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Pediatric Hematology Oncology Journal 7 (2022) 77–80

Contents lists available at ScienceDirect

Pediatric Hematology Oncology Journal

journal homepage: https://www.elsevier.com/journals/pediatric-hematology-oncology-journal/

Home isolation in transfusion-dependent thalassemia patients with SARS CoV2 infection: Experience from a developing country

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ARTICLE INFO

Article history:
Received 2 March 2022
Received in revised form
6 April 2022
Accepted 15 April 2022
Available online 19 April 2022

Keywords:
COVID-19
Transfusion dependent thalassemia
Iron chelation therapy
Deferasirox

ABSTRACT

Introduction: COVID-19 pandemic imposed challenges towards management of transfusion-dependent thalassemia patients (TDT). The need for regular blood transfusions and iron chelation therapy in these patients added further uncertainty about managing COVID-19 in this subset of patients.
Aims: To describe the clinical manifestations of SARS-CoV2 infection in patients with TDT and to evaluate feasibility of home management for patients with mild disease.
Methodology: The study involved TDT patients registered with thalassemia day care center, DMCH, who tested positive for COVID-19 by RTPCR. The demographics, clinical characteristics and baseline investigations were recorded. Patients with mild disease were managed at home and others were hospitalized. The daily home monitoring and the hospital course were noted and analyzed.
Results: The study involved 14 TDT patients who were infected with SARS-CoV2 with a mean age of 18.9 ± 6.7 years and a male to female ratio of 6:1. Five patients each were in low and high-risk groups and 4 patients were in highest risk group. The symptoms reported by these patients were fever, fatigue, sore throat etc. Two patients were hospitalized with one patient requiring oxygen therapy. He was discharged after 48 hours. The other patient had severe cardiac iron overload and diabetes mellitus. His iron chelation therapy was witheld during hospitalization. He presented with a cardiac arrhythmia later and was cardioverted. Thus, all other patients were continued on iron chelation with deferasirox. Twelve patients were successfully managed at home with regular telephonic monitoring.
Conclusion: Patients with thalassemia do not necessarily need hospitalization for management of COVID-19. Home management can be offered to patients with mild disease in a resourse limited setting. Iron chelation with deferasirox can be continued safely.

1. Introduction

Coronavirus disease (COVID-19), an infectious disease caused by the newly discovered novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was declared a pandemic by World Health Organization (WHO) in March 2020 [1].This disease posed unparallel challenges to the healthcare system, jeopardizing the lives of thousands of patients with hemoglobin disorders. In India, 34,544,882 people have been infected with SARS-CoV2 and 466,980 have died [2].Patients with pre-existing co-morbidities including obesity, cardiovascular diseases, diabetes mellitus, immunodeficiency states, and chronic liver and kidney diseases were ascertained to be at increased risk of mortality from coronavirus disease.

Thalassemia, an inherited hemoglobin disorder, is the commonest monogenic disorder that requires intensive life-long therapy and regular follow-up [3]. There is conflicting evidence on the outcome of

Abbreviations: TDT, Transfusion dependent thalassemia; COVID 19, Coronavirus diesease 2019; WHO, World Health Organisation; TDCC, Thalassemia Day Care Centre; RTPCR, Reverse Transcriptase Polymerase Chain Reaction; BMI, Body mass index; CRP, C-reactive protein; TIF, Thalassemia International Federation; MoHFW, Ministry of Health and Family Welfare; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2.

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Peer review under responsibility of Pediatric Hematology Oncology Chapter of Indian Academy of Pediatrics.

https://doi.org/10.1016/j.phoj.2022.04.024

COVID-19 in patients with thalassemia. Various authors have suggested that patients with thalassemia may be immune to SARS-CoV2 due to the absence of the potential target of the SARS-CoV2 virus and iron chelation therapy may also protect the patients against severe COVID 19 diseases due to anti-inflammatory and immunomodulatory effects. On the contrary, iron overload and its complications predispose the patients to a higher risk of severe COVID [4–6]. Studies from various parts of the world have shown an increased risk of mortality in patients with thalassemia [7–9]. We share our experience of managing patients with transfusion-dependent thalassemia with SARS-CoV2 in a resource-limited setting.

2. Aims and objectives

1. To describe the clinical features of COVID-19 in patients with transfusion-dependent thalassemia.
2. To assess the feasibility of home based management of mild COVID-19 in patients with transfusion-dependent thalassemia.

3. Materials and method

A retrospective study was conducted in the Thalassemia Day Care Centre of a tertiary care centre in Punjab after obtaining approval from the Institutional Ethics Committee. The patients with transfusion-dependent thalassemia who tested positive for SARS-CoV2 by reverse transcriptase polymerase chain reaction (RTPCR) were included in the study. Consent was obtained before enrolment in the study.

The data on patients' demographics including age, gender, height, weight, and body mass index (BMI); clinical characteristics including splenectomy status, associated complications, treatment given, and disease outcome and laboratory findings including hemoglobin, C-reactive protein (CRP), D-dimer, renal functions, liver functions, and imaging studies were collected from the patient records in a predesigned proforma.

Testing for SARS-CoV2 was performed only if a patient had symptoms of the disease or had been exposed to someone with SARS-CoV2 infection or as a part of screening for the hospital admission. No routine testing was performed before transfusion. Patients were risk-stratified as per the Thalassemia International Federation (TIF) risk assessment guidelines and the guidelines for the assessment of COVID-19 disease issued by the Ministry of Health and Family Welfare (MoHFW), Government of India [10–14]. Patients with mild COVID 19 were managed at home whereas those with moderate to severe COVID-19 were admitted. A baseline complete blood film, liver, and renal functions were done at the time of sending COVID-19 RTPCR.

Patients managed at home were followed up daily by a dedicated hemoglobinopathy nurse. Daily temperature and oxygen saturation (SpO2) recording charts were maintained till defervescence of fever. Patients obtained the home kits (Fateh Kit) issued by the Government of Punjab [15]. As per the existing guidelines, patients received zinc, multivitamins, and Ivermectin/doxycycline at home. Steroids were reserved for patients with moderate to severe COVID-19 disease and Vitamin C was not given to any of the patients. Patients were called for transfusion after they were RTPCR negative/10–14 days from the date of positive RTPCR as per the existing guidelines from the MoHFW, Government of India [11–14]. Iron chelation was held temporarily during the duration of fever for the first 3 patients, however, the subsequent patients continued deferasirox during COVID-19 illness. Imaging was performed only if the patient developed moderate to severe COVID-19 illness.

The data has been described in terms of range; mean ± standard deviation (±SD), median, frequencies (number of cases), and relative frequencies (percentages) as appropriate. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

Table 1
Baseline characteristics of patients with SARS-CoV2.

Characteristic	
No. of patients	14
Mean age	18.9 ± 6.7 years
Male: female	6:1
BMI	18.5 ± 2.7 kg/m^2
Mean Hb	8.9 ± 0.4 g/dL
Annual Requirement	224 ± 31 ml/kg/year
Average ferritin (prior to SARS-CoV2 infection)	3993 ± 2250 mg/dL
Cardiac MRI T2*	
< 6 ms	2
6–10 ms	0
11–20 s	2
>20 ms	10
Liver iron concentration	
Normal (<3)	6
Mild (3–7)	2
Moderate (7–15)	1
Severe (>15)	5
Cardiac dysfunction	1
Patients with hypothyroidism	2
Patients with diabetes	1
Splenectomized	2
Blood group	
A+	2
B+	8
O+	3
AB+	1
Iron chelation (No. of patients on)	
DFO + DFP	2
DFX	6
DFX + DFP	6

BMI: Body mass Index, Hb: hemoglobin, MRI: Magnetic resonance Imaging, DFO: Desferrioxamine, DFP: Deferiprone, DFX: Deferasirox.

4. Results

The thalassemia unit of the hospital provides regular transfusion services to 250 patients with transfusion-dependent thalassemia, 14 (0.06%) of whom had documented COVID -19 infection. The mean age of patients infected with SARS-CoV2 in our cohort was 18.9 ± 6.7 years with a range of 4–29 years. The male: female ratio was 6:1. The mean BMI in our study group was 18.5 ± 2.7 kg/m^2. The baseline characteristics of the study group are described in Table 1.

Risk stratification at the time of diagnosis with COVID-19 disease was done as per the TIF guidelines. There were 5 patients each in low-risk (Group A1) and high-risk (Group B), and 4 patients were at Highest-risk (Group C). There was no patient with Moderate risk (Group A2) (Table 2).

Eight patients were tested due to the presence of symptoms attributable to COVID-19 disease, 4 were tested due to a history of exposure, and 2 patients tested positive during screening for admission for management of fracture femur and pain abdomen respectively. The most common presenting complaint in the study group was fever (64.3% of patients) followed by fatigue (35.7% of the patients). Other chief complaints were headache, sore throat, loss of taste and smell, and vomiting. One patient complained of shortness of breath and reported desaturation at room air during home monitoring.

Two patients required hospitalization due to COVID 19 disease. One of these patients had severe cardiac iron overload with diabetes mellitus and the other patient had desaturation (<94%) on room air at home. The patient had aggravation of anemia and no

Table 2
TIF risk stratification.

Risk group→ Parameters↓	Low/ A1	Moderate A2	High B[c]	Highest C[c]
Age (in years)	<50	>50	>50	>50
Hb (last 3–4 years) g/dl	9.5 –10	9.5–10	8–9	<7
Ferritin (last 3–4 years) mg/dl	<2000	<2000	2000–3000	>3000
Cardiac MRI T2[c]	>20	>20	10–15	<10
LIC[a] (mg/g dry wt of liver)	<7	<7	7–10	>10
Comorbidities[b]	none	none	One of the following: DM, cardiac, endocrinopathy, respiratory	One of the following: DM, cardiac, endocrinopathy, respiratory
Splenectomized	no	no	Splenectomized + 1 another comorbidity	Splenectomized + 1 another comorbidity
No. of patients in the group	5	0	5	4

[a] LIC: liver iron concentration.
[b] Comorbidities: Comorbidities associated with thalassemia like diabetes, cardiac dysfunction, cirrhosis, transfusion transmitted infections, endocrine disorder like hypothyroidism, hypoparathyroidism, adrenal insufficiency.
[c] Presence of ≥2 of the following criteria.

desaturation was reported after packed cell transfusion. Computed tomography of the chest did not show any evidence of COVID pneumonia and the child was discharged after 48 h of observation. The child received 2 units of packed red blood cells during the hospital stay.

Three more patients experienced an exacerbation of anemia requiring admission for blood transfusion as a day-care treatment. None of the patients required admission to intensive care or ventilation. Oxygen therapy and steroids were used for the patient with desaturation on room air. Ivermectin, doxycycline, and hydroxychloroquine were used for 3 patients each as per the existing guidelines of MoHFW, Government of India. None of the patients were prescribed remdesivir and tocilizumab.

Iron chelation therapy was withheld in the patient with severe cardiac iron overload and diabetes mellitus. The patient presented to the emergency one-month post-discharge with cardiac arrhythmia and shock. He was given cardioversion and started on adenosine. The patient was discharged after stabilization on beta-blockers and intensive iron chelation with intravenous desferrioxamine.

5. Discussion

The current study attempts to fill the knowledge gap in the management of COVID-19 in thalassemia patients. There is not much evidence on the severity of COVID 19 and its management in this subset of patients. The current infection rate of COVID-19 is 30,045 patients per million population in India (0.03%). The infection rate in our TDCC was 0.06% (14/250) which is nearly double the general population in India. This may be due to increased chances

Table 3
The outcome of thalassemia patients with SARS-CoV2 infection.

	De Sanctis et al. [20]	Okar et al. [9]	Motta et al. [8]	Karimi M et al. [21]	Present study
Number of patients	10 8: TDT 2: NTDT	1	27 18: TDT 4: NTDT 5: SCD	48 34: TDT 14: NTDT	14 14: TDT
Mean age (years) Range	35.7 ± 11.7 (22–66)	25	43 ± 11	35.1 ± 11 (9–67)	18.9 ± 6.7
Mean BMI (kg/m^2)	19.39 ± 3.5	–		20.97 ± 1.87	18.5 ± 2.7
Male/Female	3/7	0/1	15/12	23/25	12/2
Mean ferritin (mg/dL)	1,653 ± 1,592 (Range: 225–5,960)	3.214	NA	1020 (Median) range: 142–17,000	3993 ± 2250
Blood group		NA	NA	NA	
A	5				2
B	4				8
AB	1				3
O	4				1
Disease		NA	NA		
Mild				15	13
Moderate				25	1
Severe				8	0
Symptomatic	7/10	No	22/27	33	10
Splenectomized patients	4	Yes	14	29	2
Comorbidities	3 CKD-1 Arrthymia-1 DM-1	None	20	38	DM-1
Oxygen requirement	4/10	No	6	33	1
Ventilation	1/3	No	3/6	8	None
Exacerbation of anemia		Yes	2	NA	4
Hospitalization	5	Yes	11	NA	2
Duration of hospitalization (days)	12.8 ± 5.4	4	18 ± 7	NA	Patient 1: 18 days Patient 2: 2 days
Deaths	1	0	0	8 (All with severe disease)	0

of exposure to the infection with frequent hospital visits for blood transfusions. Most patients in our cohort were either asymptomatic or had mild COVID disease with symptoms like fever, fatigue, and sore throat similar to the observation made by other authors [8,19]. A systemic review by Lee et al; showed that 61.5% of people were hospitalized for management and oxygen support was needed for 42.3% of the patients whereas only 2 patients (14.2%) needed hospitalization and one (7.1%) needed oxygen support in our cohort [19]. The remaining 12 (85.7%) patients were effectively managed at home with regular telephonic monitoring. Thus, the underlying diagnosis of transfusion-dependent thalassemia did not lead to excess morbidity and mortality in our cohort.

Hydroxychloroquine/Ivermectin are not indicated for the management of COVID-19 as per recent reviews [16–18]. However, they were used in some of our patients when they were included in the guidelines issued by the health ministry. Two patients in our study population were hospitalized for management of COVID-19. Iron chelation was stopped for the first patient who was diagnosed as COVID-19 positive in March 2020 as there was no experience in managing COVID 19 at that time and the effect of chelation on COVID-19 was unknown. The patient remained hospitalized for 18 days till his 2 specimens for RTPCR came back negative. As this patient already had severe cardiac iron overload, withholding the iron chelation proved detrimental and the patient developed cardiac arrhythmias in a month. Subsequent patients with COVID-19 continued to take iron chelation with deferasirox and recovered without any adverse effects. However, deferiprone was stopped due to fear of agranulocytosis in presence of a viral infection.

Various studies have demonstrated an increased risk of morbidity and mortality in patients with coexisting comorbidities. Patients with advancing age were more likely to need hospital admission (Table 3). The younger mean age of our patients may be a reason for better outcomes in this group.

During the second wave of COVID 19 when the entire country was reeling under the lack of oxygen and hospital beds, our ability to manage patients at home helped in better utilization of resources. Only patients with moderate to severe COVID disease needed admission. The underlying diagnosis of transfusion-dependent thalassemia did not lead to excess morbidity and mortality in our cohort.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Declaration of competing interest

The authors have no conflict of interest to declare.

Acknowledgments

Patients with thalassemia and their families for being a part of this study. Hemoglobinopathy nurses Mrs. Balwinder Kaur and Baljit Kaur for diligently following up with the patients during home isolation. Child psychologist Priyanka Dewan for counseling the patients during home isolation and keeping their morale high.

References

[1] World Health Organization. Coronavirus disease 2019 (COVID-19): situation report, 51 [online] Apps.who.int. Available at: https://apps.who.int/iris/handle/10665/331475. [Accessed 3 March 2022].
[2] India COVID - Coronavirus Statistics - Worldometer [online] Available at: https://www.worldometers.info/coronavirus/country/india. [Accessed 3 March 2022].
[3] Cappellini MD, Cohen A, Porter J, Taher A, Viprakasit V, editors. Guidelines for the management of transfusion dependent thalassaemia (TDT). third ed. Cyprus, Nicosia: Thalassemia International Federation; 2014.
[4] Lansiaux E, Pébaÿ PP, Picard JL, Son-Forget J. COVID-19: beta-thalassemia subjects immunised? Med Hypotheses 2020;142:109827.
[5] Drouin E. Beta-thalassemia may protect against COVID 19. Med Hypotheses 2020;143:110014.
[6] Dalamaga M, Karampela I, Mantzoros CS. Commentary: could iron chelators prove to be useful as an adjunct to COVID-19 Treatment Regimens? Metabolism 2020;108:154260.
[7] Zafari M, Rad MTS, Mohseni F, Nikbakht N. β-Thalassemia major and coronavirus-19, mortality and morbidity: a systematic review study. Hemoglobin 2021;45:1–4.
[8] Motta I, Pinto VM, Longo F, Bonetti F, De Michele E, Piperno A, et al. COVID 19 and hemoglobinopathies: update of the Italian experience. Blood 2020;136:17–8.
[9] Okar L, Ali M, Parengal J, Yassin MA. COVID-19 and thalassemia beta major in splenectomized patient: clinical case progression and literature review. Clinical Case Reports 2020;8:2918–22.
[10] Thalassemia International Federation. COVID-19 & haemoglobin disorders: a classification of risk groups & other considerations. - TIF. [online] Available at: . 2020. 25 March 2021], https://thalassaemia.org.cy/publications/covid-19-haemoglobin-disorders-a-classification-of-risk-groups-other-considerations-2020/.
[11] Ministry of Health and Family Welfare, Government of India. Discharge policy of nCoV case [online] Available from, https://www.mohfw.gov.in/pdf/Corona%20Discharge-Policy.pdf. [Accessed 25 November 2021].
[12] Ministry of Health and Family Welfare, Government of India. Revised national clinical management guideline for COVID 19 [online] Available at: https://www.mohfw.gov.in/pdf/RevisedNationalClinicalManagementGuidelineforCOVID1931032020.pdf. [Accessed 25 November 2021].
[13] Ministry of Health and Family Welfare, Government of India. Updated Revised Discharge Policy for COVID 19. [online] Available at: https://www.mohfw.gov.in/pdf/RevisedDischargePolicyforCOVID19.pdf. [Accessed 25 November 2021].
[14] Ministry of Health and Family Welfare, Government of India. Updated FAQs on Revised Discharge Policy. [online] Available at, https://www.mohfw.gov.in/pdf/FAQsonRevisedDischargePolicy.pdf. [Accessed 25 November 2021].
[15] Punjab CM launches Fateh kits for COVID patients in hospital and home isolation. 2020 [online] Available at, http://www.diprpunjab.gov. [Accessed 25 November 2021].
[16] NIH. COVID 19 treatment guidelines/Antiviral therapy/Chloroquine or Hydroxychloroquine and/or Azithromycin [online] Available at: https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/chloroquine-or-hydroxychloroquine-and-or-azithromycin/. [Accessed 2 March 2022].
[17] NIH. COVID 19 treatment guidelines/Antiviral therapy/Ivermectin [online] Available at: https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ivermectin/. [Accessed 2 March 2022].
[18] Hindustan Times. Govt drops Ivermectin, HCQ and favipiravir from Covid-19 treatment list [online] Available at: https://www.hindustantimes.com/india-news/govt-drops-ivermectin-hcq-and-favipiravir-from-covid-19-treatment-list-101623058343019.html. [Accessed 2 March 2022].
[19] Lee JX, Chieng WK, Lau SCD, Tan CE. COVID-19 and hemoglobinopathies: a systematic review of clinical presentations, investigations, and outcomes. Front Med 2021;8:757510.
[20] De Sanctis Vincenzo, Canatan Duran, Corrons Joan Lluis Vives, Karimi Mehran, Daar Shahina, Kattamis Christos. Preliminary data on COVID-19 in patients with hemoglobinopathies: A multicentre ICET-A study. Mediterr J Hematol Infect Dis 2020;12(1).
[21] Karimi Mehran, Haghpanah Sezaneh, Azarkeivan Azita, Matin Sara, Safaei Arash, De Sanctis Vincenzo. Coronavirus disease 2019 (COVID-19) severity in patients with Thalassemias: A nationwide Iranian experience. Mediterr J Hematol Infect Dis 2021;13(1). https://doi.org/10.4084/MJHID.2021.008.