

ACUTE MYELOID LEUKEMIA AND COVID-19

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COVID-19 pandemic has covered all parts of globe with alarming speed and has resulted not only in excessive mortality but has also led to lockdown of all major countries in the world. India has been on complete lockdown since 23 March, 2020. This has caused extraordinary situation which is unparalleled in history¹.

Cancer patients are particularly predisposed to excessive complications on getting exposed to COVID-19¹. In a report from Italy, 20 percent of the deaths from COVID-19 in the entire country were in patients with active cancer². Though no large data pertaining to acute myeloid leukemia (AML) has been reported specifically, it is reasonable to assume that AML patients if they get infected with COVID-19 will have disastrous consequences while they are on intensive chemotherapy. Delivering cancer care during this crisis is challenging given the competing risks of death from cancer versus death or serious complications from SARS-CoV-2, and the likely higher lethality of COVID-19 in immunocompromised hosts³.

AML is a rapidly fatal disease if left untreated and with a high probability of achieving a cure especially in younger patients and those with acute promyelocytic leukemia (APL or AML-M3), hence it is imperative that a rapid diagnosis and optimal therapy is attempted in this group even in the time of this crisis.

This topic will discuss issues related to balancing the risk from treatment delay versus harm from COVID-19, ways to minimize the compromise of social distancing during care delivery, how limited healthcare resources can be appropriately and fairly allocated.

Issues particular to AML and COVID-19 in India

- 1.** AML patients are likely to be managed in same hospital where COVID-19 are also admitted for care.
- 2.** Duration of neutropenia following intensive chemotherapy is one of the longest in AML among all cancers and infectious complications during this period are the leading cause of mortality in AML.
- 3.** AML patients required significant blood component support and with the extended periods of lockdown and social distancing norms, it is increasingly becoming difficult to arrange for blood component donors.
- 4.** Long duration of in hospital treatment increases exposure risk to HCW too especially if an AML patient acquires COVID-19

General points:

1. All laid down safety protocols for health care workers (HCW) to be strictly observed. Especially hematology day care staff to strictly follow all protocols to minimize risk of transmission from patients who are coming to day care from the community.
2. Diagnosis: All new patients of AML to be subjected to standard laid down diagnostic and prognostic tests without any delay.
3. Detailed travel and contact history to be elicited at first point of contact. Special emphasis on signs and symptoms of respiratory tract infection.
4. All patients should be screened for COVID-19 before initiation of induction or consolidation chemotherapy. If positive, therapy should be delayed if possible until resolution of symptoms (if present) and PCR negativity. Ideally all new patients should be admitted in a dedicated COVID suspect area in a single room until the result of negative for COVID is available following which the patient can be shifted back to the hemato-oncology unit (to avoid inadvertently infecting other patients in the hemato-oncology unit). If COVID test returns positive a case by case decision needs to be made on treatment but would recommend considering initial therapy with hypomethylating agents rather than intensive chemotherapy.
5. If feasible in non-APL cases, intensive chemotherapy to be delayed till cytogenetic and molecular test results are available, as this would help treating hematologist/oncologist in triaging the patients.
6. Restrictive transfusion policy for PRBC and platelets as it is anticipated that getting donors would be difficult in these times (target Hb 70 gm/Lt and platelet count 10×10^9 /Lt in the absence of bleeding).
7. All treatment decisions should be done after proper counselling and after discussion of risk –benefit ratio of different treatment intensity in general, and in relation to added risk involved with COVID-19. Informed consent is imperative.

Intensive chemotherapy for non-APL, AML patients <60 years with good performance score**A. Favorable & Intermediate risk category**

They should be considered for standard of care induction chemotherapy like 3+7. Daunorubicin should be administered at the dose of 60 mg/m² for 03 days while cytarabine dose should be 100mg/m² daily as continuous infusion for 07 days. Following induction if in remission patients should proceed to consolidation with high dose cytarabine for 3 monthly cycles. Cytarabine dose should be reduced to 1.5 gm/m² for all patients⁴.

B. Poor risk category

They should be considered for Hypomethylating agents (HMA). Azacytidine which can be administered subcutaneously is preferred over decitabine. Venetoclax if feasible can be added to HMA. Testing for remission status should be done only after 4 cycles.

Intensive chemotherapy for non-APL, AML patients <60 years with poor performance score

They should be considered for HMA for 1 or 2 cycles and then to be reassessed for improvement in their general condition for intensive induction therapy. Meanwhile cytogenetic and molecular tests will be available to guide further treatment (as outlined above)

Management of non APL, AML patients > 60 years

A. Favorable risk category

If performance status permits, they should be considered for standard of care induction chemotherapy like 3+7. Daunorubicin should be administered at the dose of 45 mg/m² while cytarabine dose should be 100mg/m² in twice daily dosing. Following induction if in remission patients should proceed to consolidation with high dose cytarabine for 03 monthly cycles. Cytarabine dose should be reduced to 1 gm/m² for all patients. They can be considered for D1,D2,D3 administration instead of D1, D3, D5 to reduce period of cytopenias.

B. Intermediate & poor risk category

They should be considered for HMA therapy for induction. Remission status assessment should be done only after 04 cycles of therapy.

Patients with APL

A. High risk: They should receive ATO+ATRA based induction and consolidation. For cytoreduction hydroxyurea can be used. In induction retain anthracycline to reduce risk of differentiation syndrome.

B. Low and intermediate risk: They should receive ATO+ATRA based induction and consolidation.

C. Adequate and appropriate transfusion support especially for coagulopathy in the first two weeks of induction with a target platelet count of 30 x 10⁹/Lt and target a fibrinogen level of 140 mg% with adequate cryoprecipitate support.

Patients with relapsed AML

- A. Carefully assess the risks and benefits of pursuing a curative approach on a case-by-case basis.
- B. Targeted therapies can be considered in combination with chemotherapy and risk benefit ration to be assessed on a case to case basis.
- C. Consider palliative care as an option with any adverse factors

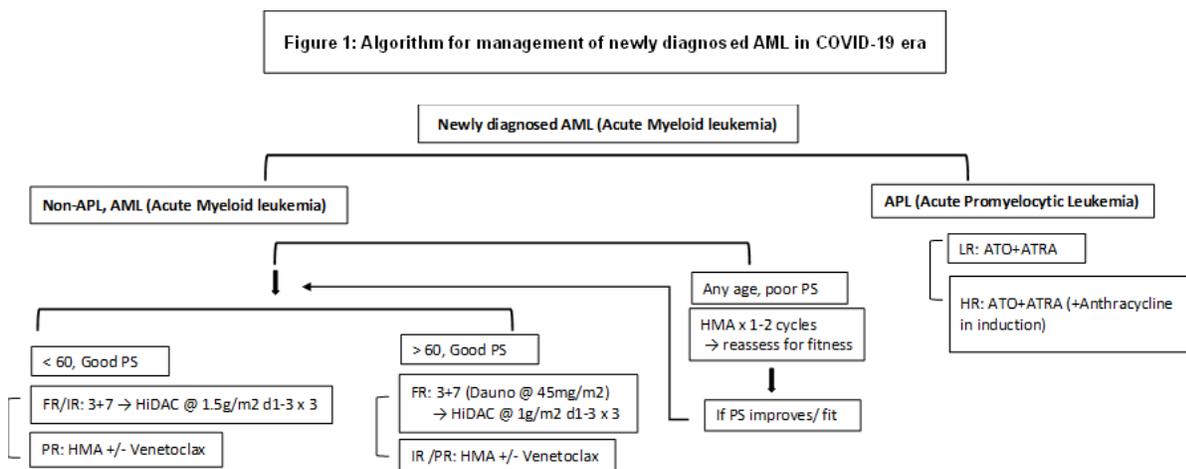
Hematopoietic Stem cell transplantation (HSCT)

At present no specific recommendations can be given on this aspect. It is imperative to carefully assess the risks and benefits of HSCT for patients with a very high risk of relapse after transplant. It is highly recommended that HSCT to be done only in large centers. Centers should take up for transplant only after due diligence and after

consultation between transplant consultant, patients and family. Clinicians may wish to restrict allogeneic transplants to patients with a HCT-CI score of less than 3 although such decisions are patient specific given the lack of precision of the HCT-CI scoring system.

References

1. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 15 April 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-15-April-2020> (Accessed on April 20, 2020).
2. Yu J, Ouyang W, Chua MLK, Xie C. SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China. *JAMA Oncol.* 2020.
3. Lewis MA. Between Scylla and Charybdis - Oncologic Decision Making in the Time of Covid-19. *N Engl J Med.* 2020.
4. Recommendations for the management of patients with AML during the COVID19 outbreak: a statement from the NCI AML Working Party. Version 2.3 dated 07-04-2020.



*HCT when indicated: decision needs to be individualized based on risk of relapse and all other logistics, preferable is to delay transplant until there is more clarity on the course of COVID-19 general status