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Abstract

The newly emerging coronavirus has affected many fields in the healthcare systems. Many resources have been declared lacking due to the high consumption during the pandemic. Among the fields that were hugely affected, cancer care is one of them that requires more attention to save what can be saved. In this review, we aimed to shed more insight into how the lockdown affected the screening and follow-up procedures of both the breast and cervix. Since the start of the pandemic, reports showed that lacking continuous screening and follow-up was remarkable which may have affected the prognosis for many potential breast and cervical cancers. These showed that delays in diagnosis and screening may have increased the incidence of mortality from breast and cervical cancers. However, many recommendations have been proposed by many relevant organizations to reduce this burden and also control the spread of the pandemic. Personal protective measures and reducing the number of individuals visiting a hospital per day are maybe the most highlighted measures. Follow-ups have been also organized to be through telemedicine for non-severe cases, and in-person and/or at a primary healthcare hospital for severe cases requiring frequent follow-up.

Keywords: Lockdown; Pandemic; COVID-19; Breast; Cervix

Introduction

The start of the COVID-19 pandemic, which is caused by the SARS-CoV-2 virus, first took place in a Wuhanian wet market in China [1]. Calling the virus SARS-CoV-2 or severe acute respiratory syndrome virus coronavirus number 2 at first was because most first reported cases were found to have respiratory illnesses. Therefore, the virus was named after previous similar viruses from the same family that causes similar manifestations [2,3]. However, COVID-19 infection was found to have more aspects than the respiratory one. Many extra-pulmonary manifestations have been reported due to the virulence of the virus and the widespread of the relevant receptors inducing the

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pathogenesis [3]. Many of these disorders are life-threatening, and therefore, precautions should be taken to avoid the infection [4]. Besides, previous reports showed that the infection is more severe in patients with comorbidities like diabetes, hypertension, and conditions causing immunosuppression as malignancy [4-6]. Therefore, better quality and more restrictions for avoiding the infection is essential in the management of these patients.

Since the start of the pandemic, no reports were published investigating cancer patients during the pandemic until February 14 when a Chinese report was published [7]. Liang., *et al.* [7] published the first nationwide report as they investigated the status of cancer patients that were affected by COVID-19 infection. The authors reported that 39% of these patients had a severe COVID-19 illness that required admission in the ICU and/or died [7]. In the months to follow, many reports were published indicating the severity of the situation of COVID-19 infection in cancer patients. Studies showed that cancer patients are at high risk for developing a severe infection that requires urgent procedures [7-9].

Although cancer is a non-communicable disease, it possesses a huge spread worldwide with big prevalence and incidence rates [10,11]. In 2012, Cancer was estimated to affect 14.9 million people globally, to be increased to 22 million cases in the coming two decades [12]. Breast and cervical cancers are one of the most common cancers worldwide [13]. Ferlay, *et al.* [12] estimated that around 1.7 million individuals are being diagnosed with cancer each year in addition to being the second most common cancer. The incidence rate for it, though, varies by region. According to previous estimates, the incidence of breast cancer is estimated to be 19.4 per 100,000 population in East Africa while in West Europe the incidence was much higher; being 89.7 cases per 100,000 population [14]. Arbyn., *et al.* [15] reported that cervical cancer followed breast cancer in prevalence being the fourth most prevalent cancer in women. The authors estimated 570,000 cases and 311,000 deaths occurred from cervical cancer, globally. These numbers indicate the severity of both lesions, and how these rates can be hugely affected by COVID-19 infection. In this study, we aim to review the effect of the pandemic on the screening, and follow-up of cervical and breast cancers.

Methods

We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases on 8th November 2020 using the medical subject headings (MeSH) or a combination of all possible related terms. Papers discussing the effect of the pandemic on the screening, and follow-up of cervical and breast cancers were screened for relevant information. We did not pose any limits on date, language, age of participants or publication type.

General considerations and recommendations

Patients are usually classified according to the degree of severity and their Breast imaging-reporting and data system (BI-RADS) scores [16-18]. For instance, patients with BIRADS 5 scores are considered as a high priority for diagnosis and screening, while others with BIRADS 4 scores are marked as medium priority patients. These findings must be also consistent with the potentiality of screening and diagnosis impact on the outcomes and severity of the diseases from a clinician perspective. According to previously published guidelines in the field, previous recommendations were also outlined for processing patients with breast cancer. These guidelines proposed some risk factors for prioritizing screening and processing [19,20]. These include: (1) Patients with suspected or diagnosed breast cancer, (2) Patients with breast cancer on a treatment regimen as chemotherapy, radiotherapy, etc. (3) patients with breast cancer that are being followed-up, and (4) age > 60, and present cardiovascular and respiratory co-morbidities have been also reported as supplementary risk factors. Based on these risk stratification factors, many recommendations have been developed. These include: (1) Patients that must pay visits to the hospital are obliged to stick to the safety measures and guidelines of each country (eg.: social distancing, and wearing masks), (2) Patients should be preliminarily assessed for general symptoms suggestive of COVID-19 infection and/or cancer which can be done by the patients through the phone. Moreover, patients should be assessed for the high temperature at the entry of the hospital, (3) patients should be tested for COVID-19 infection before conducting surgery and/or inaugurating a treatment modality as immunosuppressive, and

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radiotherapy. Discontinuation of these procedures should be done if patients tested positive until recovery from the infection occurs, (4) Hospitalization of patients should be done in COVID-19 free hospitals, and patients should be isolated in specific wards away from any potential source of infection, (5) Hospitals should not allow for any visits or accompanying individuals during screening, and/or follow-up, (6) Further Reduction in the number of people existing in the hospital is also suggested by making alternating shifts for the healthcare givers within the hospital, (7) Meetings regarding the multidisciplinary tumor boards (MDM) should be conducted via online platforms to reduce the crowdedness in the hospitals. These general measures were also described by previous reports [20,21].

Breast screening

Suggested practices

There is no doubt that the pandemic, and subsequent lockdown, has affected many aspects in the healthcare field including breast cancer care approaches as imaging, assessment of asymptomatic patients, and management of previously diagnosed individuals. Due to the lack of resources and individuals during the pandemic, previous studies and reports suggested that mass breast screening should be suspended through the pandemic, and suggested that different approaches should be applied. For instance, Hollander, *et al.* [16] suggested the use of telemedicine to reduce the crowdedness and intervene against the spread of infection. This was also in agreement with other previous reports in including the American Society of Breast Surgeons (ASBrS) and the American College of Radiology (ACR) statement on the management and screening of breast cancer during the pandemic. On the other hand, patients that present with or complain about symptoms should be processed and appointments should be given according to the availability of the resources at the local healthcare facilities. Additionally, more efforts should be conducted not to delay the diagnosis of patients that are symptomatic and with clinical and/ or imaging findings [20,22].

Effect of lockdown on screening and management

Through the difficulties induced by the lockdown, there is no doubt that many processes of breast cancer management have been affected. London., et al. [23] analyzed the data of 20 healthcare cancer institutions of different cancer types to study the effect of COVID-19 on the assessment of screening and management of the different types of cancers. As for breast cancer, the authors found that the identification of this type of cancer was reduced by -47.7%. Moreover, screening for breast cancer was also reduced by -5.0 to -9.1% between January and February. The overall decline in patients' rates seeking breast cancer screening was reported to be -89.2%. A report from Beth Israel Deaconess Medical Center also showed that the rate of breast cancer referral to the hospital was much reduced by -65% [24]. Moreover, a report from the EPIC Health Research Network estimated that a reduction of more than 90% of breast cancer screening was estimated only in March and April this year (25, 26). In Taiwan, Tsai., et al. [27] estimated the reduction in breast cancer screening rate to be -22.2%. In another Taiwanese study by Peng., et al. [28] the authors reported that significant reduction rates in the screening and diagnosis of breast cancer were noticed in March, April, and May when compared to the previous three years. The authors also showed mobile mammography was more significantly conducted than hospital-based ones. However, the rates of mobile mammography were also decreased during the pandemic. The results of these studies indicate the fact that breast cancer screening and referral have hugely reduced during the pandemic due to the recommendations to reduce the frequency of visiting hospitals and staying at home. Recommendations by Susan G. Koman; the world's largest breast cancer organization, showed that delayed screening for women should be done for the next year for patients with low risk of cancer and those that are appraently healthy [29]. On the other hand, a report from the national cancer institute recommended that breast cancer patients with high risk and a previous diagnosis are the high priority for further screening and referrals [30,31].

Cervical screening and follow-up

Cancer cervix is also one of the commonest cancers that occur worldwide. The number of 570,000 cases of cervical cancer has been estimated globally with 311,000 deaths [32]. These huge numbers indicate the high prevalence of cancer among women, and the bad

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prognosis it possesses. Therefore, it requires additional efforts to be managed and cured. Using Pap smear or Oncotic coloproctology has been considered an effective tool in the detection and management of early cervical cancer and premalignant lesions in general. However, during the COVID-19 pandemic, this procedure was recommended to be postponed to reduce the frequency of contact between patients and healthcare providers which may increase the frequency of infection. Recommendations also extended to even postpone treating intraepithelial neoplasia. This comes in agreement with the American Society of Clinical Oncology initiative to reserve medical resources during the pandemic [33]. During the pandemic, as we mentioned before, cancer care has been hugely reduced to prevent the severity of COVID-19 infection and spread. Similar to breast cancer, cervical cancer has been also affected. Kirigia., et al. [34] suggested that telemedicine modalities should be approached for the initial screening of cervical cancer. The authors described some benefits from telemedicine use in cervical screening. These include the continuous communication between the doctors and their patients in addition to providing the patients with suitable timing and places for a potential screening whenever needed. However, the author did not relate to any statistically-based investigations, and therefore, these points would have been only theoretical. However, based on the recommendations from previous guidelines for breast cancer patients, these points might also work with cervical screening. Follow-up events were also suggested to be postponed and replaced by other measures. For instance, asymptomatic patients who were previously diagnosed with cervical cancer, and have received successful management do not have to do the regular check-up visits at the gynecologist. Instead, telemedicine is considered a safe, and suitable modality that can achieve this purpose [33,35]). Estevez-Diz et al. [33] furtherly made cervical procedures prior to each other accoriding to many factors, mostly dependant on the patient's age and severity of the disease. According to the European Society for Medical Oncology (ESMO) guidelines for managing cervical cancer during COVID-19, priority should be given to the unstable conditions that might be life-threatening. For instance, follow-ups for regular imaging was indicated as a low priority. On the other hand, people with acute illnesses and symptoms were marked as a high priority for these visits and resources. Mass screening for clinical studies was marked as a medium priority while high priorities were introduced for patients with severe complications, and those that have been recently diagnosed with cervical cancer, and for the staging of the disease [36].

It is worth mentioning that during the pandemic screening for breast and cervical cancer programs have been hugely reduced when compared to the pre-pandemic ones. For instance, in the United Kingdom, a total of 210,000 individuals each week took part in the UK national screening for bowel, breast, and cervical cancer before the pandemic. In March 2020, during the early start of the pandemic and the subsequent lockdown, such events were suspended, and as a result, millions of people did not receive any invitations for these regular check-ups [37]. Despite the logical effect of the previous guidelines in reducing the rates of infections and saving more lives, many other lives are being affected due to a missed diagnosis or lack of treatment and resources. In a large study conducted by Maringe., *et al.* [38] about the effect of missed diagnosis on cancer death during the COVID-19 pandemic. The authors analyzed the data of 32,583 patients with breast cancer in England to estimate the rate of dead breast cancer patients with a previous delay in the diagnosis. Hanna., *et al.* [39] conducted a systematic review to investigate the association between diagnostic delay effects on the prognosis of many cancer types. Among the analyzed types, breast and cervical cancer mortalities were significantly associated with a four-week-delay in the diagnosis and management. Sharpless., *et al.* [40] also predicted that around additional 10,000 deaths attributable to breast and colorectal cancers will occur in the next five years in the United States while in the UK, Maringe., *et al.* [41] predicted a number of > 3,000 additional deaths from delayed diagnosis of breast cancer and other types during the lockdown over the next five years.

Conclusion

In this study, we have identified several measurements for protection against any further spread of the pandemic, and any further consequent lockdown measures by introducing the best ways and priorities for diagnosis and management of breast and cancer lesions, especially cancer based on the previous recommendations from world-known organizations. According to many reports, it appears that the lockdown measures have hugely affected the screening and follow-up procedures especially for non-severe or asymptomatic cases. Reports showed that telemedicine has been used as an effective procedure. However, we believe that further efforts should be applied in this field due to the unfortunate projections of mortality rates from delayed diagnosis.

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