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Ph.D. THESIS

"THE EFFECTS OF COVID-19 PANDEMIC ON ONCOLOGICAL PATIENTS, AND POTENTIAL FUTURE SOLUTIONS"

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T i m i ș o a r a
2022

CONTENTS

CHAPTER 1. THE IMPACT OF SARS-COV-2 PANDEMIC ON PATIENTS WITH MALIGNANT MELANOMA AT A ROMANIAN ACADEMIC CENTER: A FOUR-YEAR RETROSPECTIVE ANALYSIS

The COVID-19 pandemic's effect on the epidemiology of melanoma and other skin cancers may be evaluated using centralized databases, which also make it possible to make predictions about patient outcomes based on factors such as delayed diagnoses and visits. As a result, the objective of this study is to provide a collection of facts and statistics based on actual events involving individuals in Romania who were diagnosed with malignant melanoma during the COVID-19 pandemic. The primary objective is to examine the pre-pandemic era in comparison to the pandemic period, summarizing the clinical characteristics of patients, as well as a cancer diagnosis, progression, and treatment options. Analyzing the outcomes of patients who were treated at our center in order to identify risk factors for the advancement of illness is the secondary goal of this study.

Adult patients older than 18 years who came for treatment of skin cancer in an inpatient setting following a confirmed malignant melanoma diagnosis or in an outpatient setting for melanoma investigations and follow-up were included in the research between January 2018 and January 2022. Patients came for treatment of skin cancer in an inpatient setting following a confirmed malignant melanoma diagnosis or in an outpatient setting for melanoma investigations and follow-up. The purpose of this research was to examine how the pre-pandemic era compared to the pandemic period caused by COVID-19.

After the start of the SARS-CoV-2 pandemic in Romania in March 2020 and the subsequent implementation of lockdown precautions to prevent the spread of COVID-19, the number of patients with malignant melanoma diagnosis or suspicion addressing to specialized medical care has significantly decreased. This is due to the fact that the number of patients with malignant melanoma diagnosis or suspicion has decreased. This drop was a considerable departure from the pattern that had been seen in the preceding two years, even though there was no reason to anticipate a quick shift in epidemiological conditions (2018 and 2019). As a result, the number of new cases of malignant melanoma did not naturally decrease or remain equivalent to the year before the onset of the COVID-19 pandemic; however, during the pandemic timeframe, fewer of these new cases were effectively identified or observed in the outpatient setting, as shown in Figure 1.

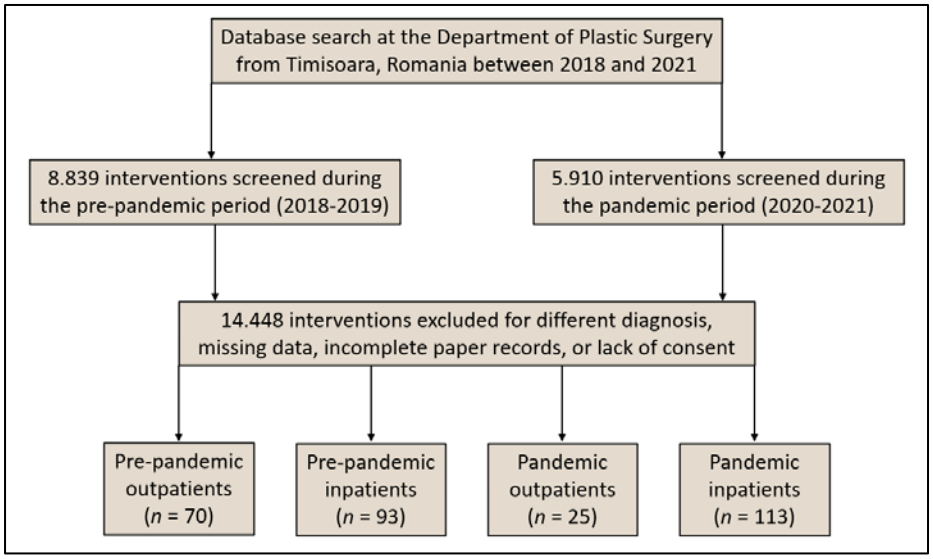

Figure 1. Flowchart displaying the inclusion process of patients with malignant melanoma during the 4-year study period.

Figure 2 presents a comprehensive profile of the patients who visited our outpatient and inpatient clinic for assessment and treatment of malignant melanoma before and during the SARS-CoV-2 epidemic. These patients were seeking care for malignant melanoma. During the first lockdown periods, which lasted from March to May 2020 and, accordingly, from October to December 2020, it was noted that a noticeably smaller number of patients with malignant melanoma arrived for specialist medical treatment. After the initial lockdown, there was a significant increase in the number of cases between June and September 2020. This rise in the number of cases is likely to be attributed to the patients who did not request medical care during the lockdown and decided to wait until there was a loosening of restrictions. The pandemic caused by COVID-19 entered its second year with a general trend toward normalization of the tendencies.

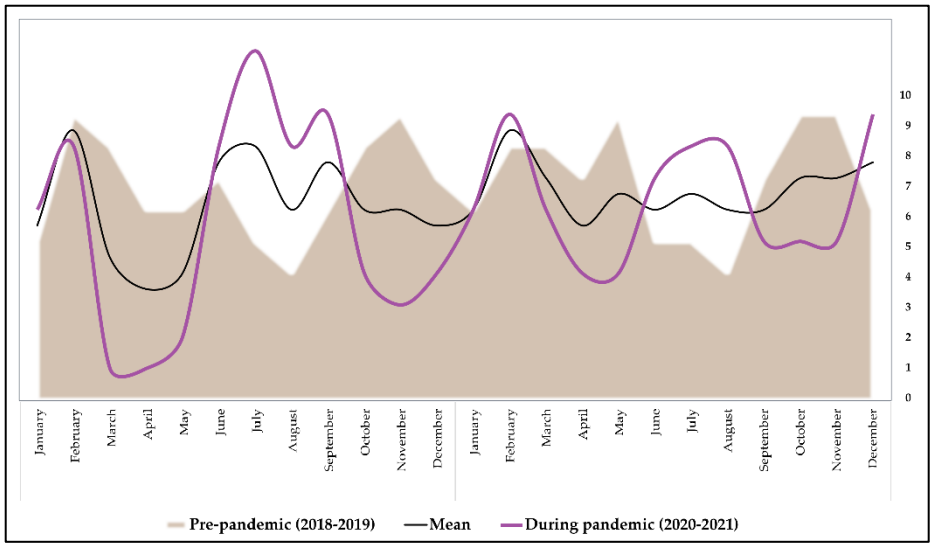

Figure 2. Evolution of malignant melanoma patient addressability before and during the COVID-19 pandemic. The X-axis represents a monthly overlay of melanoma cases during the years 2018–2019 and 2020–2021. Y-axis represents the number of patients recorded each month.

During the two years that the COVID-19 pandemic lasted, it was seen that the Breslow index of malignant melanoma cases was notably different in proportions of depth. This was one of the observations that were made. During the years 2018 and 2019, a total of 30.1 percent of patients were found to have a Breslow index that was between 1 and 2 mm. This number dropped to 20.3 percent during the years 2020 and 2021, respectively. Additionally, five patients (3.1 percent) presented with a Breslow that was higher than 4 mm, while 16 patients (11.6 percent) did not (p-value 0.001). In addition, the average Breslow depth was 1.1 millimeters before the pandemic, but it increased to 1.8 millimeters after the pandemic (p-value less than 0.001). During the pandemic, it was noticed that patients presented at later stages, which is shown by the AJCC TNM staging in Figure 3. Patients who were already in the third stage of the illness were the most common throughout both time periods of the research; however, there was a statistically significant difference during the pandemic, with the number of patients rising from 90 (55.2 percent) to 94 (68.1 percent) (p-value 0.001) Last but not least, tumor ulceration was seen in 17.2 percent of patients before the pandemic but in 24.6 percent of patients after the pandemic (p-value = 0.110).

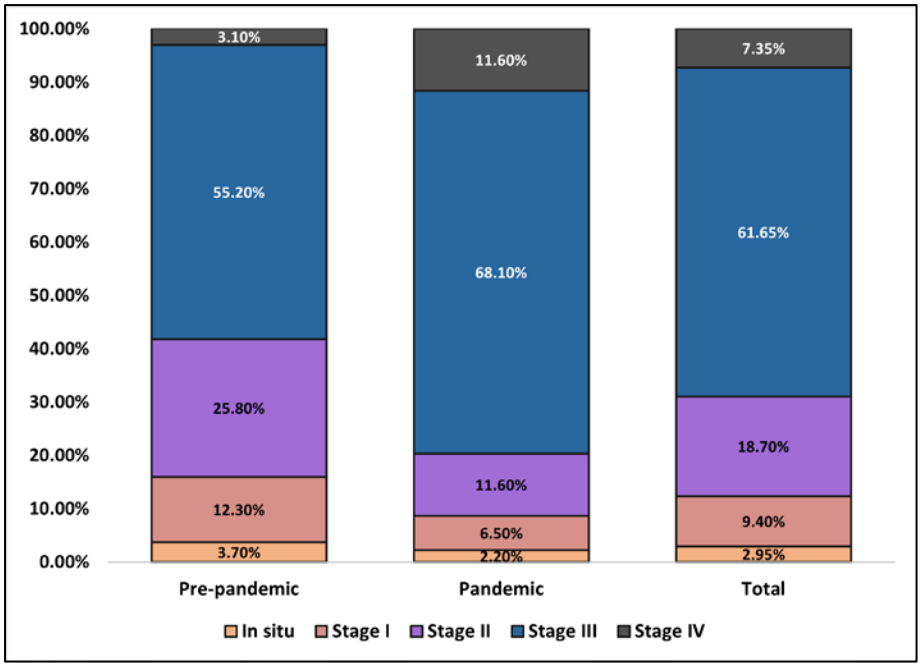

Figure 3. Comparison in AJCC malignant melanoma staging between patients seeking medical care before and during the COVID-19 pandemic.

It was discovered that extensive local excision was the most frequent technique conducted on around 90 percent of all patients, as shown in Table 3, which relates to the results and interventions that were carried out on the population that was the subject of the research. In spite of this, during the pandemic, there were 12 patients with unresectable tumors, which is a significantly higher number than the number of patients with unresectable tumors before the pandemic, which was only four patients (2.5 percent) (p-value = 0.038). There were statistically significant variations between the two study periods (29.9 percent sentinel node biopsies before the pandemic vs. 16.0 percent after the pandemic, p-value = 0.038). Lymph node assessment was conducted by sentinel node biopsy or dissection of the lymph node group. The reasons for palliation referral were found to be statistically significant, as a higher percentage of patients were found to have a poor prognosis during the pandemic (43.6% vs. 36.8%, p-value = 0.027). Other findings that were found to be statistically significant included the reasons for palliation referral. In addition, the length of time spent in the hospital was substantially longer during the epidemic (7.0 days vs. 5.9 days before the pandemic, p-value = 0.011) than it had been before the outbreak.

Before the pandemic, primary care was the referral source for 103 (63.2 percent) of the patients, but after the pandemic, secondary care was the referral source for 70 (50.7 percent) of the patients (p-value = 0.025). During the COVID-19 pandemic, it was also observed that a significantly higher proportion of patients waited longer before seeking their first medical opinion, increasing from a median of 6 weeks to a median of 9 weeks (p-value 0.001), as well as postponing treatments more frequently (18.8 percent vs. 8.0 percent, p-value = 0.005) and missing more appointments (20.3 percent vs. 11.7 percent, p-value = 0.039). Last but not least, the rate of illness progression at three months was statistically substantially greater during the COVID-19 pandemic, with 47 (34.1 percent) patients as opposed to 38 (23.3 percent) patients before the pandemic (p-value = 0.039).

The advanced AJCC stage was the most significant risk factor, with patients having a 3.48 times greater chance of disease progression (p-value 0.001), followed by a high Breslow index (HR = 3.19, p-value 0.001) as the second most significant risk factor. Other significant risk factors for the progression of the disease included delayed treatment (hazard ratio = 2.46), missed appointments (hazard ratio = 2.31), the length of time that passed after the onset of symptoms before the patient sought medical advice (hazard ratio = 2.18), anemia at

presentation (hazard ratio = 1.60), and, as a final factor, the patient's age (hazard ratio = 1.57, p-value = 0.030).

Table 4. Risk factors for melanoma progression after the initial hospital visit.

Risk Factors	HR	CI	p-value
AJCC stage	3.48	2.13–4.30	<0.001
Breslow index	3.19	2.36–4.08	<0.001
Postponed treatment	2.46	1.72–3.41	<0.001
Missed appointments	2.31	1.80–3.26	<0.001
Time from first signs until seeking medical opinion	2.18	1.13–3.15	0.001
Anemia at presentation	1.60	1.09–2.49	0.018
Age	1.57	1.04–1.94	0.030

* AJCC American Joint Committee on Cancer; HR Hazard Ratio; CI Confidence Interval.

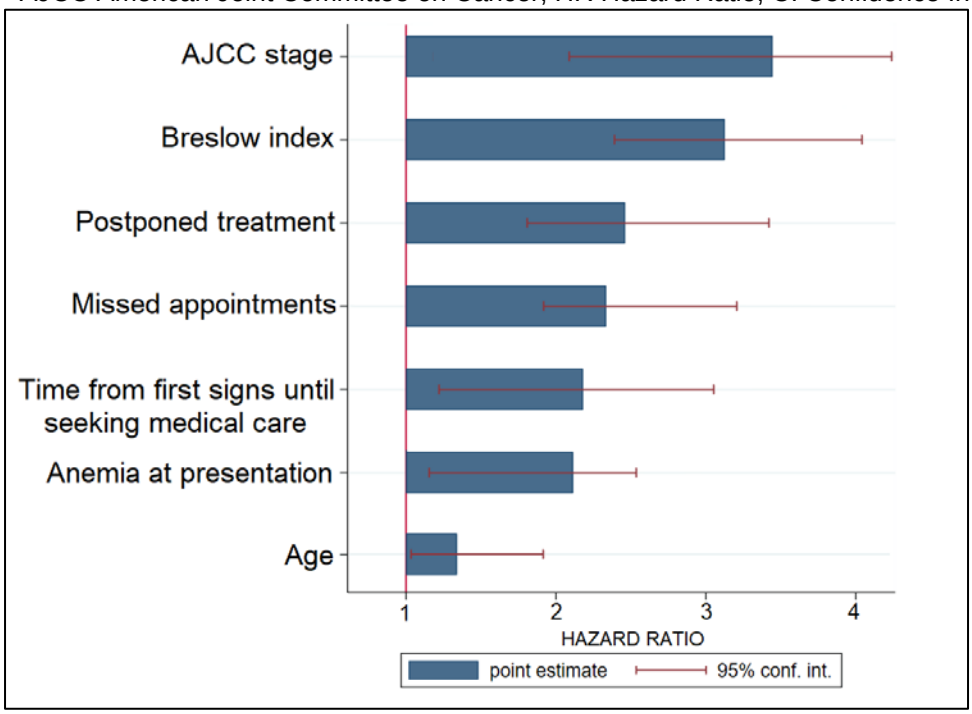

Figure 4. Risk factor analysis for disease progression in patients with malignant melanoma.

CONCLUSIONS

- It is probable that many patients remained unnoticed during COVID-19, despite the fact that malignant melanoma is not one of the most common kinds of cancer.
- Failure to do so will have long-lasting ramifications if these instances are not discovered and managed effectively.
- Although certain consultations may be delayed without major consequences, others, notably those pertaining to malignancies, must not be delayed in terms of obtaining an accurate diagnosis and initiating treatment as soon as possible.
- As soon as the restrictions imposed by the epidemic have been lifted, there should be a comprehensive screening campaign for skin cancer, in addition to one for the other prominent cancers that may be identified by screening techniques.

CHAPTER 2. THE IMPACT OF SARS-COV-2 PANDEMIC ON PATIENTS UNDERGOING RADIATION THERAPY FOR ADVANCED CERVICAL CANCER AT A ROMANIAN ACADEMIC CENTER: A FOUR-YEAR RETROSPECTIVE ANALYSIS

As the COVID-19 pandemic continued, hospitals made adjustments to their organizational procedures, including lowering the number of staff members and repurposing inpatient beds to accommodate patients better. As a consequence of this, the staffing levels and bed capacities of all non-COVID departments were reduced, which affected the provision of care for cancer patients undergoing treatment with chemotherapy, brachytherapy, or external radiation. The strategy for the administration of cancer care should be reformed to enhance patient treatment and follow-up in line with the changing recommendations for radiation therapy for gynecological malignancies during the COVID-19 pandemic. However, because of the pandemic's protracted limits requiring direct human contact, the implementation of COVID-19 rules provides a number of obstacles. This is the case even though a large-scale vaccination effort against SARS-CoV-2 is now underway. In light of this, the objective of this study is to compile a set of facts and statistics based on actual events involving women in Romania who were diagnosed with cervical cancer during the COVID-19 epidemic. The instances that needed radiation or combination with chemotherapy are the primary focus of this study. These cases are described in detail, along with the cancer diagnosis, its course, and the treatment options that are now accessible. Analyzing the outcomes of patients who were treated at our center in order to identify risk factors for the advancement of illness following radiation treatment is the secondary goal of this study.

Participants in the study were adult women over the age of 18 who presented for cancer treatment after having a confirmed cervical cancer diagnosis based on cervical screening cytology, colposcopy, and other invasive methods with biopsy, using conventional methods. The study lasted from January 2018 until January 2022. Participants were adult women over the age of 18. The research did not adhere to a particular sampling method and included all consecutive patients who were scheduled for radiation therapy or combined treatment for cervical cancer. Additionally, the research included patients who were scheduled for regular follow-up at the gynecologic oncology units of the two hospitals if they met the inclusion criteria. Patients whose test results and diagnoses could not be independently validated, as well as those who lacked the essential information or consented to take part in the current inquiry, were not considered for inclusion. Another criteria for participant exclusion was whether or not they could be located for further follow-up three months after completing cancer treatment. A total of 104 individuals were chosen from the pandemic era and case-matched by age with 104 patients who were diagnosed during the time before the epidemic began.

A total of 208 patients were chosen for the study over the course of 48 months by matching inclusion criteria and case-matching by age. This resulted in the creation of two groups: one group of 104 women who were diagnosed with cervical cancer in the 24 months prior to the start of the COVID-19 pandemic and another group of 104 patients who were diagnosed during the first 24 months of the pandemic. There were no statistically significant changes in the proportions of body mass index, smoking history, number of parties, location of origin, employment, level of income, or civil status. The average patient was 54 years old. More than thirty percent of the overall cohort of patients are smokers, with the percentage of women who have gone through menopause being almost fifty percent of those who have gone through post-menopause.

There was not a significant difference identified in the number of comorbidities discovered in the groups evaluated before and during the pandemic, with hypertension being the condition that was found in most individuals (80, or 38.4 percent of the total cohort). The histology of cervical cancer was determined to be squamous cell carcinoma in 168 (80.7

percent) of the cases, and there were no significant differences in the groups that were studied (p-value = 0.724). In addition, there was a statistically significant difference in the size of the tumors that were found before and during the pandemic. Fifty-seven of the tumors that were found before the pandemic were smaller than three centimeters in size, whereas sixty-four of the tumors that were found in the cohort during the pandemic were larger than three centimeters (p-value = 0.037).

Tumoral invasion of the vagina was significantly more extended in the patients who presented for radiation therapy during the COVID-19 pandemic, with 24.0 percent of cases extending to the lower third of the vagina, compared with 12.5 percent of cases before the pandemic (p-value = 0.046). Parametrial invasion and tumor grading did not differ between the study groups. More advanced stages of cancer were observed to be presenting for treatment during the pandemic (14.4 percent vs. 4.8 percent IVA-IVB; p-value = 0.032), as well as more cases of relapse (27.9 percent vs. 16.3 percent; p-value = 0.044), which added to the number of patients treated for palliation (63.5 percent vs. 48.1 percent; p-value = 0.034). The tumor staging was (Figure 5).

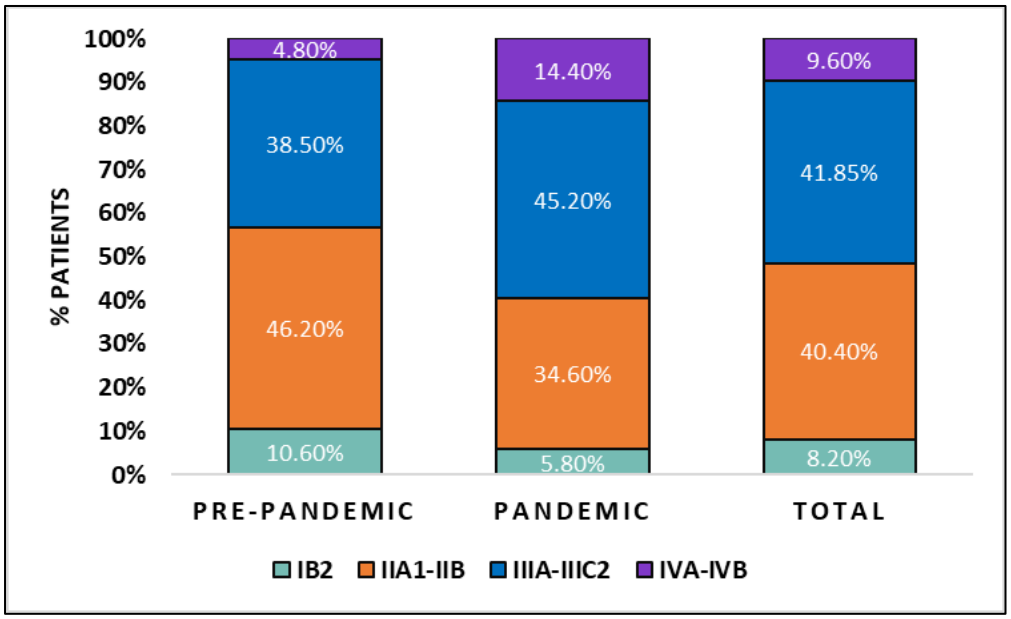

Figure 5. Graphical comparison of patients with radiotherapy-necessitating cervical cancer (IB2-IVB) before and during the COVID-19 pandemic. Cervical cancer staging is reported by the International Federation of Gynecology and Obstetrics (FIGO) staging system.

It was found that 22.1 percent of patients during the COVID-19 pandemic had disease progression after completing the radiation therapy regimen, which is significantly higher than the 11.5 percent of patients who had disease progression before the pandemic (p-value = 0.045). This was one of the significant findings. Before the pandemic, the majority of referrals came from primary care (64.4%), but after the pandemic, the majority of referrals came from secondary care (51%; p-value = 0.025). During the pandemic, there was a 13.5 percent increase in the number of people who had been referred to medical professionals but did not end up receiving treatment (p-value = 0.021). There were also significant changes in treatment outcomes, where 25.0 percent of patients had changes in their treatment plans during the pandemic, compared with 13.5 percent before the pandemic (p-value = 0.034). This was a significant increase from the percentage of patients who had treatment plans altered before the pandemic. During the pandemic, a total of 22 patients, or 21.2%, had delayed treatment, and 23.1% skipped visits due to a variety of causes; this compares to 9.6% and 12.5%, respectively, before the pandemic (p-values of 0.021 and 0.015, respectively).

Patients with an advanced FIGO stage of cervical cancer had a 3.39 higher likelihood of disease progression after radiotherapy (CI [2.06–4.21], p-value 0.001), followed by tumor

size with an HR of 3.12 (CI [2.24–4.00], p-value 0.001) Patients with an advanced FIGO stage of cervical cancer had a 3.39 higher likelihood of disease progression after radiotherapy (CI [2.06–4.21], p-value 0.001). Postponing treatment and missing appointments, both of which are associated with the COVID-19 pandemic, were shown to be significant risk factors for the advancement of cancer (hazard ratios of 2.51 and 2.24, respectively). Other characteristics that had a major role were the invasion of the vagina, the patient's age, and their response to therapy after three months.

Table 8. Risk factors for disease progression after finishing the radiation therapy regimen.

Risk Factors	HR	CI	p-value
FIGO stage	3.39	2.06–4.21	<0.001
Tumor size	3.12	2.24–4.00	<0.001
Invasion of vagina	2.58	1.82–3.73	<0.001
Postponed treatment	2.51	1.90–3.46	0.001
Missed appointments	2.24	1.18–3.53	0.001
Response to treatment at 3 months	1.66	1.09–2.52	0.014
Age	1.35	1.01–1.84	0.033

* FIGO – International Federation of Gynecology and Obstetrics; HR – Hazard Ratio; CI – Confidence Interval.

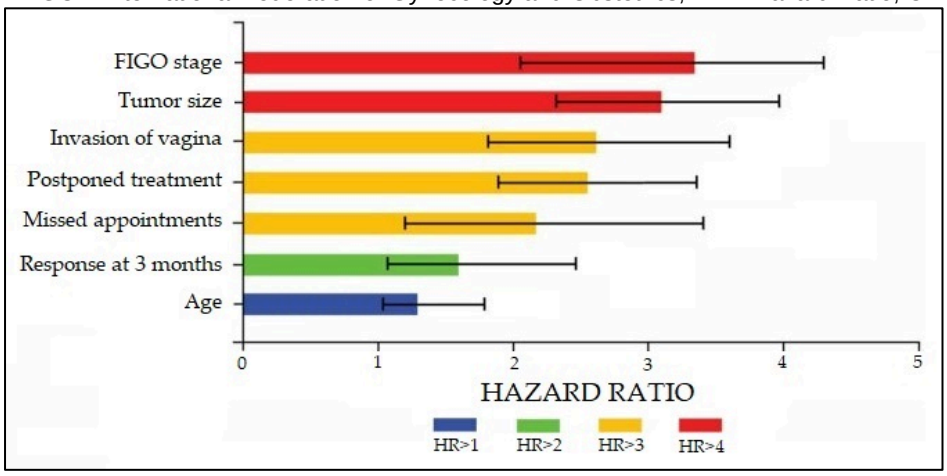

Figure 6. Graphical representation of risk factors for disease progression in patients with cervical cancer undergoing radiation therapy. The likelihood of disease progression is reported as hazard ratio (HR) and confidence interval.

CHAPTER 3. THE "INVISIBLE ENEMY" SARS-COV-2: VIRAL SPREAD AND DRUG TREATMENT

Extensive research is being carried out right now with the goal of locating pharmaceuticals that may be useful in the treatment of COVID-19 illness as well as infections caused by other coronaviruses. Following on from the previous section, this one will offer a basic summary of therapeutic drugs that have had a favorable impact in the treatment of viral infection with COVID-19.

Remdesivir is the only substance that has been given approval by the Food and Drug Administration (FDA) for use in the treatment of coronavirus disease. To this day, there is no definitive treatment for COVID-19, nor are there any drugs that have been specifically approved for the treatment of COVID-19. Care for individuals infected with COVID-19 involves a number of stages, including early detection, isolating the patient, using a variety of preventative measures to stop the spread of the illness, and providing supportive therapy.

At various stages of the COVID-19 disease, research has been conducted on a variety of drug classes. The main drug classes that have been found to be beneficial include antiviral drugs (remdesivir, ribavirin), antibodies (convalescent plasma, immunoglobulins), and

immunomodulatory drugs (tocilizumab, siltuximab), anti-inflammatory drugs (dexamethasone), and antimalarial drugs (chloroquine/hydroxychloroquine).

ANTIVIRAL MEDICATION

Patients who have COVID-19 are given antiviral medicine that was first licensed for the treatment of other illnesses, such as the flu, Ebola, or infections caused by the human immunodeficiency virus (HIV). Therefore, the objective of the medical researchers has been to conduct research on the compounds that are already available and are known to be effective in the treatment of viral infections in order to speed up the process of developing a treatment that is effective in the fight against COVID-19 disease.

It was the first medicine to be licensed by the FDA for the treatment of viral infection in adults and children (over the age of 12 and weighing at least 14 kg) who need hospitalization [209]. Remdesivir was granted approval by the FDA in October 2020 for the treatment of COVID-19 infection. It is an analog of adenosine, a prodrug, which has a broad spectrum of activity against several families of viruses, such as Pneumoviridae, Filoviridae, and Paramyxoviridae. Remdesivir is an antiviral drug that disrupts viral replication by inhibiting the ribonucleic acid (RNA) polymerase.

The most common adverse reactions to remdesivir are nausea, low blood pressure, elevated liver enzymes (aminotransferase levels), and respiratory failure. However, remdesivir is an effective therapeutic drug that is generally well tolerated. After giving remdesivir to patients with severe liver illness and renal failure, researchers came to the conclusion that the drug should not be utilized in these patient populations. Remdesivir is an antiviral medication that belongs to the family of nucleotide analogs. It was designed for the treatment of diseases brought on by RNA viruses, including Ebola, Nipah, and MERS. At this time, it is undergoing intensive research to determine whether or not it may be used in the treatment of COVID-19 infection.

ANTIMALARIAL DRUGS

Chloroquine is a medicine that is categorized as an antimalarial and has the structural foundation of 4-aminoquinoline. The activity of heme polymerase, which leads to the accumulation of harmful heme in Plasmodium species [235], is stopped by this medication, which inhibits heme polymerase. Chloroquine is widely used in the treatment of malaria, but it also has a therapeutic impact in the treatment of HIV infection and in the treatment of rheumatoid arthritis. This is due to the fact that chloroquine has both anti-inflammatory and immunomodulatory action. Headaches, sleepiness, visual abnormalities, nausea, vomiting, and hypokalemia are the most common side effects that patients experience.

In addition to its application in the treatment of malaria and rheumatic diseases, hydroxychloroquine, is a metabolite of chloroquine that is associated with fewer adverse effects. The substance accumulates in the lysosomes of the malaria parasite as well as in human organelles, raising the pH of those lysosomes. This raises the pH of the lysosomes, which inhibits the processing of antigens, prevents the chains of the major histocompatibility complex class II from dimerizing, inhibits antigen presentation by the cell, and reduces the inflammatory response.

Because of the recognized ability of the two compounds to raise the pH of the endosome, their antiviral activity is supported by the fact that it inhibits viral replication. Studies have shown that these therapeutic agents inhibit the glycosylation of the angiotensin-converting enzyme 2, which is located on the cell membranes of the lungs, kidneys, and heart. This enzyme is involved in the cellular penetration mechanism of the new virus (SARS-CoV-2). In addition, these studies have shown that the glycosylation of this enzyme is inhibited by these therapeutic agents.

Hydroxychloroquine is a human Toll-like receptor (TLR) blocker, and it has the ability to inhibit endosomal TLR3, -7, -8, and -9 signaling. As a result, it can control inflammation in COVID-19 disease, and it can also ameliorate the negative effects of SARS-CoV-2 infection. This is an important point to keep in mind. As a result, chloroquine and hydroxychloroquine

have been the subject of a great deal of focus in relation to the COVID-19 sickness. Numerous studies have emphasized the influence that these two drugs have on viral infections caused by SARS-CoV-2.

CORTICOSTEROIDS

Corticosteroids are therapeutic agents that belong to the family of pharmaceuticals known as anti-inflammatory drugs. They are medications that are employed in the treatment of a wide range of pathologies, including autoimmune illnesses, cancer, and respiratory and allergy diseases. In addition to their many beneficial benefits, corticosteroids may have a number of undesirable side effects, including hyperglycemia, hypertension, damage to the bones, an increased risk of infections, and the development of obesity.

In viral infections, such as SARS-CoV-2 infection, the immunomodulatory activity of corticosteroids is helpful and reduces the inflammatory response. This is true even though corticosteroids have the potential to cause side effects. However, owing to the fact that these medications might impact the immune system, leading to an increase in the viral load, particular attention should be given to the number of corticosteroids as well as the duration during which they are administered. Patients who are experiencing a more severe version of the sickness and who are contending with a cytokine storm are the ones who are advised to take these medicines.

Patients diagnosed with COVID-19 were the first to get corticosteroids as therapy shortly after the pandemic's first breakout. It was found in Wuhan, following a retrospective cohort study of 201 confirmed COVID-19 patients with acute respiratory distress syndrome, that patients who were treated with methylprednisolone had a lower mortality rate in comparison to patients who were not given corticosteroids. This was discovered after the study found that patients who were treated with methylprednisolone had acute respiratory distress syndrome.

IMMUNOMODULATORY DRUGS

An interleukin-6 receptor antagonist, tocilizumab is a monoclonal antibody that is also known as tocilicept. Rheumatoid arthritis and cytokine release syndrome are two examples of inflammatory disorders that may be treated with this substance. There is a correlation between the levels of interleukin-6 and the severity of COVID-19; thus, the exploration of IL-6 inhibitors is highly warranted. The most typical adverse responses to this chemical are elevated levels of cholesterol, elevated levels of alanine aminotransferase and aspartate aminotransferase, and allergic reactions.

Tocilizumab was shown to regulate temperature, decrease oxygen demand, and enhance CT imaging in multicenter research that included 21 patients with severe COVID-19. This investigation found that tocilizumab improved CT imaging. Siltuximab, an additional representative of the IL-6 inhibitors, has been explored for its effectiveness in patients with COVID-19. Siltuximab was first licensed for the treatment of Castleman's disease, which is a rare lymphoproliferative illness. It was demonstrated that administering 900 milligrams of siltuximab to patients with COVID-19 and acute respiratory distress syndrome lowers the serum level of C-reactive protein and improves clinical manifestations without causing a worsening of the patients' overall condition.

ANTIBODIES

Convalescent plasma is obtained from patients who have been cured of COVID-19 disease. This plasma contains antibodies that have been neutralized against the virus, and it is then administered to patients who are infected with SARS-CoV-2 in order to assist the immune system and increase the patient's immune response to the virus.

In addition, this treatment is effective in preventing the infection, facilitating the elimination of infected cells, and enhancing the general health of seriously afflicted individuals. This sort of therapy has shown promising results in the treatment of a variety of viral illnesses,

including Ebola and H5N1 influenza. The notion of convalescent plasma treatment is not a new one.

The effect of convalescent plasma in this pathology was followed after a study was performed on 25 patients who were diagnosed with COVID-19. As a result, for 19 of the patients, a clinical improvement of at least 1 point was observed on the ordinal route of the WHO, which is used with the help of which the severity of the disease is calculated. Convalescent plasma was given to 10 patients with COVID-19 in another trial, and the results showed that after the plasma was given, it was able to sustain or even raise the antibody titers that the patients had received. In addition, improvements were seen in clinical symptoms, leading to a lower viral load. As a result of this investigation, researchers came to the conclusion that patients are able to handle convalescent plasma treatment rather well, with no adverse effects being seen.

CONCLUSIONS OF THE STUDY

- The pandemic caused by SARS-CoV-2 has evolved into a top concern for medical professionals throughout the world. The virus has been able to speed its growth across society as a result of its ability to transmit from one person to another, which has made it more difficult to control.
- In spite of the fact that COVID-19 just seems to be a straightforward viral illness, it is nevertheless capable of causing death. Since the beginning of the pandemic, experts from all around the globe have begun cooperating with one another in an effort to safeguard the people against this "invisible foe."
- Significant work has been done in recent years to investigate the pathophysiology of COVID-19, which has led to significant scientific progress in the development of anti-COVID-19 treatments. As a result of these factors, the World Health Organization advises the use of supportive therapies in addition to the cautious management of problems.
- Although the precise pathophysiology of the COVID-19 illness is still unknown, research has shown that it often involves an abnormally heightened inflammatory response in response to viral infection. Furthermore, in addition to the host's reaction, differences in the virus strain may contribute to the severity of the sickness as well as the disease's ability to spread.
- There is currently a lack of information on the infectivity of the most common SARS-CoV-2 viral strains, as well as antibody resistance, due to high rate of viral mutations. In order to comprehend the process and put a halt to faster transmission, there has to be an increase in the number of research done on mutations in the Omicron strain.
- There are now additional medications being examined from a variety of therapeutic classes to see whether or not they are useful in treating COVID-19 illness; however, the clear proof is likely to be required before they can be used therapeutically.