

Supplementary Files

Supplementary Table 1. Search Strategy in the databases.

Database	Search Details
A) PubMed	Population: (“Thalassemia*” [MeSH Terms]) OR (“beta-thalassemia” [MeSH Terms]) OR (Hemoglobinopathy [MeSH Terms]) OR (“Anemia, Sickle Cell” [MeSH Terms]) OR (“Sickle Cell Trait” [MeSH Terms]) OR (Thalassemia* [Title/Abstract]) OR (hemoglobinopathy* [Title/Abstract]) OR (“beta*Thalassemia*” [Title/Abstract]) OR (“β*thalassemia*” [Title/Abstract]) OR (“Haemoglobinopathy “ [Title/Abstract]) OR (“Thalassaemia” [Title/Abstract]) OR (“Mediterranean Anemia*” [Title/Abstract]) OR (“Cooley*Anemia*” [Title/Abstract]) OR (“Transfusion*dependent thalassemia*” [Title/Abstract]) OR (“TDT” [Title/Abstract]) OR (“Non*transfusion*dependent thalassemia*” [Title/Abstract]) OR (“NTDT” [Title/Abstract]) OR (“Sickle cell disease” [Title/Abstract]) OR (“SCD” [Title/Abstract]) OR (“Sickle cell” [Title/Abstract]) OR (“Sickle cell anemia” [Title/Abstract]) OR (“HbSS” [Title/Abstract]) OR (“HbS β “ [Title/Abstract]) OR (“HbSc” [Title/Abstract]) OR (“Hbpathy” [Title/Abstract]) OR (“Sickle cell trait” [Title/Abstract]) AND (“COVID-19” [MeSH Terms]) OR (“SARS-CoV-2” [MeSH Terms]) OR (Covid [Title/Abstract]) OR (“Coronavirus disease-19” [Title/Abstract]) OR (“COVID-19” [Title/Abstract]) OR (“Severe acute respiratory syndrome-coronavirus-2” [Title/Abstract]) OR (“SARS-CoV-2” [Title/Abstract]) OR (“Coronavirus” [Title/Abstract]) OR (“Coronavirus disease 2019” [Title/Abstract])
B) Web of Science	Population: Topic = (“Thalassemia*” OR “hemoglobinopathy*” OR “beta*Thalassemia*” OR “β*thalassemia*” OR “Thalassaemia*” OR “haemoglobinopathy” OR “Mediterranean Anemia*” OR “Cooley*Anemia*” OR “Transfusion*dependent thalassemia” OR “TDT” OR “Non*transfusion*dependent thalassemia” OR “NTDT” OR “Sickle cell disease” OR “SCD” OR “Sickle cell” OR “Sickle cell anemia” OR “HbSS” OR “HbSβ” OR “HbSc” OR “Hbpathy” OR “Sickle cell trait”) AND Topic = (“Covid” OR “Coronavirus disease-19” OR “COVID-19” OR “Severe acute respiratory syndrome-coronavirus-2” OR “SARS-CoV-2” OR “Coronavirus” OR “Coronavirus disease 2019”)

C) Scopus	INDEXTERMS (“Thalassemia” OR “beta-Thalassemia” OR “Sickle Cell”) OR TITLE-ABS-KEY (“Thalassemia” OR “hemoglobinopathy” OR “beta-Thalassemia” OR “Thalassaemia” OR “haemoglobinopathy” OR “ β -thalassemia” OR “Mediterranean Anemia” OR “Cooley Anemia” OR “Transfusion dependent thalassemia” OR “TDT” OR “Non transfusion dependent thalassemia” OR “NTDT” OR “Sickle cell disease” OR “SCD” OR “Sickle cell” OR “Sickle cell anemia” OR “HbSS” OR “HbS β ” OR “HbSC” OR “Hbpathy” OR “Sickle cell trait”) AND INDEXTERMS (“COVID-19” OR “SARS-CoV-2”) OR TITLE-ABS-KEY (“Covid” OR “Coronavirus disease-19” OR “COVID-19” OR “Severe acute respiratory syndrome-coronavirus-2” OR “SARS-CoV-2” OR “Coronavirus” OR “Coronavirus disease 2019”)
D) Scholar	(“thalassemia” AND “covid”); (“sickle” AND “covid”)

A) PubMed: <https://pubmed.ncbi.nlm.nih.gov/advanced/>

B) Web of Sciences: <https://login.webofknowledge.com>

C) Scopus: <https://www.scopus.com/>

D) Scholar: <https://scholar.google.com>

Supplementary Table 2. Study of the quality assessment of COVID-19 infection and hemoglobinopathies.

References	[1]	[2]	[3]	[3]	[4]	[5]	[6]	[7]	[8]
Was the sample appropriate to address the target population?	yes	yes	yes	yes	yes	yes	yes	yes	yes
Were study participants sampled in an appropriate way?	yes	yes	yes	yes	yes	yes	yes	yes	yes
Was the sample size adequate?	yes	yes	yes	yes	yes	yes	yes	yes	yes
Were the study subjects and the setting described in detail?	yes	yes	yes	yes	yes	yes	yes	yes	yes
Was the data analysis done with sufficient coverage of the identified sample?	yes	yes	NA	yes	NA	yes	yes	yes	yes
Were valid methods used for the identification of the condition?	yes	yes	yes	yes	yes	yes	yes	yes	yes
Was the condition measured in a standard, reliable way for all participants?	yes	yes	yes	yes	yes	yes	yes	yes	yes
Was there an appropriate statistical analysis?	yes	yes	NA	yes	NA	yes	yes	yes	yes
Was the response rate adequate, and if not, was the low response rate managed appropriately?	yes	yes	yes	yes	yes	yes	yes	yes	yes
Total score	9	9	7	9	7	9	9	9	9

COVID-19: coronavirus-19; NA: not applicable.

[1] AbdulRahman A, AlAli S, Yaghi O, *et al.* COVID-19 and sickle cell disease in Bahrain. *Int J Infect Dis.* 2020;101:14-16.

[2] Karimi M, Haghpanah S, Zarei T, *et al.* Prevalence and severity of coronavirus disease 2019 (COVID-19) in transfusion dependent and non-transfusion dependent β -thalassemia patients and effects of associated comorbidities: an Iranian nationwide study. *Acta Biomed.* 2020;91(3):e2020007.

[3] Motta I, De Amicis MM, Pinto VM, *et al.* SARS-CoV-2 infection in beta thalassemia: preliminary data from the Italian experience. *Am J Hematol.* 2020;95(8):E198–E199.

- [4] Telfer P, De la Fuente J, Sohal M, *et al.* Real-time national survey of COVID-19 in hemoglobinopathy and rare inherited anemia patients. *Haematologica*. 2020;105(11):2651–2654.
- [5] Arlet J-B, de Luna G, Khimoud D, *et al.* Prognosis of patients with sickle cell disease and COVID-19: a French experience. *Lancet Haematol*. 2020;7(9):e632–e634.
- [6] McCloskey KA, Meenan J, Hall R, Tsitsikas DA. COVID-19 infection and sickle cell disease: a UK centre experience. *Br J Haematol*. 2020;190(2):e57–e58.
- [7] Panepinto JA, Brandow A, Mucalo L, *et al.* Coronavirus disease among persons with sickle cell disease, United States, March 20-May 21, 2020. *Emerg Infect Dis*. 2020;26(10):2473–2476.
- [8] Minniti CP, Zaidi AU, Nouraie M, *et al.* Clinical predictors of poor outcomes in patients with sickle cell disease and COVID-19 infection. *Blood Adv*. 2021;5(1):207–215. doi: 10.1182/bloodadvances.2020003456.

Supplementary Table 3. The COVID-19 incidence rate per 100,000 person-day in patients with hemoglobinopathies, transfusion-dependent thalassemia and non-transfusion-dependent thalassemia.

Refs.	Country	Incidence Rate (95% CI)				
		Hemoglobinopathy	TDT	NTDT	Thalassemia	Sickle cell disease
[1]	Turkey	1.09 (−0.42-2.61)	1.92 (−0.74-4.59)	0	1.54 (−0.59-3.67)	0
[1]	Azerbaijan	0.62 (−0.24-1.48)	0.97 (−0.37-2.31)	0	0.66 (−0.25-1.58)	0
[1]	Cyprus	1.98 (−1.90-5.87)	2.56 (−2.46-7.58)	0	2.17 (−2.09-6.44)	0
[1]	Oman	0.81 (−0.10-1.72)	0	0	0	0.95 (−0.12-2.02)
[2]	Bahrain	26.45 (5.29-47.62)	–	–	–	26.46 (5.29-47.62)
[3]	Iran	1.41 (0.99-1.83)	1.20 (0.79-1.62)	2.76 (1.12-4.39)	1.41 (0.99-1.83)	<u>?</u>
[4]	UK	21.97 (17.27-26.66)	–	–	<u>?</u>	21.97 (17.27-26.67)
[5]	Italy	1.59 (0.65-2.53)	2.00 (0.76-3.24)	0.52 (−0.50-1.55)	1.59 (0.65-2.54)	–
[6]	USA	22.99 (17.44-28.54)	–	–	–	23.00 (17.45-28.54)
Overall	Index	4.44 (2.58-6.29)	1.28 (0.90-1.66)	1.55 (−0.63-3.73)	1.34 (0.99-1.69)	17.22 (1.81-32.64)
	z	4.70	6.81	1.39	7.51	2.19
	p value	<0.001	<0.001	0.164	<0.001	0.028
I ² (%) ^a		94.4 (37.3-98.0)	0 (0.0-46.3)	80.6 (1.0-96.1)	0	97.7 (1.0-99.4)
p value		<0.001	0.720	0.023	0.617	<0.001
Egger's test ^b	95% CI for bias	(−0.13-8.29)	(−0.83-2.04)	>0.999	(−2.30-2.32)	(−5.43-19.36)
	p value	0.056	0.273	>0.999	0.992	0.137

COVID-19: coronavirus-19; 95% CI: 95% confidence interval; z: standard normal distribution.

^a Proportion of total variation in effect estimate due to between-study heterogeneity.

^b Egger's test for small-study effects.

- [1] de Sanctis V, Canatan D, Vives Corrons JL, *et al.* Preliminary data on COVID-19 in patients with hemoglobinopathies: a multicentre ICET-A study. *Mediterr J Hematol Infect Dis.* 2020;12(1):2020046.
- [2] AbdulRahman A, AlAli S, Yaghi O, *et al.* COVID-19 and sickle cell disease in Bahrain. *Int J Infect Dis.* 2020;101:14-16.
- [3] Karimi M, Haghpanah S, Zarei T, *et al.* Prevalence and severity of coronavirus disease 2019 (COVID-19) in transfusion dependent and non-transfusion dependent β -thalassemia patients and effects of associated comorbidities: an Iranian nationwide study. *Acta Biomed.* 2020;91(3):e2020007.
- [4] Telfer P, De la Fuente J, Sohal M, *et al.* Real-time national survey of COVID-19 in hemoglobinopathy and rare inherited anemia patients. *Haematologica.* 2020;105(11):2651–2654.
- [5] Motta I, De Amicis MM, Pinto VM, *et al.* SARS-CoV-2 infection in beta thalassemia: preliminary data from the Italian experience. *Am J Hematol.* 2020;95(8):E198–E199.
- [6] Minniti CP, Zaidi AU, Nouraie M, *et al.* Clinical predictors of poor outcomes in patients with sickle cell disease and COVID-19 infection. *Blood Adv.* 2021;5(1):207–215. doi: 10.1182/bloodadvances.2020003456.

Supplementary Table 4. Incidence rate of death per 1000 person-day due to COVID-19 in patients with hemoglobinopathies.

Reference	Country	Incidence Rate	95% CI ^a
[1]	Iran	0.12	0.345-1.89
[2]	France	0.70	–0.27-1.69
[3]	UK	3.78	–3.62-11.19
[4]	USA	1.17	0.53-1.81
[5]	Bahrain	0	–
[6]	Italy	0	–

Overall	Index	1.07	0.63-1.51
	z	4.78	—
	p value	<0.001	—
I ² (%) ^b		0	—
p value		0.762	—
Egger's test ^c , p value, 95% CI for bias		0.585	−2.68-3.63

COVID-19: coronavirus-19; 95% CI: 95% confidence interval; z: standard normal distribution.

^a 95% CI for incidence rate.

^b Proportion of total variation in effect estimate due to between-study heterogeneity.

^c Egger's test for small-study effects.

- [1] Karimi M, Haghpanah S, Zarei T, *et al.* Prevalence and severity of coronavirus disease 2019 (COVID-19) in transfusion dependent and non-transfusion dependent β -thalassemia patients and effects of associated comorbidities: an Iranian nationwide study. *Acta Biomed.* 2020;91(3):e2020007.
- [2] Arlet J-B, de Luna G, Khimoud D, *et al.* Prognosis of patients with sickle cell disease and COVID-19: a French experience. *Lancet Haematol.* 2020;7(9):e632–e634.
- [3] McCloskey KA, Meenan J, Hall R, Tsitsikas DA. COVID-19 infection and sickle cell disease: a UK centre experience. *Br J Haematol.* 2020;190(2):e57–e58.
- [4] Panepinto JA, Brandow A, Mucalo L, *et al.* Coronavirus disease among persons with sickle cell disease, United States, March 20-May 21, 2020. *Emerg Infect Dis.* 2020;26(10):2473–2476.
- [5] AbdulRahman A, AlAli S, Yaghi O, *et al.* COVID-19 and sickle cell disease in Bahrain. *Int J Infect Dis.* 2020;101:14-16.
- [6] Motta I, De Amicis MM, Pinto VM, *et al.* SARS-CoV-2 infection in beta thalassemia: preliminary data from the Italian experience. *Am J Hematol.* 2020;95(8):E198–E199.