



# **A Comparative Study of the Impact of Coronavirus (COVID -19) on the Therapeutic Practices of Cancer Patients in the Kingdom of Saudi Arabia and Egypt**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author MRM designed the study, performed the statistical analysis and wrote the protocol. Authors DSHA, MAA, AHA, OGA and SGA wrote the first draft of the manuscript, managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.*

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## **ABSTRACT**

Cancer patients are considered one of the most vulnerable to infection with Corona virus (COVID-19), especially who are elderly, multiple comorbidities, and are often immunosuppressed by their cancer or therapy. The immune system of cancer patients is very weak compared to the healthy individuals, so, morbidity and mortality of any serious infections expected to be high among them.

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This research aims to study the impact of COVID-19 pandemic on cancer patients practices in Saudi Arabia (KSA) and compare with the result in Egypt. It was conducted through a well-structured questionnaire, among cancer patients either online (KSA) or paper questionnaire (Egypt). The questionnaire consists of 16 questions about Scio-demographic and changes in time and method of treatment (chemotherapy and radiotherapy), postponed of surgical operations. Our results showed significant differences between KSA and Egypt hospital practices; cancer department was affected by postponed appointment (54.8% & 63.3%), diagnosis (32.7% & 60%) and treatment of cancer patients (37.1% & 63.3%) respectively. Also, postponed of chemotherapy/radiotherapy (56.8% & 73.3%), surgical operations (45% & 43.3%), an increase in the deterioration of cancer by (35.5% & 23.3%), switching from parenteral injection to oral (27.8% & 56.7%) and changing in the drug doses (19.5% & 40%) in KSA and Egypt respectively. We can conclude that management of cancer patients during COVID-19 pandemic of great importance and so, switching from parenteral to oral, prolongation of the treatment period and postponed of some surgical operations gave a good opportunity to maintain adequate care of cancer patient with minimum exposure of patients to infection.

*Keywords: Covid-19 pandemic; cancer patients; cancer practices; Saudi Arabia; Egypt.*

## 1. INTRODUCTION

A novel coronavirus was reported in Wuhan, China, in January 2020. In Saudi Arabia (KSA), the first case of the COVID-19 pandemic was confirmed on March 2, 2020 from a traveler [1]. The incidence of COVID-19 disease on May 2, 2020, from Coronavirus Resource Center at the Johns Hopkins University and Medicine (JHU) reported that > 3.4 million of people worldwide suffered from COVID-19 and > 242 thousand individuals died from the disease (7.11%), while 32% were recovered. COVID-19 pandemic inflicts more than 200 countries with various degrees (JHU, 2020). In the USA, they reported >1,126,000 were confirmed cases and > 66 thousands are died (5.86%) [2]. During the COVID-19 pandemic, healthcare systems face a challenge to balance between maintaining adequate cancer patient care and minimizing the exposure of patients as well as healthcare staff to infection. Changes in healthcare policy and practice have evolved to achieve this balance. In Egypt practice changes included different aspects of cancer care; diagnosis, surgery, chemotherapy, radiotherapy, endocrine treatment and supportive and palliative care [1]. World Health Organization (2020) stated that, COVID-19 pandemic has great effect on health care systems restriction that leads to severe worse impact on the health care of non-communicable diseases including cancer and it appears more pronounced in lower income countries [3]. Other studies showed a tight link between cancer and corona virus (COVID-19), as the immune system in cancer patients is impaired [4]. Cancer patients were more susceptible to infections due to coexisting

chronic diseases, overall poor health status, and systemic immunosuppressive states caused by both cancer and anticancer treatments [5]. There are concerns that cancer patients are at a higher risk to get infected by COVID-19 and have worse outcomes [6]. As in many countries, cancer care in KSA has been interrupted by the COVID-19 pandemic [7]. There were multiple causes for this vulnerability of Saudi patients with cancer related mainly to three factors: the underlying disease, cancer-directed treatment and the underlying comorbidities. Cancer therapy itself, whether it is surgery, radiotherapy or chemotherapy, disturbs the immune system in various ways and results in an increased risk of infection. Whether due to age or exposure to other cancer risk factors, such as smoking, obesity or lifestyle choices [8]. Oncologists in KSA and some other Gulf states appeared to show good awareness and use of virtual cancer clinics during the COVID-19 pandemic [9]. According to Canadian guideline (Cancer Care Ontario) they divided cancer patients into three groups (A, severe cases who in need for treatment, B, patients in need for treatment but not critically cases, C, healthy individuals and delaying of treatment were acceptable) This guidance is applicable to different departments such as radiation therapy, palliative care, chemotherapy and surgery [10]. The European Society for Medical Oncology (ESMO) has divided cancer patients' management during the pandemic of COVID-19 into three cancer care priority levels (high, medium and low) based on the criteria of Ontario Cancer Care, Huntsman Cancer Institute and ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) [11]. The aim of this research is to compare between the changes in oncology

practices among Saudi Arabia and Egyptian cancer patients during the COVID-19 pandemic.

## 2. SUBJECTS AND METHODS

### 2.1 Study Design

This study was conducted through Cross-sectional study design. The questionnaire was distributed among cancer patients either online (KSA) or through paper questionnaire (Egypt) starting from 1st November 2020 for two months. The questionnaire consists of 16 questions about Socio-demographic, changes that happened in the time, dosages and duration of treatment and postponed of surgical operations. Other questions about the extent of side effects that may be happen as impact on cancer patients due to COVID-19 pandemic was included.

### 2.2 Sample Collection and Statistical Analysis

The research was carried out among cancer patients at Saudi Arabia (1110) and Egypt (360). All participants were provided with clear and easy understand information about the research paper in order to allow them to make an informed and voluntary decision about their participation. Filling the questionnaire was considered their agreement about participation. Statistical analysis was performed using SPSS version 22 (SPSS, Chicago, IL, USA). Comparisons of differences between the groups were done using chi-square and 2-sample t-tests. P value of less than 0.05 was considered significant.

## 3. RESULTS AND DISCUSSION

Our study revealed that the number of respondents from the Kingdom of Saudi Arabia, was shown to be 1110, while the number of participants engaging from Egypt was 360. The majority of participants in the study were females (KSA, 95.1%) and Egypt (63.3%). This study collected data from participants of various different regions within Saudi Arabia and Egypt. Most of the contributing participants from Hail region (78.7%) compared to all the other Saudi Arabia regions. As for the age range of respondents, it was predominantly led by the 15–30-year-old age group, accounting for a significant 82.9%. According to our results most individuals who were involved in the survey were people with University degree (87.7% & 60%) for KSA and Egypt respectively.

The impact of COVID-19 has changed the global systems and more than that, the arrangement of cancer care. Cancer patients and cancer survivors are at a high risk from COVID-19. In addition, there are many risks affecting cancer patients with COVID 19 for example: patients' age, type of tumor, presence of underlying comorbidities, stage of disease, and treatment type. However, recent evidence showed that mortality in cancer patients from COVID-19 is mainly driven by an increase in age and attendance of comorbidities and less likely to be associated with the use of cytotoxic drugs. Our study compares the magnitude to which cancer patients were affected by COVID 19. It also shows that cancer patients in Egypt were more affected by the COVID 19 pandemic compared to Saudi Arabia. Consequently, the results stated that in KSA and Egypt the percentage of cancer according to type was varied, breast cancer (39.4% & 33.3%), lung (7.3% & 13.3%), bones (5.9% & 10%) and uterus (4.2% & 16.7%) respectively. According to guideline studies in Hubei, China, patients affected by breast cancer were the most frequent type of cancer (20%). [12] Likewise, another study conducted in Wuhan, China disclosed that among cancer patients, lung cancer was 25% [13]. Further related studies in Russia stated that as was expected, lung and breast cancers were the most common type malignancies within cancer patients (2.4%) [14]. In addition, another finding from a similar study indicates that in England, patients with a uterine cancer had an incidence and prevalence rate of 8.6% & 6.3% and for bone cancer were 28.3% and 5.7% respectively [15]. Patients with hematologic cancer including (leukemia, lymphoma, myeloma), lung cancer, and cancers that were within their metastatic stages demonstrated higher rate of severe events compared with other patients without cancer [6].

In this study, the results indicated that the effect of COVID-19 on cancer patients was significantly high. Our results from KSA and Egypt revealed that patients with cancer were more affected by COVID-19 which can be explained by two leading aspects. First was an increase in the death rate in cancer patients (38% & 56.7%), secondly was due to decrease in the immunity of cancer patients (51.7% & 73.3%) for Saudi Arabia and Egypt respectively which were significantly different from each other. Based on findings from similar studies, patients with cancer were in high risk of COVID infection in contrast to the general population due to weak immunity

[16]. Moreover, study in China and Italy stated at first announced that patients with cancer have a higher chance of mortality from COVID-19 [17,18]. Furthermore, according to another study in China revealed that, about 13,000 patients with COVID-19, including about 230 cancer patients who were at high risk of COVID-19 and death, with rates of 64% and 20% in cancer patients compared with 32% and 11% in 518 patients without cancer, respectively [19]. Results from our study also indicated that COVID-19 increased the death rate in patients with chronic diseases (55.4% & 83.3%) for Saudi Arabia and Egypt respectively which were significantly different from each other. As the WHO stated a statistic on chronic illnesses was the most common and leading cause of mortality worldwide. For that reason, health experts stated that the presence of any coexisting comorbidity put an individual with COVID-19 at higher risk for severe clinical consequence, including death [20]. Initial research of a similar study from Asia recommended that elderly patients with more than one comorbidity, specifically diabetes, hypertension and obesity were at higher risk of developing COVID-19 [20,21].

In our contemporaneous research we found that within KSA and Egypt, patients who exceeded 60 years of age were more susceptible to a COVID 19 infection (37.9% & 35%) followed by patients aged 56-60 years old (20% & 28.3%) and lastly subsequent by the 36–55-year-old age range accounting for (20% & 21.7%) respectively. Similarly, according to conducted studies in Korea and Italy, elderly patients had a greater probability of mortality. Patients > 70-year-old and > 60 were approximated to account for the 80% and 90% of the occurring deaths in Korea and Italy correspondingly [22,23]. Although the percentage difference in susceptibility within the different ages was not significantly remarkable in KSA, it can be explained by its youth dominated inclusion criteria of the population with only about 5% aged over 65 years old [24].

Our findings revealed that in KSA and Egypt, participants believed that patients affected by cancer were more liable to a COVID 19 infection with a very significant rate of 30% & 76.7% respectively. There was a mass evidence of studies indicating that cancer patients have a greater risk of COVID 19 infection with a higher risk for morbidity and mortality. For example, a study that conducted in the Wuhan region of china estimated that out of a total of 1,524 cancer patients, half of them had an increased

risk of COVID 19 infection compared to the overall population [16]. In United states, increased risk for COVID-19-related morbidity and mortality was found in elderly cancer patients with one or more comorbidities [25].

Under current circumstances of the global Corona pandemic, all health care systems, including medical departments, have been affected resulting in the postponed of appointments and the suspension of patients. In our paper we showed the most affected departments in hospitals of KSA and Egypt. The chronic diseases department such as diabetes mellitus and hypertension were most affected by the COVID 19 pandemic accounting (60.1% & 66.7%), followed by the oncology department (54.8% & 63.3%), hemodialysis (53% & 30%), pediatric (22.2% & 16.7%), maternity and childbirth (19.9% & 13.7%) all respectively. Other study showed some differences from our results, they found that diabetes and hypertension (30%) were the most affected departments, followed by the oncology department (6%), hemodialysis (2.5%) [26]. Another study showed the impact of COVID 19 on maternity and childbirth departments was shown by the total number of participants who did not receive antenatal care due to the COVID-19 pandemic (4%) [27].

COVID-19 pandemic produced many changes in healthcare policy and practice in cancer patient's treatment to maintain adequate cancer patient care with minimum exposure of patients to infection. These changes include cancer diagnosis, many surgery, radiotherapy and chemotherapy treatment. Our results cleared that diagnosis and treatment of cancer patients were affected by the covid-19 pandemic by about 32.7%, and 37.1% in KSA, which was significantly different from Egypt (60% & 63.3%) respectively. This study revealed that due to COVID 19 pandemic, many things were affected such as postponed of chemotherapy/radiotherapy (56.8% & 73.3%) in KSA and Egypt respectively. This action was similar to the study of Abolkasem et al. who stated that in Egypt, the main changes that happened in practice are firstly, doctors were prolonged the duration between chemotherapy cycles [1]. They treated patients with single fraction or short courses of radiotherapy in the palliative cases, also, they used hypo-fractionated radiotherapy regimen for radical treatment. They prolonged the follow up intervals and treatment of outpatient such as hormonal treatment and palliative care drugs, they

dispensed these drugs for long durations and assessed patients by phone calls. In Italy, they recommended to continue adjuvant treatment and chemotherapy for first line metastatic patients and advising delayed chemotherapy for second line treatment and further disease progression [28]. The study done in Egypt revealed that tamoxifen was administered for a longer duration in most cancer centers, LHRH analogue was administered as prolonged period (changed from monthly to every 3 months) and systemic chemotherapy also changed from every week to every 3-4 weeks [1].

In our study they postponed of surgical operations either in KSA (45%) & Egypt (43.3%) which was not significantly different. Similar study reported that they restricted patient admission to hospital and postponed surgery to patients with benign tumors [1]. Another study showed that patients with genitourinary cancers, they recommended curable treatment and delaying for surgery [29]. Others said that patients with cervical cancer, first line chemo-radiotherapy was preferred than surgery, also, neoadjuvant chemotherapy was administered initially for local advanced ovarian cancer [30]. In France, guidelines in oncology practice stated that in COVID-19 pandemic, surgery for cancer patients was postponed, adjuvant radiotherapy was delayed and hypo-fractionation was favored, and adjuvant and neoadjuvant chemotherapy were given using the shortest protocols possible [31,32]. Other study said that delaying of cancer surgery > 6 months was shown to increase the 5-year mortality in all stages of cancer and was estimated to reach >30% in stage 3 [33].

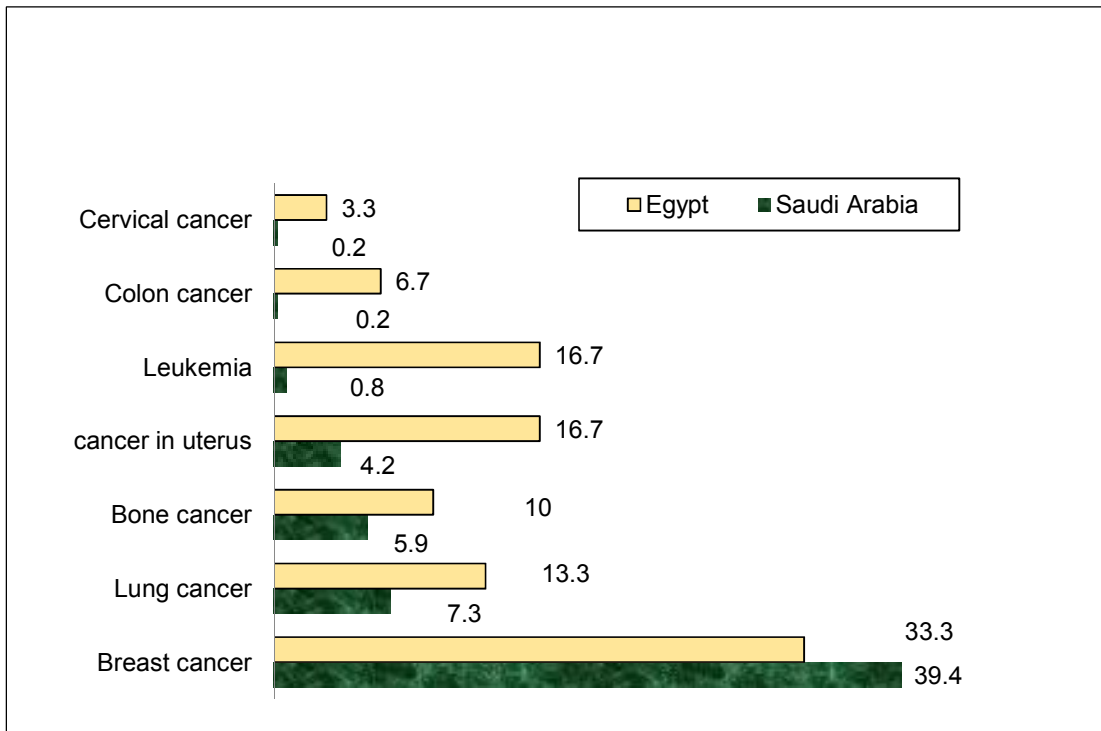
In this research delaying in treatment or diagnosis increased the deterioration of cancer in KSA (35.5%) & Egypt (23.3%). While other study of Kulikov et al. divided patients into three groups according to the risk of progression if treatment was delayed (low, intermediate and high risk). After that they stratified patients according to their risk of morbidity from COVID-19 according to age (>70 years high risk) and (<50 as low risk). According to these two factors they put their guidance to decide if cancer treatment started immediately or not during the COVID-19 pandemic [34]. Other cancer centers in Egypt minimized chemotherapy combination (triplet regimens) and encouraged single and double regimens. For patient with low-risk breast cancer the adjuvant radiotherapy was delayed when compared to radical radiotherapy for lung

and prostate cancers. Hypo-fractionated schedules were more preferable for glioblastoma multiforme and prostate cancer radical irradiation [1].

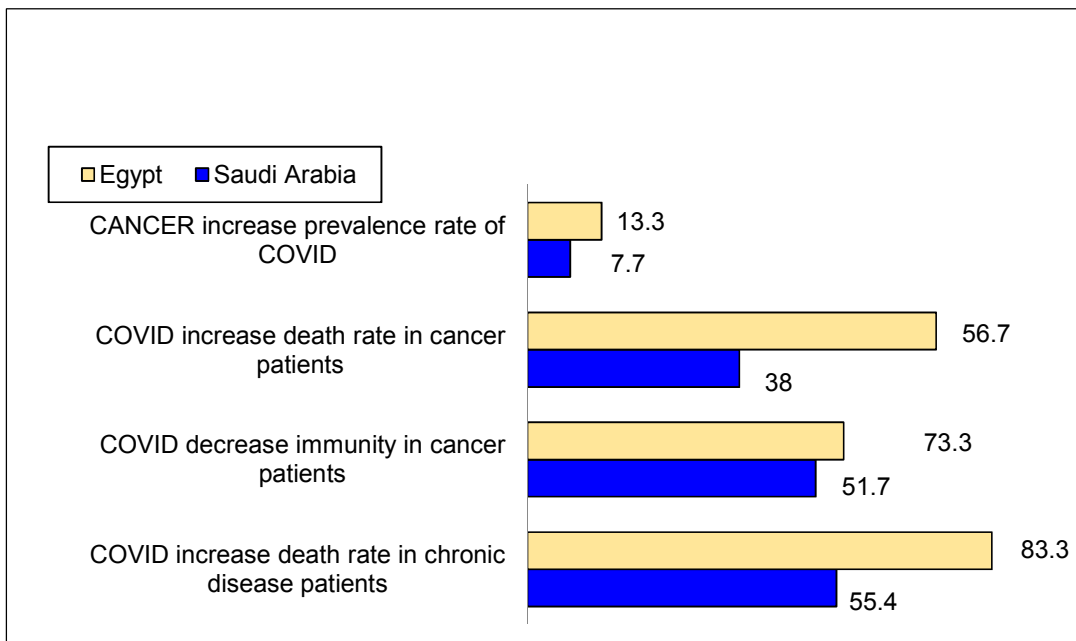
The Saudi Oncology Pharmacy Assembly (OSPA) has issued recommendations to reduce the frequency of cancer patients' visits to oncology centers during the pandemic while maintaining the access to cancer therapy and minimize the risk of exposure to coronavirus disease [35]. They recommended to delay the adjuvant chemotherapy within the range of treatment initiation such as some cases of breast cancer [36] and for colorectal and gastric cancer, starting adjuvant chemotherapy within 6-8 weeks post-surgery is associated with benefit for the patients, while delaying more than 6-8 weeks post-surgery was riskier for causing death [37]. Using of extended dosing schedule of cancer therapy such as taxanes was used every 3 weeks instead of once weekly in patients with advanced breast cancer [38]. Also, the use of medications of gonadotropin-releasing hormone analogues (Leuprolide, triptorelin and goserelin) every 12-24 weeks for treatment of prostate cancer because they were available in sustained-release formulations with different concentrations [39-41].

In our paper we switched from parental rout to oral rout in KSA (27.8%) which was significantly less than Egypt (56.7%), and also, changing in the pharmaceutical doses in KSA (19.5%) was significantly less than in Egypt (40%). Similar study by Steger et al. [42] switching from intravenous chemotherapy to oral or subcutaneous route of administration such as oral vinorelbine (60 mg/m<sup>2</sup> or 80 mg/m<sup>2</sup>) instead of IV (25 mg/m<sup>2</sup> or 30 mg/m<sup>2</sup>) was used in patients with metastatic breast cancer (MBC) to the bone [42]. The oral etoposide was given in double dose when switching from IV to oral in treatment of several hematological and solid malignancies [43]. Trastuzumab was approved in Europe since 2016, in SC injection for treatment of metastatic breast cancer in a fixed-dose of 600 mg every 3 weeks without loading dose [44]. US FDA approved in 2017 that Rituximab was given by SC injection (1400 mg in 5 to 7 min) in contrast to the IV formulation (that takes more time from 4 to 6 h) [45]. Trastuzumab and Rituximab can be given SC at home by qualified nurses to limit patient visits to hospitals and clinics during the COVID-19 pandemic [46]. Most of cancer centers in Egypt was switched cancer treatment to oral administration if it possible [1].

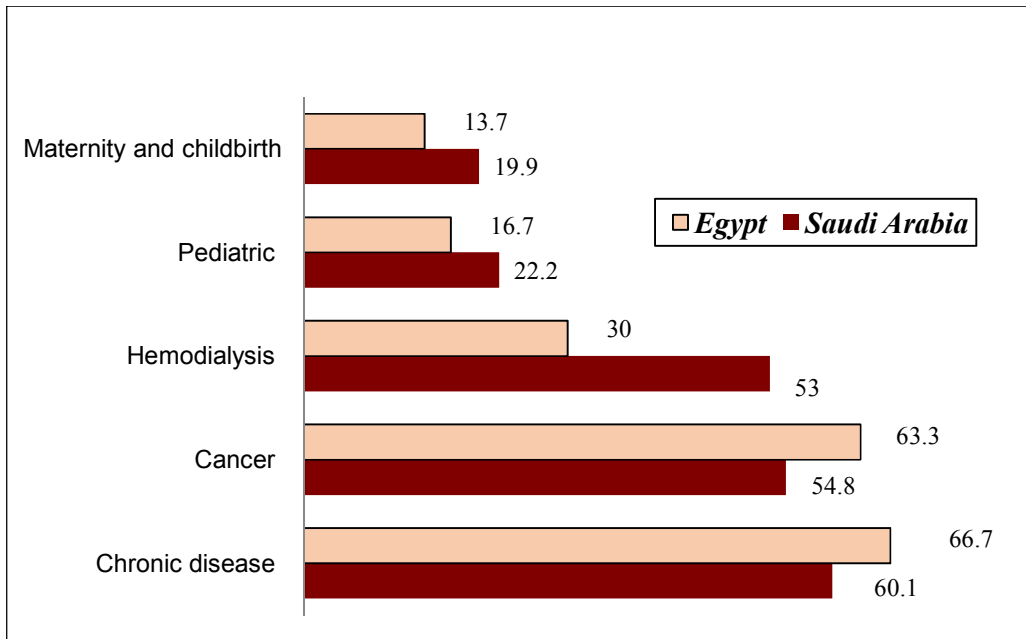
Providing more medications supply from pharmacy stock to chronic and stable cancer patients (about two to three months instead of one-month quantity) [35].



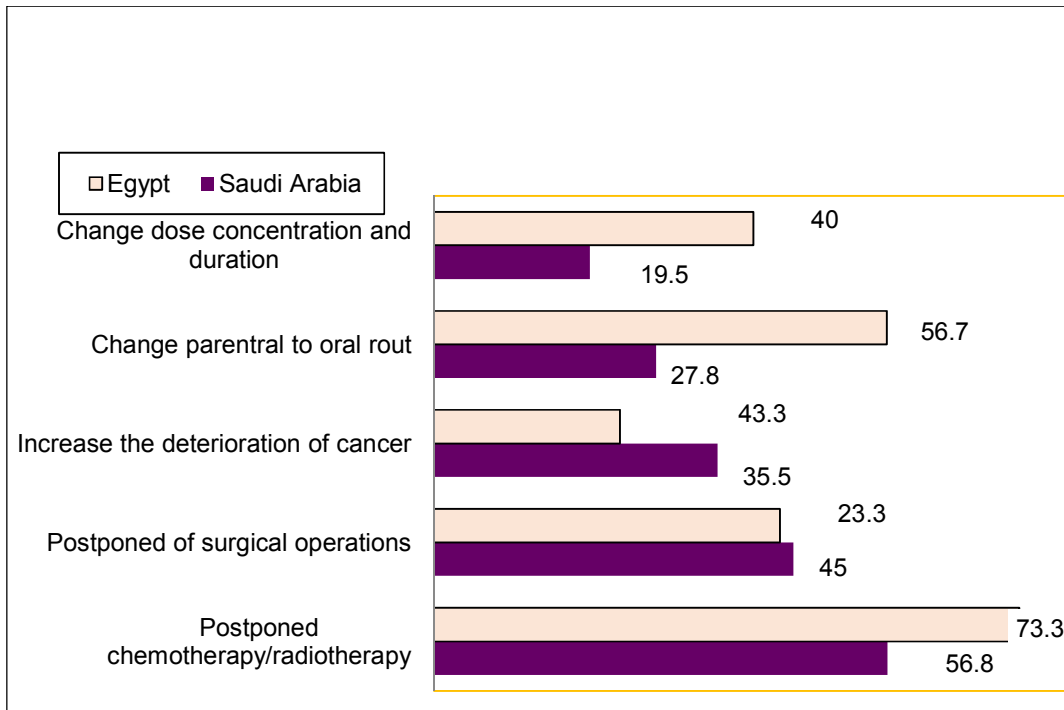
**Fig. 1. Percentage of patients who answered the question about the types of cancer**



**Fig. 2. Percentage of patients who answered the question about the link between covid-19 and cancer**



**Fig. 3. Percentage of patients who answered the question about the most affected hospital departments by postponing appointments during the covid-19 pandemic**



**Fig. 4. Percentage of patients who answered the question about which side of treatment is the most affected by covid-19 pandemic**

**Table 1. Percentages of cancer patients in Saudi Arabia and Egypt who answered the following questions about the susceptibility of cancer patient toward COVID-19 infection compared to healthy individuals [n= 1110 (KSA) & 360 (Egypt)]**

<b>Questions</b>		<b>Answers</b>						
Which is the age group more susceptible to COVID-19 infection?	Answer (%)	1-15 YEAYS		16-25 YEAYS	26-35 YEAYS	36-55 YEAYS	56-60 YEAYS	= >60 YEAYS
	KSA	3		9.3	11.8	17.9	20	37.9
	Egypt	3.3*		5*	6.7*	21.7*	28.3*	35
What is the type of cancer?	Answer (%)	Breast cancer	Lung cancer	Bone cancer	Cancer in uterus	Leukemia	Colon cancer	Cervical cancer
	KSA	39.4	7.3	5.9	4.2	0.8	0.2	0.2
	Egypt	33.3*	13.3*	10*	16.7*	16.7*	6.7*	3.3*
What is the link between COVID-19 and cancer?	Answer (%)	COVID increase death rate in chronic disease patients	COVID decrease immunity in cancer patients	COVID increase death rate in cancer patients	CANCER increase prevalence rate of COVID	Others		
	KSA	55.4%	51.7	38	7.7	2.5		
	Egypt	83.3*	73.3*	56.7*	13.3*	0*		
What is the degree of susceptibility of cancer patient toward COVID-19 infection compared to healthy individuals?	Answer (%)	Very high	High	Intermediate	Low	No relation	I don't know	
	KSA	30.9	30.4	11.8	3.8	5.5	17.7	
	Egypt	76.7*	13.3*	6.7*	3.3*	0*	0*	

\*Significant difference from Saudi Cancer Patients at P<0.05



**Table 2. Percentages of cancer patients in Saudi Arabia and Egypt who answered the following questions about the postponing appointments, diagnosis and treatment of cancer patients during COVID-19 pandemic [n= 1110 (KSA) & 360 (Egypt)]**

Questions	Answers					
	Answer (%)	Chronic disease	Cancer	Hemodialysis	Pediatric	Maternity and childbirth
Which is the most affected Department by postponing appointments during the COVID-19 pandemic?	KSA	60.1	54.8	53	22.2	19.9
	Egypt	66.7*	63.3*	30*	16.7*	13.7*
Do you think the diagnosis of cancer is affected by the covid-19 pandemic?	Answer (%)	YES		NO		I DONOT KNOW
	KSA	32.7		6.4		60.9
	Egypt	60*		6.7		33.3*
Do you think that cancer patient treatment and diagnosis has been affected by covid-19 pandemic?	Answer (%)	YES		NO		I DONOT KNOW
	KSA	37.1		10		52.9
	Egypt	63.3*		16.7*		20*
Which side of treatment is most affected by covid-19 pandemic?	Answer (%)	Postponed chemotherapy/radiotherapy	Postponed of surgical operations	Increase the deterioration of cancer	Change parentral to oral rout	Change dose concentration and duration
	KSA	56.8	45	35.5	27.8	19.5
	Egypt	73.3*	43.3	23.3*	56.7*	40*
Do you agree with the precautions that are followed to protect cancer patients from COVID-19 pandemic	Answer (%)	YES		NO		SOMETIMES
	KSA	22		37.7		40.3
	Egypt	40*		53.3*		6.7*

\*Significant difference from Saudi Cancer Patients at P<0.05

#### 4. CONCLUSION

Management of cancer patients during COVID-19 pandemic of great importance and so, switching from parenteral to oral route, prolongation of the treatment period and postponing of some surgical operations gave a good chance for maintaining adequate care of cancer patients and reducing the time of patient's exposure to infection.

#### CONSENT

As per international standard or university standard, Participants' written consent has been collected and preserved by the authors.

#### ETHICAL APPROVAL

This study has been reviewed and approved by the research Ethical Committee (REC) at the University of Hail with letter number Nr.16784/5/42 dated 23/03/1442H. (Attached file)

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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