International Blood Research & Reviews

12(3): 32-39, 2021; Article no.IBRR.68658
ISSN: 2321–7219

Survival in Patients with Acute Lymphoblastic Leukemia and COVID-19 in Mexico

Patricia Zagoya Martinez[1*], Jose Alejandro Limon Flores[1] and Jose Alfredo Vidal Vidal[2]

[1]Department of Hematology, Mexican Institute of Social Security, Hospital of Specialties, High Specialty Medical Unit, National Medical Center "Gral. Manuel Avila Camacho", Puebla, Mexico.
[2]Division of Critical Medicine, Surgical Care Unit, Puebla State Health Services "Hospital para el Niño Poblano", San Andres Cholula, Puebla, Mexico.

Authors' contributions

This work was carried out in collaboration between all the authors. The author PZM collected and analyzed data; participated in the writing of the manuscript. The authors JALF and JAVV participated in the writing and editing of the manuscript. Authors PZM and JAFL wrote the discussion and participated in literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IBRR/2021/v12i330153
Editor(s):
(1) Dr. Dharmesh Chandra Sharma, J. A. Groups of Hospital and G. R. Medical College, India.
(2) Dr. Juan Carlos Troiano, University of Buenos Aires, Argentina.
(3) Dr. Armel Hervé Nwabo Kamdje , University of Ngaoundere,Cameroon.
Reviewers:
(1) Mohammed Suleiman Obsa, Wolaita Sodo University, Ethiopia.
(2) Manash Barthakur, Pub Kamrup College affiliated under Gauhati University,India.
(3) Md. Sadique Shaikh, AIMSR, india.
Complete Peer review History: http://www.sdiarticle4.com/review-history/68658

Original Research Article

Received 05 May 2021
Accepted 31 May 2021
Published 02 June 2021

ABSTRACT

Aims: To determine the survival of patients with acute lymphoblastic leukemia and COVID-19.
Study Design: Prospective, analytical and relational.
Place and Duration of Study: Hematology department, Hospital of Specialties, High Specialty Medical Unit, National Medical Center "Gral. Manuel Avila Camacho", Puebla, Mexico, during the period June 2020-April 2021
Methodology: Patients aged 15 to 64 years, both sexes, with acute lymphoblastic leukemia and a confirmed diagnosis of COVID-19 by PCR. The variables included were; sex, age (groups: 15-20; 21-29; 30-39; 40-49; 50-59; and 60-64), comorbidities, general treatment and hematological treatment response. Survival was determined for the diagnosis of COVID-19 for 11 months, using

**Corresponding author: E-mail: patricia.zagoya@imss.gob.mx*

the Kaplan Meier estimator and the Log-Rak test; Cox regression model (univariate and multivariate); as well as Chi square and V-Cramer with a 95% confidence interval and using the statistical program SPSS Ver. 25.
Results: The study consisted of 20 patients, of which 33.3% were women, with an average age of 37.75 ± 11.63 years; The men registered an age of 28.50 ± 18.05 years. Overall survival was 50%, with a lower limit of 101.3 and an upper limit of 242.5 days, with a mean of 171.9 days; and median at 17 days. No significant differences were found in survival regarding sex, comorbidities, general treatment and hematological response. However, mortality in patients with comorbidities was higher ($p = 0.051$).
Conclusion: Survival in patients with acute lymphoblastic leukemia and COVID-19 is low, due to complications that increase mortality, mainly owing to hematological suppression, and even more so with the presence of comorbidities.

Keywords: Cancer; hematological alterations; mortality; SARS-CoV-2.

1. INTRODUCTION

Acute lymphoblastic leukemia consists of an abnormal increase in lymphoblasts, and a lack of development of mature lymphocytes, therefore, it compromises the immune response. In addition to displacing the normal cells of the bone marrow, causing a decrease in erythrocytes, leukocytes and platelets [1], predisposing the patient to severe infectious conditions [2]. Acute leukemias have a worldwide incidence of 20–35 cases per million inhabitants per year [3]. In Mexico, a global incidence of leukemia is estimated at 55.4-58.4 per million; in acute lymphoblastic leukemia of 43.2-44.9; acute myeloid leukemia of 9.8-10.6; 2.5 chronic myeloid leukemia; and unspecified leukemias of 0.5 [4].

On the other hand, the origin of human coronavirus was identified in the 1960s, when a study on respiratory viruses was carried out in England. The appearance of the Severe Acute Respiratory Syndrome (SARS) was in Guangdong province, China in 2002. It showed that human strains are mainly the cause of mild acute infections of the upper respiratory tract, being more severe in older adults with chronic degenerative comorbidities, heart disease and as well as, in immunologically depressed patients, the ability to spread SARS is high [5-6].

The new coronavirus registered at the end of 2019 was initially named “WH-Human 1 coronavirus” (WHCV), and later 2019-nCoV; finally, it was included in the same species as SARS-CoV and it was named SARS-CoV-2; the disease was designated as Coronavirus Disease 2019 (COVID-19). Owing to, its fast worldwide expansion, a pandemic situation was declared, on March 11, 2020 [7].

In March 2021, 119 million confirmed cases were registered worldwide, meaning around 15.4 thousand cases per million people, with 2.65 million deaths. In Mexico, 2.16 million confirmed cases were registered, which reflects an average of 17 thousand cases per million inhabitants, with a total of 194 thousand deaths [8-9]. Patients with acute lymphoblastic leukemia present a greater risk of morbidity and mortality from COVID-19, due to their immunological conditions, the objective of this work is to determine the survival of patients with acute lymphoblastic leukemia and COVID-19.

2. METHODOLOGY

Prospective, analytical and relational study of patients, aged between 15 and 64 years, both sexes, and with acute lymphoblastic leukemia and confirmed diagnosis of COVID-19 by PCR in the department of Hematology, Hospital of Specialties, High Specialty Medical Unit, National Medical Center "Gral. Manuel Avila Camacho", Puebla, Mexico, during the period June 2020-April 2021. The variables included were; sex, age (groups: 15-20; 21-29; 30-39; 40-49; 50-59; and 60-64), comorbidities, general treatment and hematological treatment response. Survival was determined considering, the diagnosis confirmed by COVID-19 for 11 months, using the Kaplan Meier estimator and Log-Rak test; Cox regression model (univariate and multivariate); as well as Chi square and V-Cramer with a confidence interval of 95% and using the statistical program SPSS Ver. 25.

3. RESULTS AND DISCUSSION

The study consisted of 20 patients, of which eight (33.3%) were women, between 16 and 50 years old, with an average age of 37.75 ± 11.63 years

and 12 men (66.7%) with a mean age of 28.50 ± 18.05 years, this range between 15 and 64 years, coincide with other authors, who indicate that men have a higher incidence, in acute lymphoblastic leukemia [10]. Seven patients presented comorbidities, without statistical association with sex (p = 0.370) (Table 1).

Most of the women (5) were in consolidation treatment. In the case of men, five were in induction and three were in re-induction. There was no statistical association with sex (p = 0.198) (Table 2).

In response to treatment, hematological remission predominated in both women (6) and men (5). There were no associations with sex (p = 0.471) (Table 3).

Overall survival was 50% during the eleven months (333 days) evaluated, with a lower limit of 101.3 and an upper limit of 242.5 days, mean of 171.9 days; and median at 17 days (Fig. 1). In other words, 50% of the patients died in the first 17 days after confirming the diagnosis for COVID-19, showing a clear reduction in survival, which coincides with different related investigations, noting that the immunological status, the type and stage of treatment, and the presence of comorbidities, in acute lymphoblastic leukemia, are factors that increase mortality [11-13].

Survival regarding age (p = 0.617) and sex (p = 0.411) did not present significant differences. In women it was 62.5%, with a lower limit of 103.7 and an upper limit of 320.3 days, and an average of 212 days. In the case of men, it was 41.7%, with a lower limit of 55.5 and an upper limit of 235 days, a mean of 145.2 days, and a median of 14 days (Fig. 2), which coincides with other investigations [14].

Survival regarding comorbidities, did not present significant differences (p = 0.051). All patients with diabetes mellitus, chronic kidney disease and hyperthyroidism died (Fig. 3), probably due to, the instability in the general state of health that was confirmed by COVID-19 [15,13].

Survival with respect to the general treatment did not present significant differences (p = 0.311). Patients who were in consolidation had a survival of 57.1%; those of induction 42.9%; those of palliative treatment 50%; and those of re-induction 66.7% (Fig. 4). The maintenance patient survived at the end of the study, this is confirmed by other investigations, in which they indicate that the hematological treatment administered affects the mortality of patients with acute lymphoblastic leukemia and COVID-19 [14-16].

Survival considering the type of response to hematological treatment did not show significant differences (p = 0.105). In patients under induction it was 20%, with a lower limit of 0 and an upper limit of 187.6 days, a mean of 74.2 days, and a median of 11 days. Those found in hematological remission was 72.7% with a lower limit of 161 and an upper limit of 330 days, and a mean of 245.4 days. In palliative treatment patients, it was 33.3% with a lower limit of 0 and an upper limit of 290.1 days, a mean of 171.9 days, and a median of 17 days. Patients with relapse recorded a mean of 14 days (Fig. 5), this is confirmed by other authors, who indicate that the response to hematological treatment influences, the mortality of patients with acute lymphoblastic leukemia and COVID-19 [14-16].

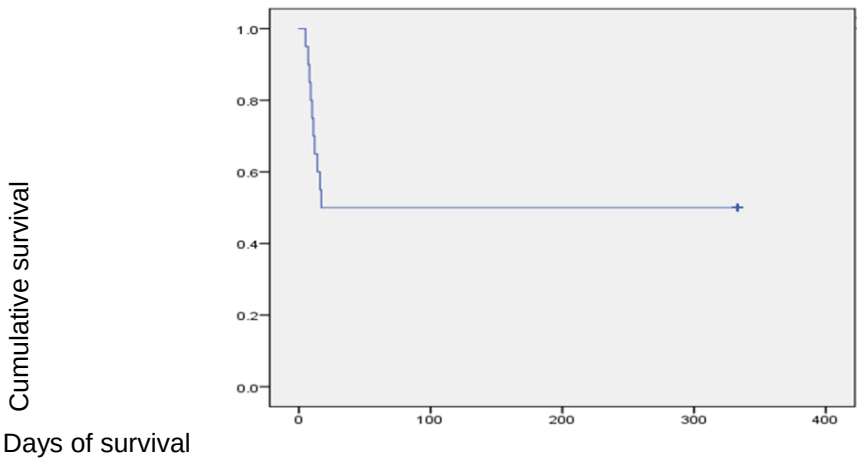

Fig. 1. Global survival in patients with acute lymphoblastic leukemia and COVID-19

Table 1. Frequency of comorbidities respect to sex

	Comorbilidades					
Sex	**Mellitus diabetes**	**Chronic kidney disease**	**Hyperthyroidism**	**Neutropenia**	**Obesity**	Total
Woman	1	0	1	1	1	4
Men	0	1	0	2	0	3
Total	1	1	1	3	1	7

Table 2. Frequency of general treatment respect to sex

	General treatment					
Sex	**Consolidation**	**Induction**	**Maintenance**	**Palliative**	**Re-induction**	**Total**
Woman	5	2	0	1	0	8
Men	2	5	1	1	3	12
Total	7	7	1	2	3	20

Table 3. Frequency of response hematological treatment respect to sex

	Hematological treatment response				
Sex	**Induction**	**Relapse**	**Hematological remission**	**Palliative treatment**	**Total**
Woman	1	0	6	1	8
Men	4	1	5	2	12
Total	5	1	11	3	20

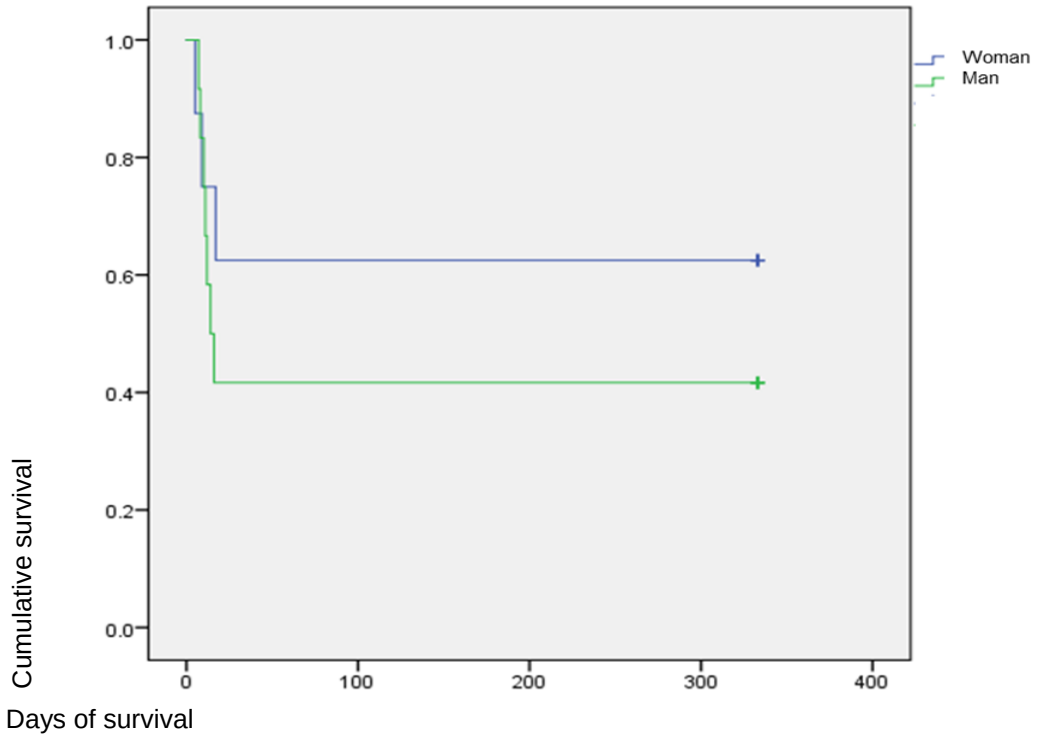

Fig. 2. Survival in patients with acute lymphoblastic leukemia and COVID-19 respect to sex

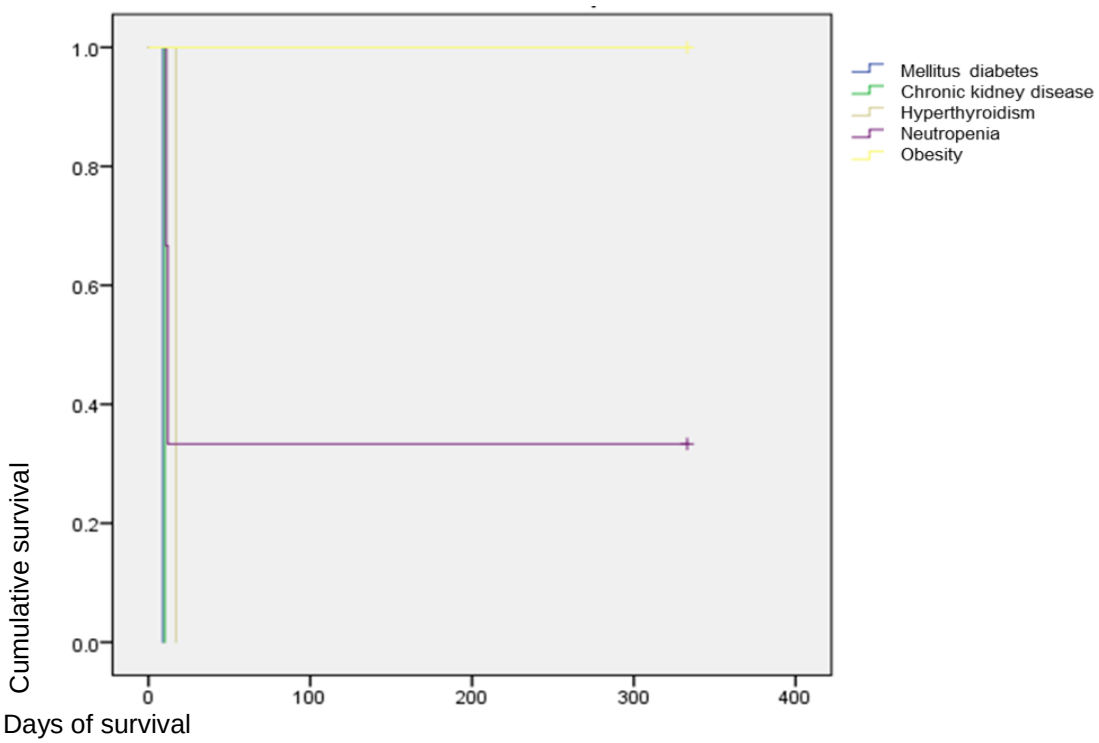

Fig. 3. Survival in patients with acute lymphoblastic leukemia and COVID-19 respect to comorbidities

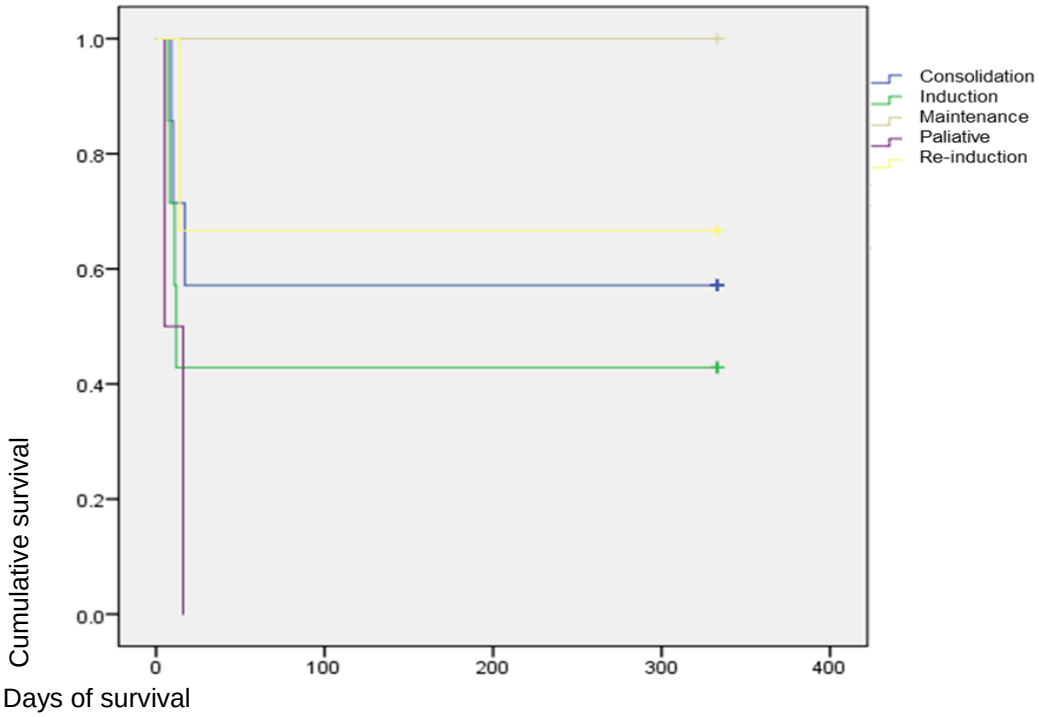

Fig. 4. Survival in patients with acute lymphoblastic leukemia and COVID-19 respect to general treatment

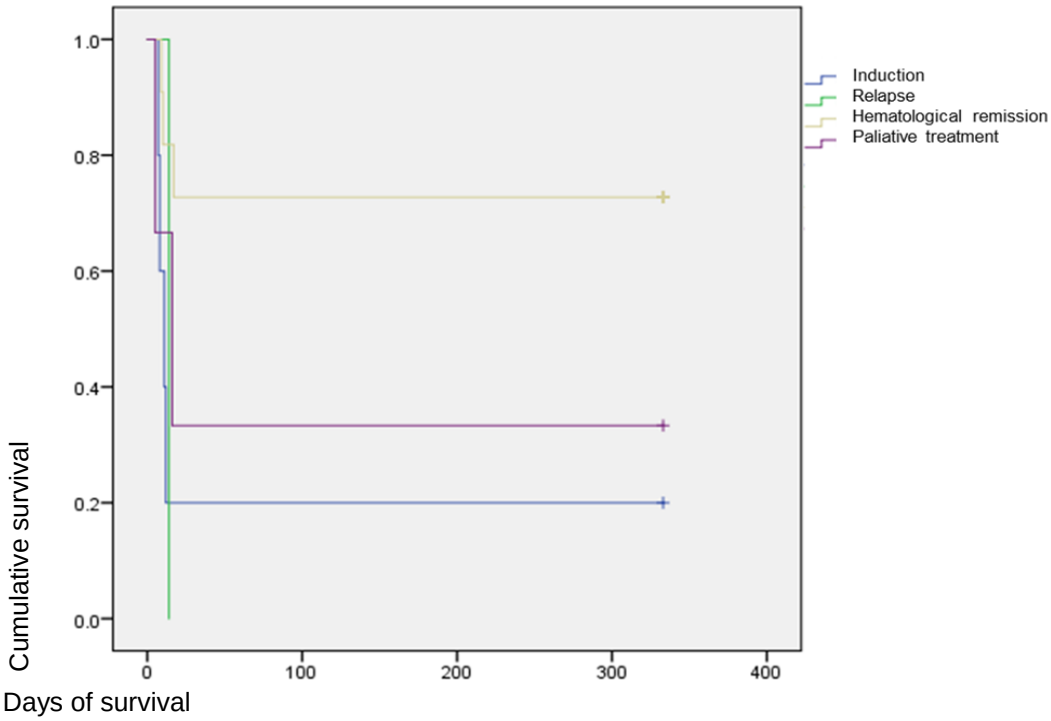

Fig. 5. Survival in patients with acute lymphoblastic leukemia and COVID-19 respect to hematological treatment response

Univariate Cox regression analysis showed no association between survival and sex (p = 0.411); age group (p = 0.617); general treatment (p = 0.331); and hematological treatment response (p = 0.105). Comorbidities (p = 0.051) showed an association with patient survival,

possibly by exacerbating the generalized inflammatory process, further compromising the immune response, mainly in diabetics [13]. In the multivariate Cox regression there were no significant associations with the variables studied.

4. CONCLUSION

Survival in patients with acute lymphoblastic leukemia and COVID-19 is low, because the complications increase mortality, due to hematological suppression, and even more so with the presence of comorbidities, that accentuate severe clinical pictures, possibly by exacerbating the generalized inflammatory process, compromising the immune response, mainly in diabetics. Therefore, it is recommended continue with research related to the subject, in order, to propose management alternatives.

CONSENT

All authors declare that written informed consent was obtained from the patients for publication.

ETHICAL APPROVAL

The research work was examined and approved by the hospital research and ethics committee.

ACKNOWLEDGEMENTS

The authors appreciate the patients that participated in this research.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Terwilliger T, Abdul-Hay MJBCJ. Acute lymphoblastic leukemia: a comprehensive review and 2017 update. Blood cancer journal. 2017;7(6):e577.
DOI: 10.1038/bcj.2017.53.
2. Inaba H, Pei D, Wolf J, Howard SC, Hayden RT, Go M, et al. Infection-related complications during treatment for childhood acute lymphoblastic leukemia. Annals of Oncology. 2017; 28(2):386-392.
DOI: 10.1093/annonc/mdw557.
3. Rendón MME, Reyes ZNC, Villasís KMÁ, Meneses JS, Núñez AE. Global trend of survival in pediatric acute lymphoblastic leukemia: a review of the last four decades. Boletín Médico del Hospital Infantil de México. 2012:69(3):153-163.
4. Sánchez LMM, Jaramillo LIJ, Hernández LFÁ, Restrepo FH, Mejía CR, Álzate JDV. Residual minimal disease: breaking the paradigm of complete remission. Revista Cubana de Hematología, Inmunología y Hemoterapia. 2018;34(1):21-32.
5. Shchelkanov MY, Popova AY, Dedkov VG, Akimkin VG, Maleyev VV. History of investigation and current classification of coronaviruses (Nidovirales: Coronaviridae). Russian Journal of Infection and Immunity. 2020;10(2):221-246.
DOI: 10.15789/2220-7619-HOI-1412.
6. Shchelkanov MY, Kolobukhina LV, Burgasova OA, Kruzhkova IS, Maleev VV. COVID-19: etiology, clinical picture, treatment. Russian Journal of Infection and Immunity. 2020;10(3):421-445.
7. Liu YC, Kuo RL, Shih SR. COVID-19: The first documented coronavirus pandemic in history. Biomedical journal. 2020;43(4):328-333.
DOI: 10.1016/j.bj.2020.04.007.
8. Coronavirus Resource Center. World Map. Jhons Hopkins University; 2021.
Accessed 14 march 2021.
Avalible:
https://coronavirus.jhu.edu/map.html
9. COVID-19 México. General information. Health Secretary; 2021.
Accessed 14 march 2021.
Avalible: https://coronavirus.gob.mx/datos/
10. Van der Plas E, Qiu W, Nieman BJ, Yasui Y, Liu Q, Dixon SB, et al. Sex-Specific Associations Between Chemotherapy, Chronic Conditions, and Neurocognitive Impairment in Acute Lymphoblastic Leukemia Survivors: A Report From the Childhood Cancer Survivor Study. Journal of the National Cancer Institute. 2020;djaa136.
DOI: 10.1093/jnci/djaa136.
11. Scarfò L, Chatzikonstantinou T, Rigolin GM, Quaresmini G, Motta M, Vitale C, et al. COVID-19 severity and mortality in patients with chronic lymphocytic leukemia: a joint study by ERIC, the European Research Initiative on CLL, and CLL Campus. Leukemia. 2020;34(9):2354-2363. DOI: 10.1038/s41375-020-0959-x.
12. Reda G, Noto A, Cassin R, Zamprogna G, Borella C, Scarfò L, et al. Reply to "CLL

and COVID-19 at the Hospital Clinic of Barcelona: an interim report" Analysis of six hematological centers in Lombardy. Leukemia. 2020;34(9):2531-2532.
DOI: 10.1038/s41375-020-0966-y.

13. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes/metabolism research and reviews. 2020; 36(7):e3319.
DOI: 10.1002/dmrr.3319.
14. Cattaneo C, Daffini R, Pagani C, Salvetti M, Mancini V. Borlenghi E., et al. Clinical characteristics and risk factors for mortality in hematologic patients affected by COVID-19. Cancer. 2020;126(23):5069-5076.
DOI: 10.1002/cncr.33160.
15. Borah P, Mirgh S, Sharma SK, Bansal S, Dixit A, Dolai TK, et al. Effect of age, comorbidity and remission status on outcome of COVID-19 in patients with hematological malignancies. Blood Cells, Molecules, and Diseases. 2021;87: 102525.
DOI: 10.1016/j.bcmd.2020.102525.
16. García SJ, De La Cruz J, Cedillo Á, Llamas P, Duarte R, Jiménez-Yuste V, et al. Impact of hematologic malignancy and type of cancer therapy on COVID-19 severity and mortality: lessons from a large population-based registry study. Journal of hematology & oncology. 2020; 13(1):1-12.
DOI: 10.1186/s13045-020-00970-7.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/68658