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Survival of Patients with Hematologic Malignancies and Covid-19

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Abstract

Purpose: The present study aimed to describe the characteristics of patients with hematological neoplasms and COVID19, treated in a reference center in Mexico City, as well as their mortality and the factors that could influence it.

Patients and methods: This retrospective study included 56 patients with hematological neoplasms and SARS-CoV-2 infection. The impact on overall survival (OS) of sex, age, malignancy status, diabetes mellitus, obesity, overweight, neutrophil count, lymphocyte count, CO-RADS was evaluated.

Results: Overall mortality was 50%. Univariate analysis identified age >50 years, history of hypertension, diabetes, and a CO-RADS score >5 as factors influencing the mortality of patients with hematologic malignancies and COVID19. Multivariate analysis only identified CO-RADS score > 5.

Conclusion: The mortality of patients with hematological neoplasms and COVID19 was high in our setting. Frequent co morbidities in our population can influence mortality.

Introduction

COVID19, caused by the SARS-CoV-2 virus, was declared a pandemic by the WHO in March 2020. Since then, multiple questions have arisen related to the prognosis and care of cancer patients. Initially, recommendations formulated by groups of experts were issued in order to guide the care of patients with hematological neoplasms and COVID19; subsequently, the experience of various regions of the planet was published, with variable mortality rates [1-4].

Various risk factors have been described that can influence the mortality of patients with hematological neoplasms and COVID19, such as age, type of neoplasm, comorbidities, certain laboratory parameters, etc [5,6].

The objective of this work is to describe the characteristics of patients with hematological neoplasms and COVID19, treated in a reference center in Mexico City, as well as their mortality and the factors that could influence it.

Methods

We include patients with hematological neoplasms and SARS-CoV-2 infection, corroborated by the polymerase chain reaction (PCR) test, which required hospitalization at the Hospital of Mexico Dr. Eduardo Liceaga between April 2020 and March 2021.

The primary analysis describes the demographic and clinical characteristics of patients with COVID19 after a previous diagnosis of hematologic malignancy. Categorical variables are presented with frequencies and percentages, and continuous variables with median and range. The secondary analysis studied the independent predictors of overall mortality in hematological patients with COVID-19, using a Cox proportional hazard model. A univariate Cox regression model was performed with variables suspected of playing a role in the mortality of patients with hematologic malignancies with COVID-19 (i.e., sex [reference woman], age [<50 years of reference], malignancy status [reference controlled disease], diabetes mellitus, obesity, overweight, neutrophils [reference >0.5 x 10^9/L], lymphocytes [reference > 0.2 x 10^9/L], CO-RADS [<5 reference]). Variables with a p value ≤ 0.1 were considered for multivariate analysis. A multivariate Cox regression model was calculated, and only those variables that were statistically significant were shown. Mortality was analyzed using Kaplan-Meier survival graphs. No a priori sample size calculation was performed for this exploratory study. SPSSv25.0 (SPSS, IBM CorpChicago, IL, United States) was used for statistical analyzes.

Results

A total of 56 patients with some hematological neoplasms and SARS-CoV-2 infection that required hospitalization were included, with a mean age of 39 years and a predominance of males. The most frequent diagnosis was Acute Lymphoblastic Leukemia (ALL), followed by Non-Hodgkin's Lymphoma (NHL) and Acute Myeloid Leukemia (AML) (Table 1).

The main symptoms at diagnosis of COVID-19 were fever (70.8%), cough (43.1%) and dyspnea (23.1%). 91% of the patients received treatment with antibiotics and supplemental oxygen, 21% assisted mechanical ventilation, the rest of the treatments are described in Table 2.

Mortality

Mortality was 50% with a median survival of 21 days (Figure 1). The highest mortality was observed in patients with non-Hodgkin's lymphoma (61.5%). Mortality by diagnosis is described in Table 3.

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Table 1: General characteristics of the patients.

	n (%)
Age	
<50 years	42 (75)
≥ 50 years	14 (25)
Gender	
Female	29 (52)
Male	27 (48)
Diagnostic	
Acute Lymphoblastic Leukemia (ALL)	27 (48.2)
Non-Hodgkin Lymphoma (NHL)	13 (23.2)
Acute Myeloid Leukemia (AML)	10 (17.9)
Chronic Myeloid Leukemia (CML)	2 (3.6)
Myelodysplastic Syndrome (MDS)	2 (3.6)
Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	1 (1.8)
Hodgkin Lymphoma (HL)	1 (1.8)
Disease status	
Under surveillance / No disease activity	5 (8.9)
In active treatment / Recent diagnosis	51 (91.1)
Time of diagnosis of hematologic neoplasia	
< 6 months	35 (62.5)
≥ 6 months	21 (37.5)
Treatment for hematologic disease in the 30 days prior to COVID19	
Chemotherapy	28(50)
Radiotherapy	0
Steroids	24 (42.9)
Target therapies	2 (3.6)
Immunomodulators	0
Comorbidities	
Hypertension	6(10.7)
Diabetes	6(10.7)
Smoking	1 (1.8)
Chronic Kidney Disease	2(3.6)
Hypothyroidism	2 (3.6)
Obesity	8 (14.3)
Overweight	18 (32.1)
Malnutrition	6 (10.7)

Table 2: Main symptoms and treatments used.

	n (%)
Symptoms	
Fever	46 (70.8)
Cough	28 (43.1)
Dyspnoea	15 (23.1)
Odynophagia	1 (1.5)
Anosmia	1 (1.5)
Dysgeusia	1 (1.5)
Headache	12 (18.5)
Conjunctivitis	3 (4.6)
Diarrhea	2 (3.1)
Myalgia	8 (12.3)
Treatments	
Antibiotics	51 (91.1)
Heparin	29 (51.8)
Oseltamivir	5 (8.9)
Steroid	36 (64.3)
Ventilatory mechanical support	12 (21.4)

Table 3: Mortality of patients with hematologic malignancies and COVID19.

	n (%)
General Mortality	28 (50)
Mortality by Diagnosis	
Acute Lymphoblastic Leukemia (ALL)	12 (44.4)
Non-Hodgkin Lymphoma (NHL)	8 (61.5)
Acute Myeloid Leukemia (AML)	5 (50)
Chronic Myeloid Leukemia (CML)	0 (0)
Myelodysplastic Syndromes (MDS)	2 (100)
Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	0 (0)
Hodgkin Lymphoma (HL)	0 (0)

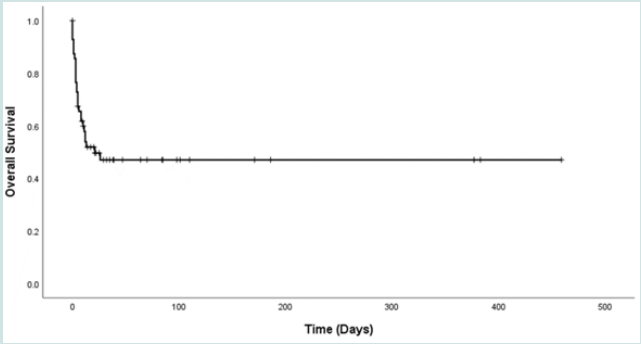

Figure 1: Overall survival of patients with hematologic malignancies and COVID-19.

Table 4: Mortality predictors in patients with hematological malignancies and COVID19.

	Univariable			Multivariable		
	p value	HR	95% CI	p value	HR	95% CI
Gender						
Female	-	-	-	-	-	-
Male	0.84	1.07	0.51-2.26	0.349	1.70	0.560-5.16
Age ≥ 50 y	0.004	3.00	1.40-6.42	0.143	2.25	0.760-6.70
Active disease	0.32	1.7	0.58-4.91	0.695	1.27	0.37-4.37
Chemotherapy in the 30 days prior to COVID-19	0.344	0.69	0.32-1.47	0.407	0.67	0.26-1.72
Hypertension	0.02	2.96	1.18-7.42	0.578	1.59	0.30-8.32
Diabetes	0.041	2.59	1.03-6.50	0.717	1.29	0.31-5.31
Obesity	0.66	1.243	0.47-3.27	0.789	1.19	0.327-4.34
Neutrophils <0.5x10^9/L	0.642	1.20	0.54-2.67	0.646	1.29	0.43-3.83
Lymphocytes <0.2x 10^9/L	0.163	1.72	0.80-3.69	0.581	1.37	0.44-4.26
CO-RADS ≥ 5	0.009	4.92	1.48-16.34	0.034	2.46	1.07-5.64

Univariate analysis identified age ≥ 50 years (HR=3.00, CI 1.40-6.42, p=0.004), history of hypertension (HR= 2.96, CI 1.18-7.42, p=0.02), diabetes (HR= 2.59, CI 1.03-6.5, p= 0.02), and a CO-RADS score ≥ 5 (4.92, CI 1.48-16.34, p=0.009) as factors associated with mortality. In the multivariate analysis, only the CO-RADS score ≥5 (HR 2.46, CI 1.07-5.64, p=0.034) was identified (Table 4).

Discussion

Coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization (WHO) on 11 March 2020 [7]. As the disease spread worldwide, uncertainty arose about the treatment and prognosis of patients with hematologic malignancies. At the beginning, only recommendations from groups of experts were published, currently we have evidence from different parts of the world. As of today (May 17, 2022), 522,278,953 cases of COVID 19 have been reported in the world population, with a mortality of 1.2%. In Mexico, 5,752,441 cases of COVID-19 have been reported in the general population, with a mortality of 5.6% [8].

In the case of patients with hematological neoplasms, different mortality ranges have been reported, for example, a multicenter study of the Spanish transplant group and cell therapy (GETH) in which 367 patients were included, reported a mortality of 17% and 18% in patients recipients of autologous (ASCT) and allogeneic

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stem cell transplantation (allo-SCT) respectively, compared with a 31% mortality in non-SCT patients, prognostic factors for 45 day overall mortality were age > 70 years, uncontrolled hematological malignancy, ECOG 3–4, neutropenia ($< 0.5 \times 10^9$/L) and a C-reactive protein (CRP) > 20 mg/dL [9]. The EPICOVIDEHA, (Epidemiology of COVID-19 Infection in Patients with Hematological Malignancies: A European Hematology Association Survey), multinational project included 3801 cases, represented by lymphoproliferative (mainly non-Hodgkin lymphoma n = 1084, myeloma n = 684 and chronic lymphoid leukemia n = 474) and myeloproliferative malignancies (mainly acute myeloid leukemia n = 497 and myelodysplastic syndromes n = 279) with an overall mortality of 31.2%, and the highest mortality observed in acute myeloid leukemia (199/497, 40%) and myelodysplastic syndromes (118/279, 42.3%); age, active malignancy, chronic cardiac disease, liver disease, renal impairment, smoking history, and ICU stay correlated with mortality [2]. A meta-analysis that included 3377 patients from Asia, Europe, and North America, found a 34% risk of death for adult patients with hematologic malignancy and COVID-19, whereas pediatric patients had a 4% risk of death [10]. A multicenter study that included patients from Mexico, Peru, Guatemala and Panama, reported a mortality of 37.7% in patients with COVID19 and hematological neoplasms, being higher in patients with acute myeloid leukemia [11].

Another study conducted in the Mexican population, which included four hundred thirty-three patients with solid tumors (79%), hematological neoplasms (21%) and COVID19 from the National Cancer Institute of Mexico, reported one hundred thirty-five (31%), 131 (30%), and 93 (21%) patients had obesity, hypertension, and diabetes mellitus (DM), respectively and a mortality within 30 days after diagnosis of 18% [12].

In our study we only included patients with hematological neoplasms and COVID19 who were treated in hospital, therefore with a more severe disease, which could explain the high mortality (50%), patients with acute leukemia, mainly lymphoblastic leukemia (ALL) were the most affected, and this is explained by the high population that is treated in our institution with this disease. The prognostic factors that we identified were age over 50 years and comorbidities with a high prevalence in the Mexican population, such as diabetes and hypertension, however, in the multivariate analysis, the CO-RADS score ≥ 5 was the only factor associated with mortality which can be related to COVID19 with well-defined radiological changes and a more severe disease.

Conclusion

Different percentages of mortality and risk factors for patients with COVID19 and hematologic malignancies have been reported, depending on the geographical area and the characteristics of the patients treated at their centers; however, it is common for the mortality of patients with hematological neoplasms to be increased. In Mexico, factors such as the heterogeneity of hospital services, as well as the comorbidities of the population can influence mortality. Thanks to vaccination and prevention programs, COVID19 seems to have decreased in our country, however, in other regions of the world the activity of the disease is intense, so it is important to report previous experience and take it as a basis to improve strategies for patient care, especially those who are immunosuppressed, such as patients with hematological malignancies.

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