

Review Article

Chemotherapy in COVID-19 pandemic: to give or not to give?

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Received: 16 April 2020

Accepted: 08 May 2020

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ABSTRACT

COVID-19 is a new pathogen for humans, not much is known how it affects cancer patients, but definitely there is high risk for cancer patients contracting this disease. So to find a solution to this very challenging situation the oncologists need to formulate certain guiding principles for cancer treatment in this pandemic era. Authors have divided this cancer patients into four categories depending upon the urgency of giving chemotherapy. The lowest priority being Priority A where delaying chemotherapy till this pandemic gets over will not harm the patients much and the highest priority being given to Priority D where authors do not want even a delay of days/ week. It is Priority B and C where the decision needs to be made by the clinicians. However, in case authors decide to give chemotherapy in present setting there are certain changes that need to be made both on patient as well as the hospital end. Like higher degree of awareness among patients, rational usage of resources of the hospital etc. It is indeed a very difficult time for cancer patients who are trying to cope up with malignancy and for most of them; the coronavirus is an extra concern and worry. Till the time authors learn how best to treat and care to these patients during this pandemic era do what you can do to keep you and your family safe and healthy.

Keywords: COVID 19, Cancer, Chemotherapy, SARS-cov-2, Pandemic

INTRODUCTION

The novel Coronavirus is a new pathogen identified in patients of pneumonia in a city of Wuhan, in Hubei province of China. The term COVID-19 is an abbreviation for Coronavirus Disease 2019 given by WHO in February 2020.¹ It is also referred to as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2).

Since this is a new pathogen for humans, our body does not have any immunity against this disease, and hence it spreads rapidly, infecting almost everyone who comes in its contact. What started as a seasonal flu in China has now spread to nearly the entire world, killing over one lakh individuals. This disease has now been declared as a pandemic by WHO.²

Since it is a very new disease, not much is known how it affects cancer patients, but one thing which we all know is that cancer patients come under the groups of patients who are at high risk for contracting this disease. All the patients who are on either chemotherapy, immunotherapy, radiation therapy, targeted therapy and even those who have earlier been treated for cancer are much more vulnerable to contracting the infection by COVID 19.

This is indeed a very challenging time for both cancer patients and their treating oncologists. It raises a few fundamental questions related to patients as well as health care providers.

First, should cancer patients leave their homes to visit the cancer clinic and thereby possibly expose themselves to

infection? Second, should we be giving cancer treatments in prevailing situations and predisposing this patients to the more harmful severe effects of COVID-19? Studies published by Liang et al, clearly showed that patients with prior history of cancer had a higher incidence of severe infections defined by patients requiring ICU admission, mechanical ventilation or death among Chinese patients.³

The third important question is, should we be exposing our healthcare workers to this infection as this cancer patients are more prone to be infected and thus transmitting this infection to this health care workers. 9% of cases detected in Italy were health care workers, and there have many doctors and nurses who have died fighting this Coronavirus pandemic.

These issues are further worsened by the fact that many of these infected individuals may in initial stage be asymptomatic. Another ethical issue to be considered is that in the present scenario of limited resources, are we willing to divert this limited resources to manage a terminal stage cancer patient on palliative care versus a young COVID-19 infected patient?

And believe me, the world requires much more resources to fight this pandemic, than what it presently has.

Nobody knows the answer to these questions as never before has such a pandemic with so many complications ever occurred. This article is an attempt to answer those question based on published data available and shared experiences of oncologists in India.

DISCUSSION

There has never been a time when the urgency of knowledge for any particular disease been more than what it is at present. In the absence of any clear cut understanding of the disease, its morbidity, and its response one can just make an intelligent guess to how things would evolve. With this little understanding and the recent guidelines. By the major cancer society's authors have tried to answer the two most pertinent questions i.e. whom to give chemotherapy in present setting and in case authors decide on giving chemotherapy what needs to be done by patient and the hospital for safe out comes

So should giving chemotherapy be stopped during COVID-19 pandemic?

It is true nobody knows the answer to this question. It is truly a very challenging time for both the patient as well as their oncophycians. The anxiety of progression of disease after withholding chemotherapy in cancer patients versus the fear of getting COVID 19 infection in these vulnerable group of patients has led to a lot of confusion. There are institutions across the world which have stopped administering chemotherapy all together, and there are others which are continuing with chemotherapy. Published data reveals that cancer patients have 3.5 fold times more

chances of having a severe infection compared to other general population. On the other side, there is enough data to support that if authors delay chemotherapy in specific settings, there is a definitive inferior outcome. Authors already know that there is an increased risk of death of about 16% in case authors delay radiotherapy for head and neck cancer patients.⁴ Similarly, delaying adjuvant chemotherapy for breast cancer has been associated with greater mortality (RR 1.08, 95% CI 1.01-1.15 per 4 weeks) and also in colon cancer (HR 1.14, 95% CI 1.10-1.17 per 4 weeks).⁵

So in this present condition, authors will have to formulate some working model to weigh this pros and cons for giving or not giving chemotherapy to a particular patient. There has to be a precautionary approach. Precautionary approach as defined by UNESCO "when human activities may lead to morally unacceptable harm that is scientifically plausible but uncertain, actions shall be taken to avoid or diminish that harm".⁶

An approach which will help this patients and their treating team formulate some guiding principles on which they can work. The final decision has to be shared decision between the patient and the doctor considering the various factors like an indication of treatment, risk of continued treatment, earlier response to therapy and the outcome of delayed therapy.⁷

So to have a more pragmatic solution to the present problem, authors have divided this cancer patients into four categories depending upon the urgency of giving chemotherapy (Table 1). The lowest priority being Priority A where delaying chemotherapy till this pandemic gets over will not harm the patients much and the highest priority is given to Priority D where authors do not want even a delay of days/ week.

Oncophycians all over the world agree that they would not like to withhold chemotherapy for patients with aggressive lymphoma and leukaemia. In contrast, the ones in Priority A, which are of palliative intent, can be withheld. It is Priority B and C where the decision needs to be made by the clinicians.

In the patients whom authors need to chemotherapy, prior testing for COVID-19 by RT PCR should be done. This will help us in detecting any asymptomatic patient and would help us in deciding whether authors need to continue with chemotherapy or not.

Though there is definitely a chance of false negativity in early setting, it is still would help us in deciding for therapy. For positive patients, they need to be first treated for COVID infection. Chemotherapy to be started only when they are found to be negative.

It is definitely not a very exhaustive list but an effort to categorise this patients into subheadings and helping the clinicians to take a final decision. However, one must

realise that the final decision would still be based on various other important factors like:

- Depending on your hospital/community resources
 - Preparedness by your hospital to tackle any adverse events
- Place on graph for COVID Pandemic where your particular community is located
- Resources availability i.e components like blood/platelets as most of this patients could require these supportive measures.
- Patient related
 - Compliance of patients
 - Duration of delay in chemotherapy
 - Response to early therapy
 - Age
 - Comorbidities etc.
 - Level of anxiety

This present scenario is very fluid, and there has to be an ongoing prioritisation based on the data produced all over

the world to follow the principle precept of bioethics of “*Primum non nocere*” first do no harm.

The above-mentioned prioritization can be done to address the issues of chemotherapy.

However, there are multiple other reasons for which patients come to hospitals like OPD follow-ups, diagnostic procedures, surgery, etc.

These also need to be divided under low, medium and high priorities. Many of the cancer patients report to the hospital for flushing of chemoport, frequency of these can be increased to once every 12 weeks.

To have a detail prioritisation for each and individual cancers is beyond the scope of this article. NCCN, ESMO, ASCO have all come up with detail prioritization of individual cancers about their OPD visits, diagnostic procedures, chemotherapy, surgery, and follow up appointments. Readers are requested to visit those sites for further details.⁸

Table 1: Cancer divided on the basis of urgency of giving chemotherapy priority A, B, C, D. Lowest priority being given to priority A and Max priority to priority D.

Priority A: palliative therapy with no survival or symptomatic advantage	Priority B: palliative therapy with substantial/modest survival benefit or symptomatic relief	Priority C: Neoadjuvant / adjuvant with substantial/modest benefit/	Priority D: Imminent risk of mortality
Second/ third line palliative chemotherapy for solid tumours	Immunotherapy for melanoma	Adjuvant for stage III colon cancer	Acute leukaemias
Bone metastasis manageable with medications	Systemic therapy for metastatic Breast cancer	Chemotherapy for breast cancer	Aggressive lymphomas
Prostate cancer under surveillance	Metastatic colorectal cancer	NACT / adjuvant for bladder cancer	Definitive CCRT for head and neck and anal cancer
	Palliative therapy for Upper GI cancers	NSCLC both chemotherapy and immunotherapy <6 month of treatment	
	Radiotherapy for pain palliation	Germ cell tumor	
	Metastatic / adjuvant carcinoma Prostate	New Brain Metastasis	
		NACT/ Adjuvant For carcinoma ovary	
	Metastatic carcinoma Pancreas	NACT For carcinoma Pancreas May be given for 12 cycles	
		High Grade Gliomas/ Recurrent gliomas/ Anaplastic astrocytoma/	

What needs to be done?

As authors have seen even in the COVID Pandemic environment, there is a huge section of cancer patients who are meriting chemotherapy. So, authors do have to find a

way out to give chemotherapiest these patients without harming them. So, let us look at some of the necessary changes that authors need to make in our day to day interaction with cancer patients.

Cancer patients should be made aware of the potential dangers of taking chemotherapy in the present scenario by giving them handouts/web-based communications. They should follow the following guidelines very strictly

- Washing of hands often with soap and water for at least 20 seconds.
- Use hand sanitizer with 60% or more alcohol.
- Avoid touching your eyes, nose, and mouth without washing your hands first.
- Clean and disinfect surfaces often.
- Avoid handshakes, hugging, and standing or sitting close to people who are coughing or sneezing.
- Be as healthy as you can. Get plenty of sleep, eat healthy, exercise, and manage your stress.
- Call your doctor right away if any of these happen to you:
 - Fever higher than 100.3 degrees F.
 - Short of breath.
 - Develop a cough, runny nose, or congestion.

Similarly, the hospital should come up with certain policies like:

- Rescheduling follow up visits and elective surgeries.
- Utilising more of tele medicine/video conferencing for consultation.
- Reinforcing a strict “stay at home when ill” policy
- Deferring second opinion consultations
- Reducing palliative chemotherapies
- Limited no persons to enter patients’ rooms
- Considering lower thresholds for component support. There are guidelines to administer prophylactic myeloid growth factors in patients with a lower level of expected risk for febrile neutropenia with treatment (eg, >10%). The normal cut off for prophylactic administration of growth factors is that of 20%.⁸
 - Restricting OPD follow-ups
 - Restricting visitors
 - Reallocation of hospital resources.⁹
 - In COVID 19 positive patients to discuss proactive palliative and end of life conversations with cancer patients.¹⁰

CONCLUSION

It is indeed a tough time for cancer patients who are trying to cope up with malignancy and for most of them; the coronavirus is an extra concern and worry. Since for all of us such a pandemic has occurred for the first time in the lifetime with no previous guidelines or experience; it’s indeed a night mare.

This article has been written on the basis of limited knowledge available to help physicians and cancer patients to tide over this crisis. However, one needs to understand that it is an evolving field, and many of the points presented here might need reconsideration.

The highly recommended telemedicine and its legal and regularity landscape have to be modified accordingly to evolve better strategies by consensus towards the management of cancer patients in the existing scenario through relevant webinars and web conferences.

Till the time we learn how best treat and care to this patient during this pandemic era do what you can do to keep you and your family stay safe and healthy.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Pathak A, Ranjan S, Rathore A, Kapoor R, Gupta A. Chemotherapy in COVID-19 pandemic: to give or not to give?. *Int J Adv Med* 2020;7:1035-9.