCD) resources and services; the underlying causes for existing disruptions in NCD services vary across income groups with disruptions to transport, insufficient personal protective equipment (PPE), insufficient staff, unavailability / stock out of essential medicines and services impacting low- and lower-middle-income countries to a greater degree.¹⁰

The rising number of cancer patients and the persistence of cancer drugs shortage and resultant

effects necessitated the need for concerted effort and collaboration amongst oncologists and pharmacists involved in managing cancer patients. This collaboration will enhance the best treatment options with resultant improved survival and less toxicities to therapy and the impact of drug shortage.

The aim of this study is to establish the presence of cancer drug shortage due to COVID-19 lockdown, affected drugs and the remedies offered to the patients in Ahmadu Bello University Teaching Hospital (ABUTH). A further study of the impact of the shortage on the outcome of the patients is ongoing.

MATERIALS AND METHODS

This was a descriptive cross-sectional study carried out at the Radiotherapy and Oncology Department, Ahmadu Bello University Teaching Hospital, Nigeria. The institution is a tertiary referral center for cancer patients located in Kaduna State in the North-west geopolitical zone and one of the designated centers as Center of Excellence for Oncology by the Federal Government of Nigeria. It included all histologically confirmed cancer patients receiving chemotherapy and or targeted therapy at the Chemotherapy unit of the department between the period of 27th march, 2020 to 30th June, 2020 during the Lockdown by the Kaduna State and Federal Government of Nigeria due to COVID-19 pandemic. During the study period, consecutive patients seen experiencing drugs shortage irrespective of diagnosis, histology report, stage of disease and performance status were analyzed. The bio-data and all relevant clinical information were extracted using a structured proforma designed for the study. The sources of data were the departmental registry, oncology pharmacy registry, patients' case notes and interview of patients at every chemotherapy visit. A total of 170 patients came for cancer chemotherapy within the study period excluding the 2

with incomplete data. A total of 16 cancer patients were affected by cancer drugs shortages with complete data retrieved and analyzed. Clinical staging was based on general examination, results of investigations at presentation and findings at examination under anaesthesia (EUA). Stage of disease was considered early stage if there is no extension into adjacent structures or regional lymph node involvement; locally advanced if there is involvement of adjacent structures, regional lymph node involvement, inoperable, bilateral or widespread in the absence of distant metastasis; and metastatic stage if there is distant metastasis.

The patients in this study included those referred from other clinical departments within the hospital and those referred from other hospitals within and outside the geopolitical zone. The histology reports from referring physicians were used for the study. Patients' information retrieved included age, sex, histology, site of cancer, stage of disease, aim of treatment, indications and types of chemotherapy regimen, affected drugs, reasons for drugs shortage and proffered solutions.

Data were analyzed using Microsoft Excel sheet and results presented in simple tables.

RESULTS

Table i shows the sociodemographic and clinicopathological characteristics of the patients. A total of 170 patients (excluding the 2 patients with missing data) were on chemotherapy within the study period, out of which 16 experienced drugs shortage (9.4%). Analysis of the 16 patients revealed M: F = 1:1.7; median age 55.5 years and age range of 24 – 74 years. Cancer of the ovary was the commonest cancer (4 patients) followed by cervical cancer and cancer of the lower limb with 3 patients each respectively. The disease was locally advanced in 10 patients and 5 patients have metastatic disease.

Table 1: Showing Patients sociodemographic and clinicopathologic characteristics.

Patients Characteristics	Frequency (n)	Percentage %
Age (Yrs)		
21 - 30	1	6.25
31 - 40	4	25.0
41 - 50	2	12.5
51 - 60	4	25.0
> 60	5	31.25
Sex		
Male	6	37.5
Female	10	62.5
Cancer Type / Site		
Gastric (Adenocarcinoma)	1	6.25
Mandible (Squamous Cell Carcinoma SCC)	1	6.25
Cervical (Embryonal rhabdomyosarcoma, SCC)	3	18.75
Scalp (angiosarcoma)	1	6.25
Rectal (Adenocarcinoma)	1	6.25
Mediastinal (Malignant Thymoma)	1	6.25
Lower limb Dermatofibrosarcoma, Fibrosarcoma, SCC)	3	18.75
Ovary (Serous Cystadenocarcinoma)	4	25.0
Lungs (Large Cell Carcinoma)	1	6.25
Stage of Disease at Presentation		
Early	1	6.25
Locally advanced	10	62.5
Metastatic	5	31.25
Aim of Treatment		
Curative	11	68.75
Palliative	5	31.25

Table 2: Showing COVID-Induced drug shortages, reasons and remedies

Covid-Induced Drug Shortages, Reasons And Remedies		Frequency N	Percentage %
Type of Chemotherapy Regimen			
Regimen	Single	-	-
	Combination	16	100.0
Brand Type	Branded	5	31.25
	Generic	11	68.75
Indication for Chemotherapy			
	Neoadjuvant	9	56.25
	Adjuvant	2	12.5
	Definitive (for metastatic)	5	31.25
Chemotherapy Course affected			
	1 st line	13	81.25
	2 nd line	2	12.5
	3 rd line	1	6.25
Chemotherapy Regimen used			
	Epirubicin / Cisplatin	1	6.25
	Paclitaxel / Cisplatin	5	31.25
	Carboplatin / Epirubicin / Cyclophosphamide	1	6.25
	Vincristin / Adriamycin / Cyclophosphamide (VAC)	3	18.75
	Capecitabine / Oxaliplatin	1	6.25
	5FU / Cisplatin	1	6.25
	Cyclophosphamide/Vincristin/Adriamycin/Dacarbazine	2	12.5
	Docetaxel / Carboplatin	1	6.25
	Gemcitabine / Carboplatin	1	6.25
Targeted Therapy Used			
	Bevacizumab	5	31.25
Drugs affected by Shortage (Out of Stock)			
	Cisplatin	5	31.25
	Epirubicin	1	6.25
	Cyclophosphamide	5	31.25
	Adriamycin	1	6.25
	Vincristine	1	6.25
	Oxaliplatin	1	6.25
	Dacarbazine	2	12.5
	Bevacizumab	5	31.25
Cycles affected by Drugs shortage			

Cure was the aim of treatment in majority (11) of the patients.

Table ii shows COVID-Induced drugs shortages, indications, reasons for shortages and the remedies. Combinations of chemotherapy were prescribed for all the affected patients and 5 patients were prescribed targeted therapy in addition to their chemotherapy. Generic drugs were prescribed to 11 patients on chemotherapy and all patients receiving targeted therapy (5) were on branded drugs. The indication for the use of chemotherapy was as neoadjuvant in majority (9) followed by definitive (5) in metastatic disease. All patients prescribed targeted therapy had metastatic disease at presentation.

Cancer drugs shortage affected predominant patients on the first line chemotherapy (13) with only 3 patients receiving treatment beyond first line. Cisplatin, Cyclophosphamide and Bevacizumab are the most affected by COVID-19 lockdown with 5 patients affected each. This also mirrors the regimens as those containing these drugs (Cisplatin/ Paclitaxel, Bevacizumab, CYVADIC and VAC) were most affected. Patients already receiving chemotherapy and targeted therapy (16) were affected as none on first and last cycles of treatment were affected by the cancer drugs shortage.

The reasons for drug shortage were multifactorial as shown in table ii. Exhaustion of cancer drugs in the hospital oncology pharmacy store and that of neighboring facilities was the cause of cancer drug shortage in all the patients (16). Out of these, 3 patients were further affected after exhausting the stock in neighboring tertiary health institution. In the course of the protracted lockdown, 4 patients were affected due to break in the supply chain (interstate transport and importation).

Out sourcing of cancer drugs was the initial remedy for all the patients (16) and this led to delay of less than 3 days in majority of the patients. Only 3 patients had

more than 7 days delay before administering the cancer drugs due to interstate restrictions. Eventually, 7 patients completed the recommended cycle of treatment with substitution of the unavailable cancer drugs in 2 patients and 5 patients without the complete cancer drugs.

DISCUSSION

The declaration of COVID-19 as a pandemic and the resultant lockdown affects various aspect of human endeavours. It affected those already on treatment and the newly diagnosed cancer patients.

In this study, a total of 170 cancer patients came for cancer chemotherapy at the time of the lockdown with 16 patients affected by cancer drugs shortages accounting for 9.4% of the study population. The total number of patients on chemotherapy was reduced as the department was not receiving new patients due to COVID-19 pandemic restrictions during the study period. There were also changes in departmental operations, such as having a specific number of patients that can be seen each day and reducing number of clinical staff working and creating shift duties to limit the number of staff and patients visiting the department.^{11,12} The proportion of patients who experienced drug shortage requiring cancer drug regimen changes or continuation without the affected cancer drug was worth noting during the COVID-19 lockdown period.

As shown in table i, the preponderance of females, a median age of 55.5 years and age range of 24-72 years of the affected patients reflected the already established pattern in the study institution which shows that the median age of cancer in adult is 5 – 10 years younger in this environment compared to the pattern in developed countries.¹³⁻¹⁶ There were more females affected by drug shortage. This reflects the

high proportion of cervical cancer in northern Nigeria and the high incidence and prevalence of gynaecological cancers as previously documented in the study environment.¹³⁻¹⁶ This high gynaecologic cancer prevalence also accounts for ovarian cancers (25%) followed by cervical cancers (19%) being the commonest cancers affected by cancer drug shortages (Table i).

Late presentation is the norm in the study environment due to confounding factors including lack of screening uptake, apathy for orthodox treatment, prevailing poverty amongst others.^{14,15} Most of the patients who experienced drug shortage had locally advanced and metastatic disease. This pattern is not uncommon in developing countries due to factors such as fear, misconception, misdiagnosis, ignorance and prolonged investigation that are obtainable in our setting.¹⁴⁻¹⁸ In this study; most of the patients affected by cancer drug shortage were having locally advanced disease followed by metastatic disease justifying the need for chemotherapy. As a result of this late and advanced stage disease, 31% of the patients were for palliative care. Despite this, the main aim of treatment was curative as most of the patients had locally advanced disease which can be cured with definitive surgery and or radiotherapy after being down staged with neoadjuvant chemotherapy.¹⁹

Table ii revealed the various drugs and regimen affected by the drug shortage, reasons for the shortage and the remedies offered. In view of the pattern of presentation, stage of disease and the aim of treatment, all the patients were on combination chemotherapy and the indication for chemotherapy was neoadjuvant in majority (56%) so as to down stage the disease and render it amenable to surgery and or radiotherapy.

The policy of the oncology pharmacy is to stock both the branded and generic products due to prevailing poverty. Majority of the patients affected by cancer drug shortage were on generic which is cheaper than

the branded. Presently, the targeted therapy bevacizumab (anti-VEGF) stocked in the pharmacy is branded as biosimilars is not yet available in the country. All the patients on targeted therapy have metastatic disease and treated according to standard protocol.¹⁹ The cancer drugs mostly affected include cisplatin, cyclophosphamide and bevacizumab. This mirrors the regimen used for most gynaecological cancers and soft tissue sarcomas using the regimens Cisplatin/Paclitaxel/Bevacizumab and CYVADIC or VAC respectively.^{20, 21} The high demand of these chemotherapy regimens and the limited storage of Bevacizumab resulted in these cancer drugs being exhausted faster than other cancer drugs. This caused more patients with epithelial ovarian cancer to be affected by its shortage as the addition of bevacizumab to platinum and taxane based chemotherapy has now become the standard of care for metastatic ovarian cancers.²¹

In the course of the lockdown, new patients did not present to the department because there was shut down of some aspect of the oncology clinic and preference was given to patients already on treatments. Similarly, bias was given in favour of those having only one cycle to complete the first line chemotherapy so as to enable them complete their treatment and proceed to the next phase of treatment, either definitive surgery or radiotherapy. Patients on 2nd and 3rd line chemotherapy regimen were also given priority in getting their chemotherapy drugs compared to those on 1st line chemotherapy due to the burden of disease and worsening quality of life. This accounted for the high number of those on 1st line chemotherapy being affected (81%). Those patients due for the 6th cycle were favoured and none of the patients was affected by drug shortage. Similarly, due to modifications of the oncology clinic, with reluctance to enroll new patients, no patient on 1st cycle was affected because prescription

was subsequently tailored to drug availability in the pharmacy store. As a result, none on first and last cycles of chemotherapy treatment affected by cancer drugs shortage. Several reasons were identified in this study as responsible for cancer drug shortage. The most significant was the exhaustion of the hospital stocks. This is in keeping with a Jordanian study that identified lack of coordination in controlling inventory between medical stores, regional medical stores and health facilities as the cause of drug exhaustion especially in the public hospital.²² Efforts to restock the hospital pharmacy was further compounded by delay of payment to suppliers due to several factors affecting the financial institutions at that time such as closure of banks. Despite the reason for drug shortage being multifactorial as shown in table ii, exhaustion of cancer drugs in the hospital oncology pharmacy store and that of neighboring facilities were the major cause of drug shortage affecting all the patients (100%). Due to the protracted nature of the lockdown, there was further shortage due to break in the supply chain due to restriction of interstate movement and shut down of international airports which affected the transportation and importation of drugs affecting 25% of the patients. Even when drugs were sourced from alternate facilities outside the state, this remedy was faced with transportation challenges due to interstate movement restriction.²⁻⁴ Furthermore, the drug reserve from neighboring facilities also got exhausted due to high demand and inability to restock them. This is related to the effect of the pandemic which caused disruptions to domestic and international supply chains, as well as globally increased demand for medications, further straining an already broken system.^{2-5,22-24} This was the case in a global study done during the COVID-19 pandemic which showed that drug shortage in Africa and Europe were mostly caused by limitations in drug supply.²⁵

The challenges caused by these drug shortages were enormous necessitating precise management decisions regarding treatment of patients affected. Such decisions to remedy this include delay in administration of the cycle by a few days to make alternative sourcing of the drug. It can be noted that the delay was for short period as extended timeframe of drug shortage may increase the risk of patient deterioration, worsens the patient illness, postpone or cancel crucial surgical procedures, prolong the hospital stay, and increase the rate of mortality.²⁶ Cancer drug shortages have been shown to be more challenging in management decisions for cancer patients than other therapeutic areas as cancer drug alternative with equivalent supportive evidence may be lacking.²⁷ Therefore, the treatment was continued without the unavailable drug when there was no substitute, pending when it becomes available. In this study, the major remedy used to solve the immediate out of stock phenomenon was to source for the drugs in neighboring institutions in neighboring states which all the patients benefited from (100%). This was associated with some delays in patients receiving the chemotherapy as scheduled. Most of the patients had less than 3 days delay (75%). Five patients continue the regimen used without any substitution for the unavailable drugs (31%) and another two (12.5%) patients had their drugs substituted with available alternative. The affected drug was replaced with another drug of similar activity and efficacy. In our study, Cisplatin was replaced with carboplatin in regimes that had Cisplatin.^{28, 29} This was supported by the availability of diverse regimen available in literature for common cancers which are effective.¹⁹ The limitations in this study include the inability to capture patients unable to come to the hospital during the lockdown. A lot of the patients may have died at home without presenting in the hospital either

due to the lockdown or fear of COVID 19 infections. Other limitations include the small study population and missing folders.

CONCLUSION

In this study, we identified cancer drug shortage being experienced by cancer patients receiving treatment in our facility. The cancer drugs most affected by the shortage were Cisplatin, Cyclophosphamide and Bevacizumab. The causes for these shortages were identified as being multifactorial with exhaustion of hospital stocks being the most significant causative factor. Delaying the administration of chemotherapy for a few days while the unavailable drug was sourced from neighboring facility was our major approach to resolving this problem.

REFERENCES

- Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed.* 2020; 91:157-60. Medline 3219675
- NCDC. COVID-19 in Nigeria [Internet]. [cited 2020 May 21]. Available from: <https://ncdc.gov.ng/news/227/first-case-of-coronavirus-disease-confirmed-in-nigeria>
- NCDC. Covid-19 in Nigeria [Internet]. [cited 2020 May 21]. Available from: <https://covid19.ncdc.gov.ng/>
- Shiklam J. Nigeria: El-Rufai Eases Lockdown On Kaduna After 75 Days. *thisday* [Internet]. 2020; Available from: allafrica.com/stories/202006100565.html
- U.S. Food and Drug Administration. FDA coronavirus (COVID-19) response; 2020 [accessed 2020 Apr 18]. Available from: [https://www.fda.gov/emergency-preparedness-and-response/courterterrorism-and-emerging-](https://www.fda.gov/emergency-preparedness-and-response/courterterrorism-and-emerging-threats/coronavirus-disease-2019covid-19)
- Ventola CL. Drug shortage crises in United states; causes, impacts and management strategies. *PT.* 2011;36(11):740-757
- Holcombe B, et al. Drug shortages; Effects on parenteral nutrition therapy. *Nutr Clin Pract.* 2018;33(1):53-61
- Hishman AB, Bassam A. Global drug shortages due to covid-19:impact on patient care and mitigation strategies. *Research in social and administrative pharmacy.* 2020: <https://doi.org/10.1016/j.sapharm.2020.05.017>
- Ali M,Lisa MH, Colleen W, Margaret S, Niesha G Raymond JM, James MH. National survey on the effect of oncology drug shortage on cancer care. *Am J Health-Syst Pharm.* 2013;70:609-617
- World Health Organization. (2020). The impact of the COVID-19 pandemic on noncommunicable disease resources and services: result of a rapid assessment. World Health Organization. <https://apps.who.int/iris/handle/10665/334136>.
- Olabumuyi AA, Ali-gombe M, Biyi-olutunde OA, Gbolahan O. Article Special feature Oncology practice in the COVID-19 pandemic? a report of a Nigerian expert panel discussion (oncology care in Nigeria during the COVID-19 pandemic). 2020;36(153):1–9.
- Okunade KS, Okunowo AA, Ohazurike EO, Anorlu RI. Good clinical practice advice for the management of patients with gynaecological cancer during the COVID-19 pandemic in Nigeria and other resource-constrained countries. *Ecancermedicalscience.* 2020;14:1–10.
- Adewuyi S, Oguntayo A, Kolawole A, Samaila M, Adewuyi K. Age distribution, site of origin and HIV status of cases of gynaecological malignancies seen at a radiotherapy facility in Northern Nigeria. *Arch Int Surg.* 2015;5(1):11.
- Oguntayo OA, Zayyan M, Kolawole AOD,

- Adewuyi SA, Samaila MOA. Epidemiology of Gynaecologic cancers in Zaria, Northern Nigeria. *Italian Journal of Gynaecology & Obstetrics*. 2012; 24(4):168-173.
15. Oguntayo OA, Zayyan M, Kolawole AOD, Akpar M, Adewuyi SA. The burden of Gynaecological cancer management in Northern Nigeria. *Journal of Obstetrics and Gynaecology*. 2013; 3(8):634-638.
16. Adewuyi SA, Shittu SO, Rafindadi AH. Sociodemographic and Clinicopathologic Characterization of Cervical Cancer in Northern Nigeria. *Eur. J. Gynaec. Oncol (EJGO)*. 2008; vol. 29(1):61 - 64.
17. Awofeso O, Roberts A, Salako O, Balogun L, Okediji P. Prevalence and pattern of late-stage presentation in women with breast and cervical cancers in Lagos University Teaching Hospital, Nigeria. *Niger Med J*. 2018;59(6):74.
18. Kene TS, Odigie VI, Yusufu LMD, Yusuf BO, Shehu SM, Kase JT. Pattern of presentation and survival of breast cancer in a teaching hospital in North Western Nigeria. *Oman Med J*. 2010;25(2):104-7.
19. Klaus Herdrich, Heinz Weinberger. Selected schedules in the therapy of malignant tumors. 17th ed. California: Baxter; 2013.
20. Santoro A, Tursz T, Mouridsen H, Verweij J, Steward W, Somers R, et al. Doxorubicin versus CYVADIC versus doxorubicin plus ifosfamide in first-line treatment of advanced soft tissue sarcomas: A randomized study of the European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. *J Clin Oncol*. 1995;13(7):1537-45.
21. Robert AB, Mark FB, Michael AB, Gini FF, Bradley JM, Helen H, Robert SM, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. *N Eng J Med*. 2011;365:2473-83
22. Awad H, Al-Zu'bi ZMF, Abdallah AB. A Quantitative Analysis of the Causes of Drug Shortages in Jordan: A Supply Chain Perspective. *Int Bus Res*. 2016;9(6):53.
23. Andrew GS, Yoram U. Covid-19 and drug shortages; A call to action. *JMCP*. 2020;26(8):945-947
24. Andrew GS, Erin F, Yoram U. preparing for Covid-19 related drug shortages. *Ann Am Thorac Soc*. 2020;17(8):928-931
25. Marliese A, Jennifer J, Grace C, Shaun O, Alexandre C. Global oncology pharmacy response to COVID-19 pandemic: medication access and safety. *J Oncol Pharm Practice*. 2020;0(0):1-5
26. Walker J, Chaar BB, Vera N, et al. Medicine shortages in Fiji: a qualitative exploration of stakeholders' views. *PloS One*. 2017;12(6):e0178429 <https://doi.org/10.1371/journal.pone.0178429> Published 2017 Jun 5.
27. Jill CB, Laurie DS, Bruce GG, Jeremy RG. An ethical framework for responding to drug shortages in pediatric oncology. *Pediatr Blood Cancer*. 2015;62:931-934
28. Lorusso D, Petrelli F, Coinu A, Raspagliesi F, Barni S. A systematic review comparing cisplatin and carboplatin plus paclitaxel-based chemotherapy for recurrent or metastatic cervical cancer. *Gynecol Oncol [Internet]*. 2014;133(1):117-23. Available from: <http://dx.doi.org/10.1016/j.ygyno.2014.01.042>
29. Sebastião AM, Da Silva Rocha LS, Gimenez RD, De Barros LAB, Fukushima JT, Da Silva SCS, et al. Carboplatin-based chemoradiotherapy in advanced cervical cancer: An alternative to cisplatin-based regimen? *Eur J Obstet Gynecol Reprod Biol*. 2016 Jun;201:161-5