COVID-19 IN ADOLESCENT PATIENTS IN THE BRAZILIAN POPULATION WITH SICKLE CELL ANEMIA: A REVIEW

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Abstract

Introduction: *Sickle cell anemia due to recent scientific evidence suggests that individuals with disease are considered a risk group and SARS-CoV-2 and spreads rapidly in this group of patients with diseases due to lack of inherited immunity, has a high lethality rate among young people and children and patients with associated comorbidities such as Diabetes Mellitus.* ***Objective:*** *to analyze the profile of patients with sickle cell anemia and their immunological motivations for worsening in positive cases of COVID-19 from a systematic review.* ***Results:*** *Initially, 217 articles were identified, of which 213 were removed because they were not related to the theme of the review, or because they were duplicated or did not have the abstract. The 04 selected articles were classified into two thematic axes to be performed the analysis.* ***Discussion:*** *This systematic review study is the first with sickle cell anemia and COVID-19 in the adolescent population with a limited resource configuration that shows the inherent need in the management of both diseases. However, in this systematic review, the four included studies showed a favorable evolution of the infectious process by COVID-19, and deaths occurred in adolescent patients who concomitantly had multiple comorbidities, for example, DM.* ***Conclusion:*** *It was found in this systematic review study that COVID-19 infection may accentuate the presence of vasculopathy in patients with sickle cell anemia and may increase pain to varying degrees.*

Keywords: COVID-19; sickle cell anemia; Coronavirus; Sickle-cell anemia; Treatment.

1. INTRODUCTION

COVID-19 in the period from 2020 to 2021 in the Brazilian adolescent population has caused a debate of a preventive, diagnostic and therapeutic action in public health researchers in Brazil, especially in patients with sickle cell anemia [01-04].

Sickle cell anemia due to recent scientific evidence suggests that individuals with the disease are considered a risk group and SARS-CoV-2 spreads rapidly in this group of patients with diseases due to lack of inherited immunity, has a high lethality rate among young people and children and patients with associated comorbidities such as Diabetes Mellitus [09,10,12,14,17].

Patients with COVID-19 present as symptoms cough, fever, tiredness, dyspnea, and other signs and symptoms [08, 09, and 10]. These signs and symptoms are aggravated in sickle cell anemia [10-18].

In the Brazilian population of young people with sickle cell anemia, little is known about the relationship between COVID-19 [12, 14, and 17]. However, in the literature, a specific discussion about the socioeconomic, ethnic and gender profile has not been identified, as well as the immunological motivations of patients with sickle cell anemia for worsening in cases positive with COVID-19 [17, 18, and 20].

The aim of this article was to analyze the profile of patients with sickle cell anemia and their immunological

motivations for worsening in positive cases of COVID-19 in the period from 2020 to 2021.

1.1 Methodology

A review of the literature on the subject was conducted in the PubMed of the National Library of Medicine for the period 2020 to 2021, using the keywords COVID-19, and sickle anemia, Coronavirus, Sickle-cell anemia and Treatment [22].

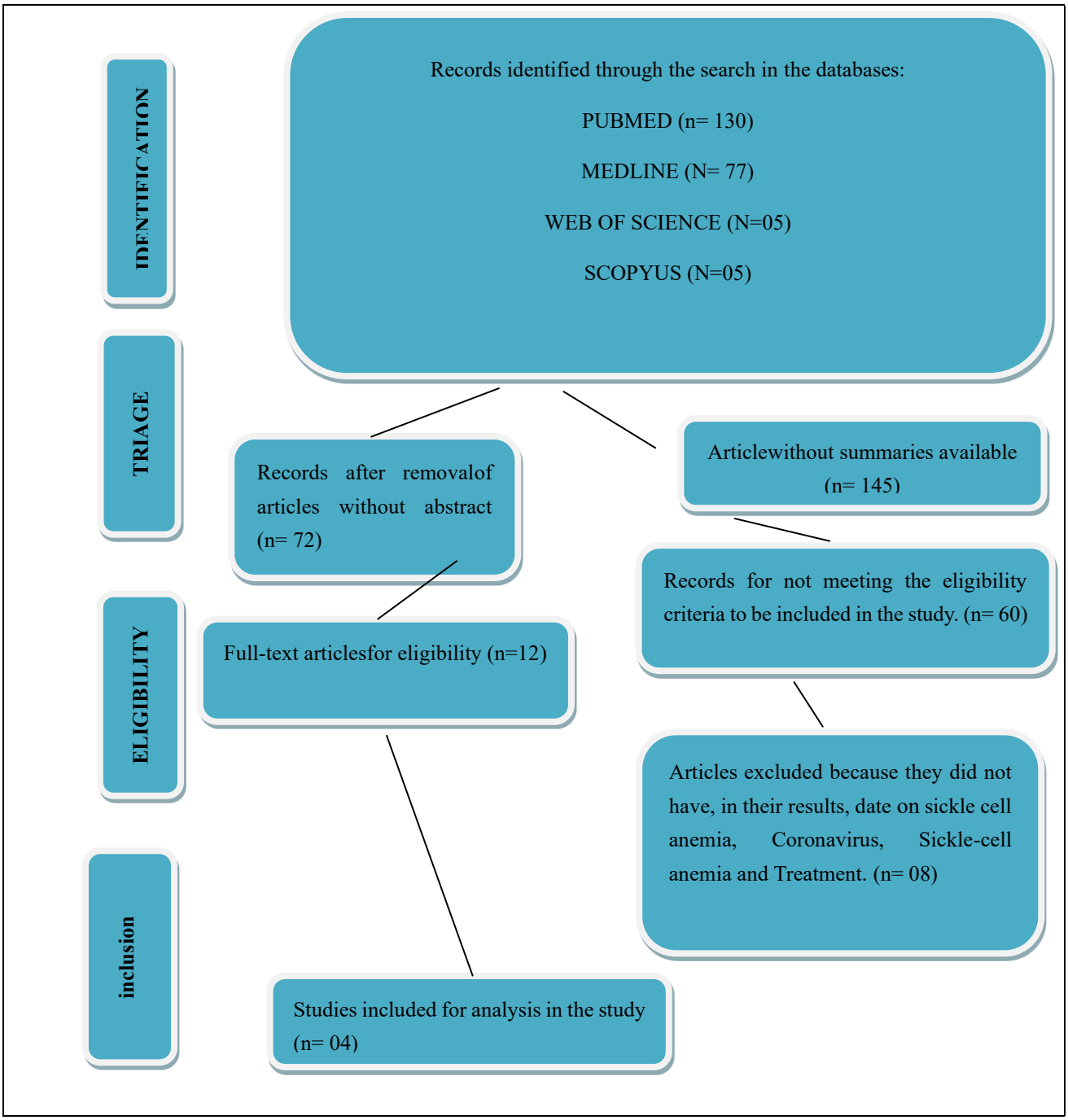
The criteria for selecting the articles were: contain all the complete descriptors or in parts of the title of the article, be written in Portuguese, English and Spanish, have been carried out with the young population in Brazil, aged over 12 years and less than 18 years [04, 12, 15, and 20].

Initially, 217 articles was identified, of which 213 were withdrawn because they were not related to the theme of the review, or because they were duplicated or did not have the abstract. The 04 articles selected were classified into two thematic axes to be performed the analysis [17-20].

Sociodemographic profile from the perspective of patients or groups of patients (45%, n= 01) [17, 18, 20]. Percentage of the complication rate in patients with sickle cell anemia undergoing treatment for COVID-19 (45%, n=01) [17-20]. We analyzed 04 articles related to patients with sickle cell anemia with worsening possibility for COVID-19 [17-20]. These were included the 04 articles that dealt with the immunological characteristics of the young population with sickle cell anemiarme that presented worsening the positive cases of COVID-19 [17-20].

1.1.2 Findings

Figure 1



Flowchart of the selection process of studies for inclusion in a systematic review[17, 18, 19, and 20]

In the end, four studies contemplated all inclusion criteria (FIGURE 1) and were included in the systematic review [22, 23].

When evaluating the quality design of the selected articles, which was expressed in Figure 02, it was possible to observe that the mean for the total score was 21 points (presenting SD= 1.07) according to the Down and Black instrument [22.23].

The article by Rocha et al (2020) (Article 01) reached a score of 22 points, being considered excellent. The authors' articles; Appiah-kubi et al (2020) (Article 03), Oliveira et al (2021) (Article 02) and Esposito et al (2021) (Article 04) obtained the score for quality assessment totaling 22 points, thus being considered good

[17-20].

Regarding the judgment of the items present for evaluation in the instrument, in this case, Down and Black, the dilemmas encountered were those related to the methodology, such as, external validity, internal validity (confounding) and confounding (selection images) [22,23].

Figure 02 -

ARTICLE	REPORTING (0 – 10)	EXTERNAL VALIDITY (0 – 03)	INTERNAL VALIDITY - VIEIS (0 – 07)	CONFOUNDING - SELECTION BIASES (0 – 06)	POWER (01)	TOTAL SCORE
ARTICLE 01	10	03	04	04	01	22
ARTICLE 02	09	03	04	04	01	21
ARTICLE 03	09	03	05	03	01	21
ARTICLE 04	09	03	04	04	01	21

Analysis of the risk of video from the studies included in accordance with the Down and Black criteria[22, 23].

In the analysis of the 217 articles, few publications were observed with the theme of the review, and when analyzing the four articles on patients with sickle cell anemia with COVID-19 included in this study in adolescents, it was verified that it was from the period of 2020 that the first studies with this approach began to appear [14,17-20].

Regarding the methodology used, it is observed that 03 articles are quantitative in nature and one qualitative [11,17,18,20]. Brazil conducted more studies on the theme (50%), followed by Italy (25%) and England (25%) (Table 01) [17-20].

The four articles were classified according to the main theme developed: Sociodemographic profile from the perspective of patients or groups of patients and percentage of the complication rate in patients with sickle cell anemia undergoing treatment for COVID-19 [04, 08, 12, and 17].

Table 01

ARTICLE INCLUDED	PARENTS OF STUDY	POPULATION STUDIED
ARTICLE 01	BRAZIL	Adolescents undergoing treatment for COVID-19 with sickle cell anemia in a university hospital.
ARTICLE 02	BRAZIL	Adolescent patients with injuries in COVID-19 in a

		university hospital.
ARTICLE 03	ITALIA	Adolescent patients undergoing outpatient treatment for sickle cell anemia with COVID-19 in a public health unit.
ARTICLE 04	ENGLAND	Adolescent patients undergoing private outpatient treatment for sickle cell anemia with COVID-19.

Information on the included articles with characterization of the sociodemographic profile in patients with sickle cell anemia undergoing treatment for COVID-19.

Table 01 shows the demographic characteristics of cases confirmed by RT-PCR for COVID-19 of adolescent patients with sickle cell anemia in the period from 20 to 2021 in the studies included for this study [17-20].

Overall, the included studies were conducted with adolescents aged over 12 years and less than 18 years, the country with the highest percentage of publication included was Brazil (n=02) [17-20].

Three studies presented the population studied with treatment in a public health unit, only one study performed outpatient treatment of pacientes in a private health unit [17-20].

The included studies conducted in the period of 2020 showed the correlation of sickle cell anemia with infection by the SARS-CoV-2 or COVID-19 virus with a higher risk for death due to the presence of elevated sickle cell erythrocytes with higher presence of pneumonia [17-20].

In the four studies included the presence of sickle cell erythrocytes were verified, and the four articles showed no evidence of severe damage to important organs due to this indicator [17-20].

It was verified that patients with sickle cell anemia with positive RT-PCR results for COVID-19 developed different levels of pain with a higher frequency of severe pain due to increased frequency of vasculopathy (Table 02) [17-20].

The included studies showed that the absence of dyspnea occurred in 80% of patients in the included studies and 60% of the patients analyzed in the included studies developed hypoxemia without initial signs of dyspnea [17-20].

Moreover, 12 patients with multiple morbidities died in the studies included for this systematic review (Table 02), 04 needed to be admitted to an intensive care unit bed [17-20].

Simultaneously, in the four articles included for analysis in this systematic review, fever, chest pain and dry cough was reported. The mean hospitalization period was 10 days [04, 17, and 20].

Table 02

TOTAL PATIENT	**PRESENCE OF SICKLE CELLIRETHRATICS**	**COVID-19 (RT-PCR POSITIVE) WITH INJURIES**
10	YES	08
07	YES	05
12	YES	07
12	YES	09

Thenalysis of complications in patients with sickle cell anemia undergoing treatment for COVID-

19[17,18,19,20].

The percentage of general lethality was 61% in the studies included for analysis of this systematic review and the result seems consistent with those observed over time in other studies [17-20]. In general, in the four studies, 16 patients were affected by comorbidities, specifically sickle cell anemia simultaneously with diabetes Mellitus [17-20].

In all cases in the articles included in the analysis of this systematic review, the SARS-CoV-2 favored to worsen the prognosis of patients with sickle cell anemia and cause death mainly from pneumonia [08, 17-20].

The main limitation of this systematic review study, although it can report the vast majority of cases of sickle cell anemia by analyzing included studies of patients with COVID-19 in the adolescent population with sickle cell anemia, cannot be considered representative of the Brazilian situation [17-20].

2. Discussion

Sickle cell anemia in adolescents and COVID-19 have presented significant challenges in screening, treatment and management and control of infection [05, 06, and 17].

This systematic review study is the first with sickle cell anemia and COVID-19 in the adolescent population with a limited resource configuration that shows the inherent need in the management of both diseases [08, 13, and 14].

The majority of deaths included in this systematic review of the selected studies were nosocomial in 2020 that occurred in Italy, England Brazil [17, 20].

The presence of sickle cell anemia in the adolescent population brings a much stronger chance ratio to increase mortality in adolescent patients with COVID-19 than other groups of patients with other diseases that may worsen with the development of pneumonia or other injuries [09, 16, and 20].

It is known that sickle cell traits affect about 300 million patients worldwide [10, 11]. Adolescent patients with sickle cell anemia should be included in the high-risk group to acquire COVID-19 because of low immune response, usually due to functional hypersplenism and systemic vasculopathy [14, 15, and 20].

Sickle cell anemia is a disease that leads to occlusion of vessels with hypercoagulability and that presents as a response the severe complications and failure of multiple organs and this can be aggravated through infection by the COVID-19 virus mainly through pneumonia [16, 17, 19].

However, in this systematic review, the four studies included showed a favorable evolution of the infectious process by COVID-19, and deaths occurred in adolescent patients who concomitantly had multiple comorbidities, for example, DM [17, 18, 20].

3. Conclusion

Taking into account the results found in this systematic review, both sickle cell anemia and COVID-19 are two diseases considered challenges for public health in Brazil and worldwide. It was found in this systematic review study that COVID-19 infection may accentuate the presence of vasculopathy in patients with sickle cell anemia and may increase pain to varying degrees.

4. References

1. Naik RP, Streiff MB, Lanzkron S. Sickle cell disease and venous thromboembolism: what the anticoagulation expert needs to know. J Thromb Thrombolysis. 2013; 35(3):352–8. DOI: 10.1007/s11239-013-0895-y
2. Johnston RB Jr, Newman SL, Struth AG. Increased susceptibility to infection in sickle cell disease: defects of opsonization and of splenic function. Birth Defects Orig Artic Ser. 1975; 11(1):322–7. PMID: 238677.
3. Hussain FA, Njoku FU, Saraf SL, Molokie RE, Gordeuk VR, Han J. COVID-19 infection in patients with sickle cell disease. Br J Haematol. 2020; 189(5):851–852.
4. From Luna Gonzalo, Habibi Anoosha, Deux Jean-Franc_ois, Colard Martin, Pham Hung d'Alexandry d'Orengiani Anne-Laure, Schlemmer Fr_ed_eric, Joher Nizar, Christian Kassasseya, Pawlotsky Jean Michel, Ourghanlian Cl_ement, Michel Marc, Mekontso-Dessap Armand, Pablo Bartolucci. Rapid and severe Covid-19 pneumonia with severe acute chest syndrome in a sickle cell patient successfully treated with tocilizumab. Am J Hematol. 2020; 95(7):876–878.
5. Heilbronner C, Berteloot L, Tremolieres P, Dupic L, De Saint Blanquat L, Lesage F et al Patients with Sickle cell disease and suspected COVID-19 in a pediatric ICU. Br J Haematol. 2020.
6. Odievre MH, by Marcellus C, Ducou Le Pointe H, Allali S, Romain AS, Youn J et al Dramatic improvement after tocilizumab of severe COVID-19 in a child with sickle cell disease and acute chest syndrome. Am J Hematol. 2020.
7. Nur E, Gaartman AE, van Tuijn CFJ, Tang MW, Biemond BJ. Vaso-occlusive crisis and acute chest syndrome in sickle cell disease due to 2019 novel coronavirus disease (COVID-19). Am J Hematol. 2020; 95 (6):725–6.
8. Deza Leon, M.P.; Redzepi, A.; McGrath, E.; Abdel-Haq, N.; Shawaqfeh, A.; Sethuraman, U.; Tilford, B.; Chopra, T.; Arora, H.; Ang, J.; et al. COVID-19-Associated Pediatric Multisystem Inflammatory Syndrome. J. Pediatric Infect. Dis. Soc. 2020, 9, 407–408.
9. McCloskey KA, Meenan J, Hall R, Da Tsitsikas. COVID-19 infection and sickle cell disease: a UK centre experience. Br J Haematol. 2020.
10. Beerkens F, John M, Puliafito B, Corbett V, Edwards C, Tremblay D. COVID-19 pneumonia as a cause of acute chest syndrome in an adult sickle cell patient. Am J Hematol. 2020.
11. Sahu KK, Siddiqui AD, Cerny J. Managing sickle cell patients with COVID-19 infection: the need to pool our collective experience. Br J Haematol. 2020.
12. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW et al Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020.
13. Kassir R. Risk of COVID-19 for patients with obesity. Obes Rev. 2020;21 (6):e13034.
14. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ et al Lymphopeni predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther. 2020; 5(1):33.
15. Cron RQ, Chatham WW. The Rheumatologist's role in COVID-19. J Rheumatol. 2020; 47(5):639–42.
16. Eloseily EM, Weiser P, Crayne CB, Haines H, Mannion ML, Stoll ML et al Benefit of Anakinra in

treating pediatric secondary hemophagocytic lymphohistiocytosis Arthritis Rheumatol. 2020;72(2):326–34.

17. Esposito, S.; Marchetti, F.; Lanari, M.; Caramelli, F.; From Fanti, A.; Vergine, G.; Iughetti, L.; Fornaro, M.; Suppiej, A.; Zone, S.; et al. COVID-19 Management in the Pediatric Age: Consensus Document of the COVID-19 Working Group in Paediatrics of the Emilia-Romagna Region (RE-CO-Ped), Italy. Int. J. Environ. Res. Public Health 2021, 18, 3919. https://doi.org/10.3390/ijerph18083919
18. APPIAH-KUBI et al. Varying presentations and favorable outcomes of COVID-19 infection in children and young adults with sickle cell disease: an additional case series with comparison to published cases. British Society for Haematology and John Wiley & Sons Ltd. 2020. https://doi.org/10.1111/ibjh.17013.
19. Oliveira et al. Educational technology on COVID-19 for families of children and adolescents with sickle cell disease. Rev Bras Enferm. 2021; 74(Suppl 1): https://doi.org/10.1590/0034-7167-2020-1045 e20201045.
20. F.G.F. Rocha, A.L.J.F. Campos, M.R.F. Teixeira, M.G. Vanderlei, L.F.B. Botelho. INFECTION BY COVID-19 AND SICKLE DISEASE ANEMIA: A LITERATURE REVIEW. Hematol transfuse cell ther. 2020; 42(S 2):S1–S567.
21. Langford, B.J.; So, M.; Raybardhan, S.; Leung, V.; Westwood, D.; MacFadden, D.R.; Soucy, J.R.; Daneman, N. Bacterial co-infection and secondary infection in patients with COVID-19: A living rapid review and meta-analysis. Clin. Microbiol. Get infected. 2020, 26.1622–1629.
22. Santos, C.M.C.; Pepper, C.A.M.; Noble, M.R.C.N. The PICO strategy for the construction of the research question and search for evidence. Latin American journal of nursing. v.15. n.3. 2007.
23. DE-LA-TORRE-UGARTE-GUANILO, M.C.; TAKAHASHI, R.F.; BERTOLOZZI, M. R. Systematic review: general concepts. Journal of the School of Nursing USP. v. 45, n. 5, p. 1260 - 1266, Oct. 2011.