

# An immune-centric investigation of Coronavirus in the women with cancers; A review article

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## ABSTRACT

Cancer is one of the growing chronic diseases in the world that kills large numbers of people every year. The disease affects the human immune system. The function of the body's organs under the influence of this disease loses its main function. Studies have shown that people with cancer are at higher risk of dying from Coronavirus. Because of the outbreak, wide clinical spectrum, pathogenesis of infection in Coronavirus, recognition and evaluation of this virus in populations with a risk factor for cancer is important. Many women develop chronic diseases such as cancer throughout their lives. Examining and recognizing Coronavirus in the women with cancer can increase our awareness of the disease. In this article, considering Coronavirus, we discuss the function of the immune system in cancer and corona, the concepts related to the topic, and the known solutions with an emphasis on cancer.

**Keywords:** Corona, COVID-19, immune system, women, women's cancer

## Introduction

The new Coronavirus was first identified in China, and genetic studies at the time showed that the virus was similar to that of bats in the genome sequence of about 96%.<sup>[1]</sup> Coronavirus infects a wide range of mammals and birds. The virus can cause respiratory illness in all its hosts. Coronaviruses are based on the genetic structure of the four genera alpha, beta, gamma, and delta Coronaviruses. These viruses have low-risk types and high-risk types such as SARS and MERS. Coronavirus, meanwhile, bears the closest resemblance to MERS.<sup>[2,3]</sup> Coronavirus is caused by a virus that enters the body and infects the target cells, which are usually squamous cells, and at the proper time uses the cell

replication machine to destroy the epithelial cells of the lungs, bringing about the illness and severe inflammation.<sup>[4,5]</sup> The modes of transmission in the coronavirus are inhalation of the air containing the droplets of the mouth or nasal mucosa and the lungs of the people with the virus, and touching contaminated surfaces or objects and subsequently touching the mouth, nose or eyes.<sup>[6]</sup> According to the World Health Organization, by May 2020, about five million people in the world have been infected with the new Coronavirus, of which more than 315,000 have died, a third of whom are women.<sup>[7-9]</sup> Due to their role in the family and their great importance in human society, women are among the important issues in the study and monitoring of diseases. Despite the spread of cancer in women such as breast cancer, uterine cancer, ovarian cancer, and so on, given the high rates of outbreak, mortality from Covid-19, and the significant effect that the virus has on older people and cancer patients, attention to the pathogenesis of the virus in people at risk requires health care and therapeutic actions.<sup>[10,11]</sup> In this

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article, by examining Coronavirus in women with cancer and the important points about Coronavirus and the people with cancer, we try to investigate the role of cancer risk factor in patients with cancer, especially women, the damage caused by the new Coronavirus, the role of the immune system in cancer and Coronavirus in these cases, provide preventive solutions for people.

## Materials and Method

The present study, aiming at immune centrically investigating Coronavirus in the women with cancer from 2010 to 2020, expresses the problematic aspects of the virus for the people with cancer and society. The search was conducted on scientific databases such as PubMed, ISC, NCBI, and the articles published around the world, and the clinical records and laboratory findings were examined. The Aspects and topics related to the spread of the virus, pathogenesis in different populations, and clinical manifestations were searched and investigated. To gather information on Coronavirus, in terms of content, the keywords in over-mentioned databased include cancer, cancer in women, cancer types, cancer statistics, Coronavirus infections, COVID-19, Corona outbreak, Corona in the world, the onset of the pneumonia, and the like. Searching a total of 209 articles, 62 cases that covered the topic and were consistent in the content were used in this article.

### Corona and its clinical symptoms

Coronavirus belongs to the Orthocoronavirinae subfamily. Viruses in this subfamily generally cause pneumonia in their hosts and include four species:  $\alpha$ -coronavirus,  $\beta$ -coronavirus,  $\gamma$ -coronavirus, and delta-coronavirus. Coronaviruses have the largest genome among all viruses. The surface of the virus has spike (S), membrane (M), and envelope (E) protein. The virus binds to the host cell surface with the help of the spike protein and initiates pathogenic stages.<sup>[4,12,13]</sup>

After infection with the virus, the patients show general symptoms including fever, cough, muscle aches or fatigue and bruising, stenosis, acute respiratory distress syndrome (ARDS), severe kidney damage, which 25% of the patients require transfer to the ICU and eventually 12% death. Another symptom is lymphopenia, which is seen in 80% of the adult patients. Also, ground glass opacity (GGO) was seen on CT scan. Moreover, the symptoms that the patients may experience include an increase in CRP protein, erythrocyte sedimentation rate, lactate dehydrogenase, creatinine, and prothrombin clotting time.<sup>[9,14,15]</sup>

### Corona in the women with cancer

Coronavirus appears in the people with cancer more severely. Various reports have indicated that cancer weakens the immune system, which can lead to adverse and critical outcomes. The clinical complications and severity of Corona have been higher in the people with cancer. Studies in the patients undergoing

chemotherapy have shown a negative effect of Corona in the people with cancer and an increase in pneumonia.<sup>[16-18]</sup>

In their study, Liang *et al.* found that 1% of COVID-19 cases had cancer, which was generally higher than 0.3% in the Chinese population.<sup>[19]</sup> This suggests that the cancer patients are at higher risk. There has been no study on the risk of Corona and its outbreak in the people with cancer. However, studies suggest that delaying the treatment may help reduce the incidence of the disease.<sup>[20,21]</sup>

Studies on the outbreak of Coronavirus in the women with cancer have not been conducted specifically, but cancer findings in the infected women and men illustrate that due to weaknesses in the immune system the risk of complications and mortality from Corona in the people with cancer is high.<sup>[16,17]</sup> but paying attention to this issue can lead to an important step in women's health.

### The role of the immune system in cancer and Corona

The human immune system is responsible for protecting organs against diseases caused by certain pathogens such as viruses, bacteria, and cancer. The immune system consists of two parts: Inherent safety and acquired safety.<sup>[6]</sup> The Inherent immunity in the early stages is responsible for combating pathogens, and the acquired safety at a more professional level identifies the causative agent of the disease. T cells, or T lymphocytes, play an important role in viral infection and cancer, and by recognizing the main pathogen of the immune system, help the body to diagnose the virus more quickly. In creating an acquired immune response, B lymphocytes also play a significant and considerable role in recognizing external factors by creating memory cells.<sup>[22-24]</sup>

The important role of the immune system in cancer is well proven. Studies have shown that one of the causes of cancer is a decrease in the strength of the immune system and the lack of recognition of the destruction of tumor tissue in the early stages by the immune system and subsequent long-term inflammation. At least 25% of cancers are associated with chronic inflammation. Microbial agents such as human papillomavirus (HPV) that induce inflammation and are responsible for 90%–100% of all cervical cancers. Similarly, a chronic infection with *Helicobacter pylori* increases the risk of gastric cancer. The significant role of the immune system's dysfunction in reduction has been well established.<sup>[25-27]</sup>

One of the characteristics of tumors is escape from the immune system. In the early stages of tumor growth, cytotoxic immune cells such as natural killer (NK) cells and CD8 + T cells, detect and kill cancer cells, but in the people with malignancy, cancer cells by producing new antigens against the immunity cell, escape from the immune system. In many cases, the immune system cells such as immature dendritic cells (DCs), cause the tumor's spread. However, the presence of T lymphocytes and natural lethal cells is always beneficial to the immune system.<sup>[28-30]</sup>

Processes such as angiogenesis, regeneration, and escape from the immune system are performed by tumor associated neutrophils (TANs) and immature DCs, leading to rapid tumor progression and metastasis. In contrast, cytotoxic macrophages and TANs, NK cells, and immature DCs lead to the destruction of tumor cells after proliferation.<sup>[30,31]</sup>

The immune system respond to viruses generates by detecting the molecular parts of pathogens such as virus-free RNA, cellular stress, metabolic changes, or cellular damage caused by infection. After detecting the viral components, the immune system initiates an appropriate and effective antiviral response, which involves the production of a variety of cytokines and various cells of the immune system.<sup>[32,33]</sup>

The immune response to the coronavirus is that after the infection of the cells in the body, the macrophages or DCs provide Corona antigens to T lymphocyte cells [Figure 1]. This process leads to the activation and detection of T cells and the production of cytokines associated with different subsets of T cells. In the people with weaker immune systems, the inflammatory response of cytokines increases dramatically and has a negative effect on NK and CD8 T cell's activation. An important function of the immune system against viruses is the interaction of lymphocytes and accurate identification of the invasive virus.<sup>[34-36]</sup>

### Women with cancer

More than half of the world's population is made up of women. Every day, a large number of women around the world are diagnosed with cancer. These women form the main body of the family and their exposure to cancer affects the family and society. In Iran, cancer is the third leading cause of death.<sup>[37]</sup> The most common cancers in women include breast, colon, lung, uterus, lymph nodes, ovaries, pancreas, blood, and so on. Among these diseases, breast cancer is the second leading cause of cancer-related death in the women worldwide, and about 7,000 new cases of breast cancer are reported in Iran each year.<sup>[38,39]</sup> This disease is the most common type of malignancy and the most important cause of cancer death in women all over the world.<sup>[40]</sup> More than 1.2 million people are diagnosed with breast cancer each year, and more than 500,000 die from the disease.<sup>[41]</sup> In Iran, every 10 to 15 women are at risk of cancer. In addition, skin, intestinal, and uterine cancers kill large numbers of women in Iran and around the world every year.<sup>[39,42]</sup> The need to identify and address the types of cancer in women is felt despite the high mortality rate.

### Prevention and treatment

Preventive health measures such as not being in crowded environments, washing hands, not being in close contact with sick people, using a home moisturizer, not touching the eyes, nose and mouth, and drinking plenty of fluids can prevent the spread of respiratory viruses such as COVID-19.<sup>[43]</sup> In Iran, the results of a review of guidelines for breast cancer during COVID-19 epidemiology have shown that physicians and cancer patients

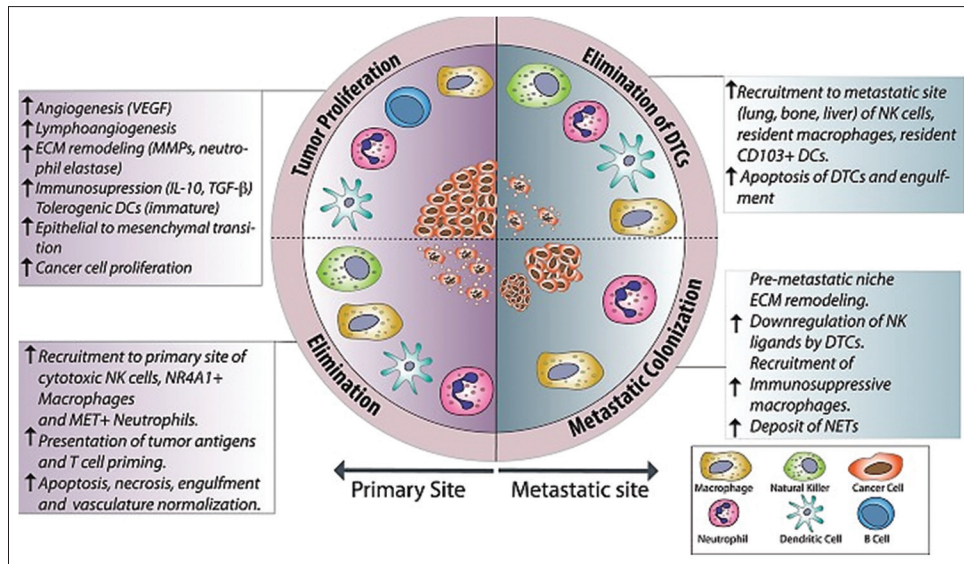
should choose the least contact and referral for treatment. Reforms are aimed at reducing the workload of medical centers and also providing the least interaction between the patients and medical centers.<sup>[44]</sup>

As mentioned, the immune system is greatly weakened in the people with cancer. This weakened immune function makes it easy for the people to become infected with the virus. Research has shown that viruses develop in the people with weaker immune systems more easily. Viruses are destroyed by the immune system in the first line of defense, but in the immunocompromised people (such as people with cancer), this line does not work well. The inflammatory response is more severe in the people with weaker immune systems, which in turn helps to increase the rate of inflammation. For example, the secretion of enzymes in the body is one of the most important factors in destroying the walls of bacteria and viruses. Increased immune function also assists improving pneumonia after a virus infection. Decreased cellular stress and better immune function are directly related to each other. Paying attention to the use of antioxidants and exercise is effective in increasing the immune system. Pneumonia is directly related to stress levels in infectious cases of influenza and secondary lung infections.<sup>[45-48]</sup> Research has shown that advanced stages of pneumonia are associated with increased cellular stress.<sup>[49,50]</sup> Studies in 2017 have indicated that exercise reduces oxidative stress in the people with cancer, and this has affected the better functioning of the immune system.<sup>[48]</sup>

In terms of treatment, several vaccines have been evaluated in the laboratory, but have not yet been fully approved for public use. Vaccines are made based on the S protein of these viruses, which are located on the surface structure of the virus. There is currently no known information about epitopes in the patients with Corona, and scientists are trying to identify different epitopes in the virus to make the vaccine effective.<sup>[51,52]</sup>

Clinical treatments for Coronavirus have been based on Codeine tablets and the anti-malarial drug Chloroquine which is only used to reduce the severity of Coronavirus. Corticosteroids are used in small doses during treatment, as they have been illustrated to increase the risk of prolonged virus replication, as seen in the patients with MERS. Drugs such as Ritonavir, Lopinavir, and the anti-malarial drug Chloroquine are currently being used in various parts of the world, but the full effect of these drugs in the treatment of the disease has not yet been proven. With the least side effects, the antiviral drug Favilavir has been indicated to have acceptable results in 70 patients who took the drug experimentally.<sup>[53-56]</sup>

Other adjunctive remedies are herbal remedies that are very effective in reducing inflammation and have a beneficial effect on the recovery of chronic lung disease. Some plant extracts have been utilized as adjunctive therapy. Herbal ingredients contain antioxidant and anti-inflammatory substances that help cure the disease.<sup>[57-59]</sup>



**Figure 1:** The role of innate immune cells in metastatic cancers. An overview of the prominent and anti-tumor role of innate immune cells in cancer, which indicates its specific functions and complications

## Discussion and Conclusion

We found a common ground between the findings of the various studies on cancer and Corona, which is to reduce the function of the immune system in the people with cancer and the effect of the immune system on specific immune cells. Specific immune cells such as lymphocytes, play an important role in reducing viral infection and cancer, and in contrast, the inflammatory response of the immune system and the increase in innate immunity increase the severity of the disease in these individuals. Antibodies are more secreted in the people with stronger immune systems. A study in France unearthed that the patients with cancer who had Corona were significantly lower in terms of SARS-COV2 antibodies at 15 days or later after COVID-19 and RT-PCR symptoms. Antibodies were often undetectable in the patients receiving anticancer therapy one month before the test, indicating a decrease in the immune system in the people with cancer. They emphasized that further studies are needed to confirm the immune response to the virus under the influence of recent cancer treatments.<sup>[60]</sup>

However, some cancers, such as skin cancer, which is known as a common cancer in women in some countries such as Iran, have decreased during the Corona era. A group of Dutch researchers have reported a significant reduction in the detection of skin cancer in the country since the onset of the COVID-19 epidemic. Significant reductions in cancer detection have been reported in all age groups, geographies, and almost all cancer types, with the greatest impact on skin cancers. They described the reasons for their findings from the perspective of the patient, the physician and the health care system. From the patients' point of view, it is said that the patients who attend the health care centers are worried about being infected with COVID-19. From a physician's point of view, in the case of not showing severe symptoms of cancer, due to attention to Coronavirus, the patients do not

undergo special examinations, and the medical centers have concentrated the most services on fighting the virus.<sup>[61]</sup>

Vaccines are currently being reviewed and there are no vaccines to prevent COVID-19 or any specific treatment. The best way to prevent the disease is to avoid exposure to the virus. Despite all the advances in treatment, it is important to pay attention to the performance of the physicians in the guidance and prevention of the cancer patients with Corona. In Iran, the physicians have been shown to be well-informed about preventive measures and behaviors at the time of Coronavirus outbreak.<sup>[62-65]</sup> According to the mentioned studies, cancer treatments such as chemotherapy can weaken the immune system and may increase the risk of COVID-19. As a result, it is important to insist reducing contact with the cancer patients.

In a general conclusion, the proposed solutions of this article are to increase the immune system of the cancer patients with the proposed solutions and reduce the patients' contact with the medical centers and crowded places. The proposed solutions can be presented to the patients with cancer in the form of a health protocol.

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## Conflicts of interest

There are no conflicts of interest.

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