findings provide further evidence for a high prevalence of VTE in critically ill patients with SARS-CoV-2 infection. These findings are important for identifying a high risk group for adverse outcomes and to raise clinicians' awareness of VTE risk amongst critically ill COVID-19 patients.

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Author contributions

JAH and SEJ collected and analysed the data. JAH, ELB, and SEJ designed this research study and wrote this manuscript.

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Prevalence and mortality in β-thalassaemias due to outbreak of novel coronavirus disease (COVID-19): the nationwide Iranian experience

In late December 2019, an ongoing outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that was termed Coronavirus Disease 2019 (COVID-19), was reported in Wuhan, China.[1]

A total of 3 018 681 patients have been reported globally and 92 584 confirmed cases have been documented in Iran, until April 29th, 2020. The death toll from the COVID-19 outbreak at that time was 207 973 worldwide, and 5877 in Iran.

Transfusion-dependent and non-transfusion-dependent thalassaemia (TDT and NTDT) patients may have coexistent comorbidities due to iron overload[2,3] that can expose them to a potentially higher risk of complications attributable to COVID-19, compared to the normal population.[4]

Limited data about frequency and outcomes of infected COVID-19 patients with thalassaemia are currently available in the literature. In this study, the primary aim was to

determine the prevalence, severity and mortality rate of COVID-19 in patients with TDT and NTDT living in Iran. Moreover, we evaluated the associated risk factors in this vulnerable group of patients.

A multicentre, retrospective, cross-sectional study was obtained across all comprehensive thalassaemia centres in Iran, from January to 29 April 2020. All suspected and confirmed COVID-19 cases from a total of 15 950 TDT (regular transfusion every 2–4 weeks) and 2 400 NTDT patients registered by the Iranian Ministry of Health (MOH) were evaluated.

Epidemiological data, demographics, clinical characteristics (type of thalassaemia, splenectomy status, and associated complications), laboratory, imaging, and outcome data were collected by analyzing patients' electronic medical records.

A coronavirus test was performed based on the Berlin protocol by the real-time reverse-transcription polymerase chain reaction (RT-PCR).[5]

Clinical and imaging manifestations for diagnosis of suspected cases were: fever, shortness of breath, fatigue, dry cough, and chest computed tomography scan suggestive of SARS-CoV-2 pneumonia infection.

All patients were classified as mild, moderate, severe, and critically ill according to the guidance issued by the National Health Commission of China (accessed February, 2020).[6]

Hydroxychloroquine combined with lopinavir/ritonavir or atazanavir were the suggested treatment regimens according to guidelines issued by the Iranian MOH.

The study protocol was approved by the Ethical Committee of Shiraz University of Medical Sciences (Code:1399.228). The patients or their legal guardians signed a consent form to protect the confidentiality and their identity.

Qualitative and quantitative variables were compared using Fisher's exact test and the Mann–Whitney test respectively between the two groups of confirmed COVID-19 cases with the outcomes of recovery or death. COVID-19 prevalence and mortality rate were calculated in confirmed cases and compared, by the chi-square test, with those reported in the general Iranian population. A P value <0·05 was considered statistically significant.

Fifteen confirmed cases (12 TDT and 3 NTDT) and eight symptomatic β-thalassaemia patients (6 TDT and 2 NTDT) suspected of being infected with COVID-19 without performing the test, were detected in a total of 18 350 Iranian β-thalassaemia patients.

Detailed data of confirmed cases are presented in Table SI. Clinical characteristics and laboratory data of confirmed and suspected COVID-19 cases are summarized in Table I below. Almost all the thalassaemia patients with COVID-19 were from Northern and Southern Iran as well as the central part, which were the epicentres for COVID-19 disease.

Seventeen patients (73·9%) had mild to moderate symptoms and recovered, while six patients died (26·1%, two TDT and four NTDT). More than 60% of all patients had at least one comorbidity (Table I).

The clinical and laboratory data were compared in RT-PCR positive β-thalassaemia patients who recovered versus those who deceased (Table II).

The two groups were comparable in nearly all variables except for the thalassaemia type. Moreover, major underlying diseases including diabetes, heart disease, hypertension, and pulmonary artery hypertension showed a significantly higher frequency in the deceased group compared to the recovered group (100% vs. 27·3%; $P = 0·026$). Eighty per cent of our patients with confirmed COVID-19 were splenectomized but splenectomy was not significantly associated with the fatal outcome (II).

The prevalence of confirmed COVID-19 was 11·01/10 000 in the general population compared to 8·17/10 000 in patients with β-thalassaemia up to 29 April 2020 ($P = 0·246$). On the other hand, at the same date, the mortality rate was significantly higher in patients with β-thalassaemia (26·6%) compared to the general population (6·34%) ($P = 0·001$).

According to a COVID-19 webinar presented by the European Hematology Association, 51 patients with TDT and COVID-19 have been reported from nine countries (https://ehaweb.org/COVID-19/webinars.session 3; 16 April 2020). Most of them presented mild to moderate respiratory symptoms (46 out of 51) and three out of five hospitalized patients died.

A small cohort study from Northern Italy, which was the epicentre for COVID-19 in Europe, experienced relatively mild to moderate COVID-19 disease (11 cases: 10 with TDT and one with NTDT) compared to the general population and all infected thalassaemia patients recovered despite all of them having associated comorbidities.[7]

Our survey is the first nationwide investigation that systematically evaluated the prevalence of COVID-19, the presence of comorbidities and the prognosis in patients with TDT and NTDT in Iran.

Most of our patients showed mild to moderate disease, as reported in Italy, but six cases developed severe symptoms contributing to the patients' mortality while no deaths were reported in Italian patients with thalassaemias.[7]

The significantly higher mortality rate in COVID-19 thalassaemic patients compared to the general Iranian population may be attributed to the presence of additional risk factors in patients with thalassaemias.[4]

Moreover, a significantly higher frequency of major underlying diseases in the deceased group compared to the recovery group emphasizes the importance of adherence to iron chelation regiment in thalassaemia patients.

No cases of paediatric or adolescent thalassaemia with COVID-19 were observed in our study, which was similar to fewer children being infected by COVID-19 in the general population.[8]

One observational study reported subjects with blood group A were at higher risk while subjects with blood group O were associated with a lower risk for SARS-CoV-2 infection.[9] Our

Table I. Summary of clinical characteristics and laboratory data of confirmed and suspected COVID-19 cases in patients with β-thalassaemias.

Parameters	COVID-19 (RT-PCR positive; *n* = 15)	Suspected COVID-19 (*n* = 8)
Age (year), mean ± *SD*, min–max	36·1 ± 12·1, 22–66	39·6 ± 9·03, 30–54
Sex (m/f)	7/8	7/1
Thalassaemia type (*n*, %)	=	=
TDT	12 (80)	6 (75)
NTDT	3 (20)	2 (25)
Splenectomy (yes) (*n*, %)	12 (80)	4 (57·1)
Serum ferritin (ng/ml)		
Mean ± *SD*	1725 ± 2245	2847 ± 3189
Median (min–max)	830 (225–8200)	2000 (545–9556)
(*n*, %)	=	=
≤2000	11(78·6)	4 (57·1)
>2000	3 (21·4)	3 (42·9)
Haemoglobin (g/l), mean ± *SD*	89 ± 6·8	84 ± 14·4
White blood cell count (per μl), mean ± *SD*	15 885 ± 11 579	22 914 ± 15 830
Platelet count (per μl), mean ± *SD*	530 820 ± 289 787	514 428 ± 213 550
Heart or liver iron overload (moderate and severe) (*n*, %)	5 (33·3)	3 (37·5)
Hydroxycarbamide (yes) (*n*, %)	3 (20)	4 (50)
Comorbidities (yes) (*n*, %)	12 (80%)	5 (62·5)
Major underlying disease*	7 (46·7)	4 (50)
Symptoms (*N*, %)	=	=
Fever	10 (66·7)	3 (37·5)
Cough	9 (60)	2 (25)
Dyspnoea	4 (26·6)	2 (25)
Rhinorrhoea and sneezing	1 (6·6)	NR
Sinusitis	1 (6·6)	NR
Myalgia	NR	1 (12·5)
Diarrhoea	NR	1 (12·5)
Anosmia and hearing loss	1 (6·6)	NR
Weakness in lower extremities	1 (6·6)	NR
Condition	=	=
Recovered	11 (73·3)	6 (75)
Death	4 (26·6)	2 (25)

RT-PCR, reverse-transcription polymerase chain reaction; TDT, transfusion-dependent β-thalassaemia; NTDT, non-transfusion-dependent β-thalassaemia; NR, not reported.

*Heart disease, diabetes, pulmonary artery hypertension, and hypertension.

Table II. Comparison of demographic and clinical characteristics between confirmed COVID-19 cases in patients with β-thalassaemias based on disease outcome.

	Recovered *N* = 11	Dead *N* = 4	*P* value
Age (year), Median (min–max)	36 (22–66)	32·5 (30–60)	0·949
Sex (m) (*n*, %)	5 (45·5)	2(50)	>0·999
Thalassaemia type (TDT) (*n*, %)	11 (100)	1(25)	0·009
Splenectomy (yes) (*n*, %)	9 (81·8)	3 (75)	>0·999
Haemoglobin (g/l) median (min–max)	87 (79–97)	95 (82–99)	0·226
Serum ferritin (ng/ml) >2000 (*n*, %)	3 (27·3)	0	>0·999
White blood cell count (per μl), median (min–max)	12 300 (63–31 900)	12 000 (3775–34 360)	>0·999
Platelet count (per μl), median (min–max)	589 500 (840–848 000)	582 500 (147 000–965 000)	0·808
Hydroxycarbamide (yes) (*n*, %)	1 (9·1)	2 (50)	0·154
Heart or liver iron overload (moderate and severe) (*n*, %)	4 (36·4)	1 (25)	>0·999
Comorbidities (*n*, %)	8 (72·7)	4 (100)	0·516
Major underlying disease* (*n*, %)	3 (27·3)	4 (100)	0·026

*Heart disease, Diabetes, pulmonary artery hypertension, and hypertension.

study showed a low frequency of blood group O among confirmed COVID-19 cases (13%, two out of 15).

In conclusion, our study showed a low number of β-thalassaemia patients with COVID-19 that most of them developed mild to moderate disease and recovered but having multiple comorbidities predisposed these patients to have a severe disease and a significantly higher risk of mortality compared to cases in the general population infected with COVID-19. These findings provide objective evidence which further variables should be taken into account in the comprehensive risk assessment and prognosis of thalassaemic patients with COVID-19.

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Author contributions

MK made substantial contributions to the study concept, design of the protocol, and in drafting the manuscript. SH performed the statistical analysis and participated in drafting the manuscript. AA, ZZ, MA, AS, and AB were responsible for data collection and confirmation. TZ participated in drafting the manuscript. VDS participated in preparation of the protocol survey and in drafting and revising the manuscript.

Conflicts of interest

The authors declare to have no potential conflicts of interest regarding the present work.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table SI. Data of confirmed COVID-19 in patients with β-thalassaemias.

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