LETTER TO THE EDITOR

Mortality by COVID-19 in adults with acute myeloid leukemia: a survey with hematologists in Brazil

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Dear Editor,

COVID-19 caused by the novel coronavirus SARS-COV-2 and first detected in Wuhan, China in 2019, has become one of the worst pandemics in history [1, 2]. Although approximately 50% of the infected individuals are asymptomatic, some may develop severe cytokine release syndrome with intense immune response and endothelial damage [3]. Obesity, hypertension, diabetes, COPD, advanced age, and malignancy have been listed as risk factors for severe disease, hospitalization, admission in intensive care unit, and death [4, 5]. Patients with hematological malignancies also have a higher risk of severe events and among all of them, acute myeloid leukemia (AML) seems to have the highest risk for death by COVID-19 [6].

Because avoiding medical services visits or prolonged stays in hospital is not an option for AML patients, these individuals have a higher chance of getting in contact and being infected by SARS-COV-2. Once infected, these patients may be at high risk for severe complications and death as they have immunosuppression, neutropenia, and epithelial mucosal barrier damage [7]. AML affects individuals of all ages whom may be in different hematological scenarios such as in remission or with active disease that may be treated with intensive chemotherapy or low intensity treatment. The impact of COVID-19 in those different AML scenarios is unknown. Our aim is to report a survey conducted with Brazilian hematologists who attended AML patients with COVID-19, to evaluate the mortality rate seen by those doctors among their patients and any potential risk factor for death.

Methods

From May 5 to May 19, 2021, we conducted a survey with 178 hematologists within different regions of Brazil. We asked about adult patients (> 18 years) with AML who had the COVID-19 diagnosis confirmed by RT-PCR. We collected data about age, gender, possible source of contamination by SARS-COV-2 (hospital vs community), previous vaccination, moment of the AML treatment (pre-treatment, during induction, post remission, off treatment), the status of AML when COVID was diagnosed (remission vs active disease) and the outcomes related to COVID-19 (death, delay of treatment, relapse of AML). We considered the answers provided by the doctors as events that are reported as counts and percentages. We use Mann–Whitney U, Fisher's exact, or chi-square tests when appropriate. The p value < 0.05 considered significant. Statistics were performed using the Social Science Statistics at https://www.socscistatistics.com.

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Results and discussion

We received answers from 10 doctors representing 10 cancer centers. Four medical centers involved in this survey were exclusively part of the Brazilian Public Health System and 5 exclusively part of the private system. One center was part of both public and private systems. Seven were general hospitals, while 3 were exclusive for cancer treatment. Only one hospital has high-efficiency particulate air (HEPA) filtration for leukemia patients. The patients were treated in private isolate rooms in five hospitals. According to the protective measures to diminish SARS-COV-2 transmission, we found that only one center regularly screens health personnel, only two tested patients prior to hospital admission and all of them allowed companions with patients, although only one center screens them for COVID-19 pre-admission. The doctors surveyed provided data on 33 patients (22 females), that were admitted mainly through urgent and emergency care unit. The median age at the COVID-19 diagnosis was 60 years (19 to 79 years). Only one had been previously vaccinated. The place of contamination with SARS-COV-2 could not be identified in two cases, while in 21 cases (63%) in-hospital transmission was presumed to be the source of infection. In 20 patients (60.6%), COVID-19 was diagnosed when the patient had active AML, while in 13 patients, (39.3%) AML was in remission. The diagnosis was done in the context of symptomatic patients except for one whose diagnosis was done in the context of investigation for febrile neutropenia. Twelve patients had COVID-19 diagnosis before starting AML treatment, 6 during intensive chemo induction remission, 3 during intensive chemo consolidation, 9 while in low-intensity therapy and 2 during treatment of relapse. Only one patient had completed AML treatment and was in remission. There were 18 deaths attributed to COVID-19 (54.5%), of which 15 (83%) had active AML and 3 (17%) were in AML remission ($p = 0.0052$). We did not identify any other factor that could be associated to death. Among the 15 patients who survived COVID-19, 8 (53%) had some delay in their AML treatment.

Despite its limitations, this exploratory report addressing specifically AML and COVID-19. It brings up some points to consider: First, most patients were presumed to be infected in hospital, which reinforces the need for taking measures to control the dissemination of COVID-19 inside the hospital environment. This is particularly relevant since the seroconversion rate after COVID-19 can be lower in AML patients than that expected for the general population. Besides, the viral shedding may be prolonged in immunocompromised persons which may facilitate dissemination in hospital if protective precautions are not taken [8]. In this survey only one patient had been vaccinated before the diagnosis of COVID-19. This patient was in AML remission and did not die. The question of whether previous SARS-COV-2 vaccine could diminish the mortality rate in our population cannot be answered. In fact, this may be an intriguing point since patients with hematologic malignancies, particularly those with B-cell lymphoid neoplasm and multiple myeloma, may not have a good immune response [9]. Second, published recommendations on management of patients with hematological malignancies and COVID-19 were based more in common sense rather than on scientific evidence [7, 10, 11]. Our work adds to this, suggesting that patients with active AML possibly have more risk of death from COVID-19 and that patients on AML treatment did not have better outcomes. Together, these findings lead us to speculate that the best strategy could be postponing the beginning of AML treatment as long as it is safe, as others have also suggested [11]. This suggestion is supported by retrospective studies indicating that the time from diagnosis to treatment may not affect the final outcome for AML patients [12]. Of note, 5 of 12 patients who had COVID-19 diagnosis before beginning AML treatment were alive and COVID free by the time the survey was made. Patients in remission who needs post remission therapy should be screened for SARS-COV-2 before starting chemotherapy and in case of positivity consideration should be given to postponing it for two or more weeks [11]. Third, although the role of SARS-COV-2 cannot be ascertained, our survey seems to confirm the high risk of death due to COVID-19 in patients with AML. Fourth, more than 50% of patients who survived COVID-19 had a delay in their treatment; the impact of this delay on AML survival remains uncertain and should be evaluated in future studies.

In conclusion, AML patients seem to have a very high risk of death when infected by SARS-COV-2. Furthermore, even when recovered from COVID-19, those patients may suffer a delay in their treatment. Further reports are needed to formulate evidence-based recommendations.

Declarations

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