β-Thalassemia Heterozygotes

Subjects: Obstetrics & Gynaecology

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β-Thalassemia is the most prevalent single gene blood disorder, while the assessment of its susceptibility to coronavirus disease 2019 (COVID-19) warrants it a pressing biomedical priority.

β-thalassemia risk coronavirus

1. Introduction

Identifying medical conditions with a high or potentially deadly impact on the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a critical initial step towards containment of associated morbidity and mortality risks. Given that viral stress from SARS-CoV-2 elicits anabolic responses supported by increasing blood pressure to meet enhanced oxygen needs of vital organs and organ systems, hypoxemia is rendered a high-risk medical condition [1][2]. As the most common blood disorder affecting approximately one third of the global population, anemia presents a low tolerance to hypoxemia and may have either acquired polysystemic or inherited poly- or monogenic background [3]. Monogenic anemia—which is caused by abnormal hemoglobin—is a rather prevalent medical disorder with 270 million carriers worldwide [4][5][6]. β-Thalassemia is the most common inherited single gene disorder in the world. Approximately one-third of all hemoglobinopathies and/or nearly 1.5% of the global population carry the β-thalassemia trait [7]. In this context, β-thalassemia heterozygosity is a strong candidate condition for assessing an individual's susceptibility to COVID-19.

2. Associations

Association of β-thalassemia heterozygosity with severe and critical COVID-19 symptoms.

Considering the clinical spectrum of COVID-19 as a primary outcome, patients were categorized into three groups (asymptomatic and mild/ moderate/ severe and critical). No difference in chest X ray or CT scan was observed among study participants. In univariate analysis, sex (p = 0.047), age (p < 0.001), atrial fibrillation (p = 0.022), coronary disease (p = 0.041), hyperlipidemia (p = 0.014), hypertension (p < 0.001), and being heterozygous for thalassemia (p = 0.004) were associated with severe COVID-19 symptoms (**Table 1**). In multivariate analysis, male sex (p = 0.023), increased age (p < 0.001), and being heterozygous for thalassemia (p = 0.002) were identified as independent risk factors for severe and critical clinical COVID-19 symptoms. Specifically, males had a 1.81 times (95% CI, 1.09 to 3.01) increased possibility for severe or critical clinical symptoms; increased age was associated with increased odds of severe and clinical symptoms with OR = 1.06 (95% CI, 1.04 to 1.08). A finding of great

interest is that patients who were heterozygous for thalassemia were 2.89 times (95% CI, 1.49 to 5.62) more likely to have severe and critical clinical symptoms of COVID-19 (**Figure 1**).

Table 1. Characteristics and COVID-19 clinical spectrum.

Severity			Univariate	Multivariate Ordinal Logistic Regression (Severe and Critical vs. Others)		
Mild (%)	**Moderate (%)**	**Severe and Critical (%)**	***p*-Value**	***p*-Value**	**aOR with 95% CI**	
Sex (M/F)	34/34	67/46	52/22	**0.047** *	**0.023**	1.81 (1.09–3.01)
Age (median, IQR)	51.5 (34)	64.0 (17)	70.5 (15)	<**0.001** ±	<**0.001**	1.06 (1.04–1.08)
Atrial Fibrillation	17 (25.0)	32 (28.3)	33 (44.6)	**0.022** *	0.787	0.92 (0.49–1.71)
Respiratory Disease	5 (7.4)	13 (11.5)	14 (18.9)	0.104 *	0.325	1.47 (0.68–3.15)
Coronary Disease	7 (10.3)	23 (20.4)	20 (27.0)	**0.041** *	0.955	1.02 (0.50–2.09)
Diabetes	10 (14.7)	25 (22.1)	18 (24.3)	0.331 *	0.619	0.85 (0.45–1.60)
Neoplasia	7 (10.3)	11 (9.7)	11 (14.9)	0.529 *	0.209	0.61 (0.28–1.32)
Hyperlipidemia	21(30.9)	60 (53.1)	32 (43.2)	**0.014** *	0.138	0.65 (0.37–1.15)
Hypertension	24 (35.3)	62 (54.9)	56 (75.7)	<**0.001** *	0.104	1.67 (0.90–3.08)
β-Thalassemia Heterozygotes	5 (7.4)	19 (16.8)	21 (28.4)	**0.004** *	**0.002**	2.89 (1.49–5.62)

* Chi-square test, ± Mann–Whitney test; Bold is for the statistically significant results (*p*-value < 0.05).

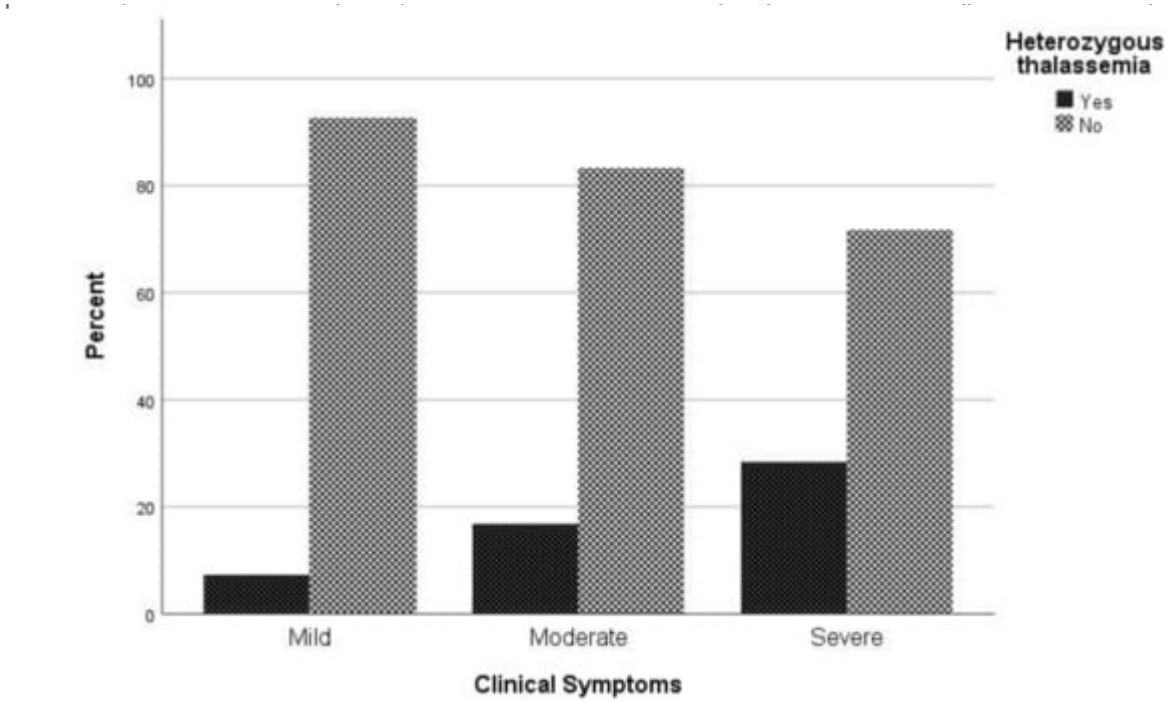

Figure 1. Proportion of β-thalassemia heterozygotes relative to non-carriers regarding clinical symptoms to COVID-19.

2.1. Association of β-Thalassemia Heterozygotes with Mortality Due to COVID-19

Regarding mortality associated with COVID-19 infection, in univariate analysis sex (p = 0.022), age (p < 0.001), atrial fibrillation (p = 0.002), respiratory disease (p = 0.027), coronary disease (p = 0.027), hypertension (p < 0.001), and being heterozygous for thalassemia (p = 0.005) were associated with mortality (**Table 2**). In logistic regression analysis, male patients had a 2.09 times (95% CI, 1.05 to 4.18) greater possibility of dying and patients with increased age were 1.06 times (95% CI, 1.03 to 1.09) more likely to die. It is worth noting that hyperlipidemia plays a beneficial role in COVID-19 mortality, as the odds ratio of mortality in patients with hyperlipidemia is 0.65 (95% CI 0.37–1.15). It should be highlighted that patient who are heterozygous for thalassemia have a 2.79 times (95% CI, 1.28 to 6.09) greater possibility of dying than other patients (**Figure 2**).

Table 2. Characteristics and mortality due to COVID-19.

Mortality			Univariate		MultivariateBinary Logistic Regression		
Yes (%)	**No (%)**	***p*-Value**	**OR with 95% CI**	**RR with 95% CI**	***p*-Value**	**aOR with 95% CI**	
Sex (M/F)	50/20	103/82	**0.022** *	1.99 (1.10–3.61)	1.67 (1.06–2.64)	**0.036**	2.09 (1.05–4.18)
Age (median, IQR)	72.5 (15)	61.0 (24)	<**0.001** ±	-	-	<**0.001**	1.06 (1.03–1.09)

Mortality			Univariate		MultivariateBinary Logistic Regression		
Yes (%)	No (%)	*p*-Value	OR with 95% CI	RR with 95% CI	*p*-Value	aOR with 95% CI	
Atrial Fibrillation	33 (47.1)	49 (26.5)	**0.002** *	2.48 (1.40–4.39)	1.88 (1.28–2.78)	0.201	1.64 (0.77–3.48)
Respiratory Disease	14 (20.0)	18 (9.7)	**0.027** *	2.32 (1.08–4.97)	1.74 (1.11–2.74)	0.297	1.61 (0.66–3.95)
Coronary Disease	20 (28.6)	30 (16.2)	**0.027** *	2.07 (1.08–3.96)	1.64 (1.08–2.49)	0.808	0.90 (0.39–2.09)
Diabetes	18 (25.7)	35 (18.9)	0.233 *	1.48 (0.77–2.84)	1.32 (0.85-2.05)	0.758	0.87 (0.41–1.91)
Neoplasia	10 (14.3)	19 (10.3)	0.367 *	1.46 (0.64-3.31)	1.30 (0.75–2.24)	0.395	0.67 (0.26–1.70)
Hyperlipidemia	30 (42.9)	83 (44.9)	0.773 *	0.92 (0.53–1.61)	0.94 (0.63–1.41)	**0.008**	0.38 (0.19–0.78)
Hypertension	52 (74.3)	90 (48.6)	<**0.001** *	3.05 (1.66–6.60)	2.30 (1.43–3.70)	0.198	1.67 (0.77–3.62)
β-Thalassemia Heterozygotes	20 (28.6)	25 (13.5)	**0.005** *	2.56 (1.31–4.99)	1.87 (1.24–2.80)	**0.010**	2.79 (1.28–6.09)

* Chi-square

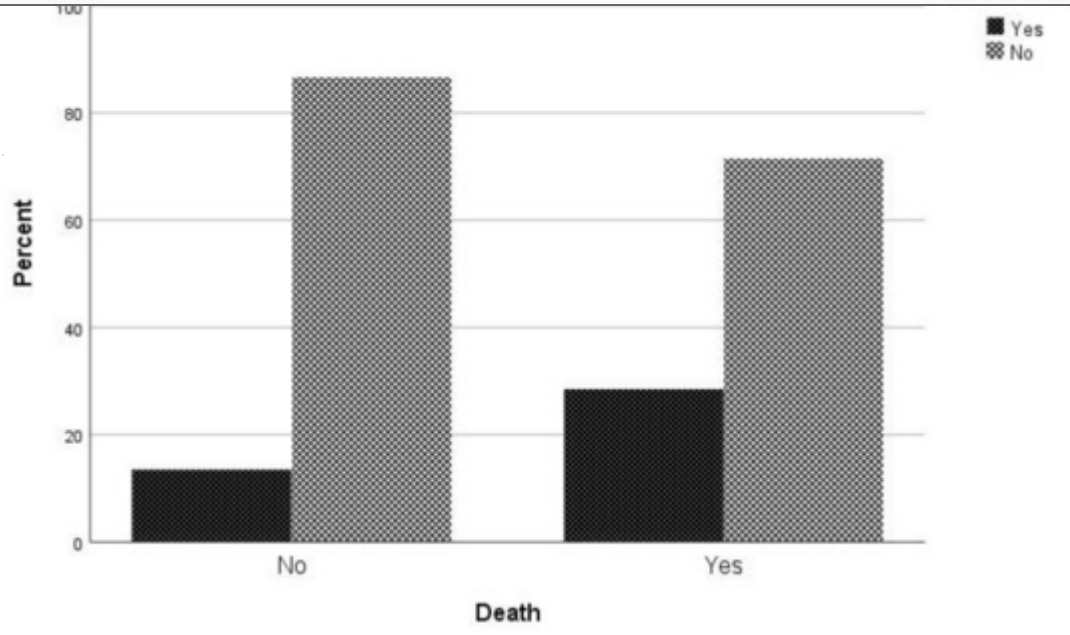

Figure 2. Proportion of β-thalassemia heterozygotes relative to non-carriers regarding mortality due to COVID-19.

2.2. Admission of COVID-19 Infected β-Thalassemia Heterozygotes to the ICU

Regarding the requirement for ICU care, it was found through univariate analysis that age (p = 0.03), respiratory disease (p = 0.043), coronary disease (p = 0.029) and hypertension (p < 0.001) were associated with ICU admission (**Table 3**). Through logistic regression analysis, patients with hypertension had 5.12 times (95% CI, 2.04 to 12.87) greater risk of requiring ICU care than patients without hypertension. On the contrary, hyperlipidemia was identified as a protective factor against ICU admission, with OR = 0.44 (95% CI, 0.21 to 0.94). Furthermore, in relation to the requirement for ICU care, being heterozygous for thalassemia had no effect on the possibility of admission to the ICU (p = 0.505).

Table 3. Characteristics and ICU admission due to COVID-19.

ICU		Univariate			Multivariate Binary Logistic Regression		
Yes (%)	**No (%)**	***p*-Value**	**OR with 95% CI**	**RR with 95% CI**	***p*-Value**	**aOR with 95% CI**	
Sex (M/F)	36/17	117/85	0.186 *	1.54 (0.81–2.92)	1.41 (0.84–2.37)	0.305	1.45 (0.72–2.93)
Age (median, IQR)	66.2 (17)	60.4 (24)	**0.030** ±	-	-	0.649	1.01 (0.98–1.04)
Atrial Fibrillation	21 (36.9)	61 (30.2)	0.191*	1.52 (0.81–2.84)	1.39 (0.85–2.25)	0.966	0.98 (0.43–2.23)
Respiratory Disease	11 (20.8)	21 (10.4)	**0.043** *	2.26 (1.01–5.04)	1.83 (1.05–3.17)	0.205	1.80 (0.73–4.46)
Coronary Disease	16 (30.2)	34 (16.8)	**0.029** *	2.14 (1.07–4.27)	1.77 (1.08–2.92)	0.393	1.48 (0.61–3.59)
Diabetes	10 (18.9)	43 (21.3)	0.699 *	0.86 (0.40–1.85)	0.87 (0.48–1.64)	0.098	0.49 (0.21–1.14)
Neoplasia	4 (7.5)	25 (12.4)	0.466 †	0.58 (0.19–1.74)	0.64 (0.25–1.63)	0.102	0.37 (0.11–1.22)
Hyperlipidemia	22 (41.5)	91 (45.0)	0.644 *	0.87 (0.47–1.60)	0.89 (0.55–1.45)	**0.033**	0.44 (0.21–0.94)

ICU		Univariate			MultivariateBinary Logistic Regression		
Yes (%)	No (%)	*p*-Value	OR with 95% CI	RR with 95% CI	*p*-Value	aOR with 95% CI	
Hypertension	42 (79.2)	100 (49.5)	<**0.001** *	3.90 (1.90–7.99)	3.04 (1.64–5.63)	**0.001**	5.12 (2.04–12.87)
β-Thalassemia Heterozygotes	11 (20.8)	34 (16.8)	0.505 *	1.29 (0.61–2.77)	1.22 (0.68–2.18)	0.508	1.33 (0.57–3.06)

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median duration of hospitalization among carriers and non-carriers was 12 and 17.5 days, respectively.

* Chi-square sults (*p*-value < 0.05).

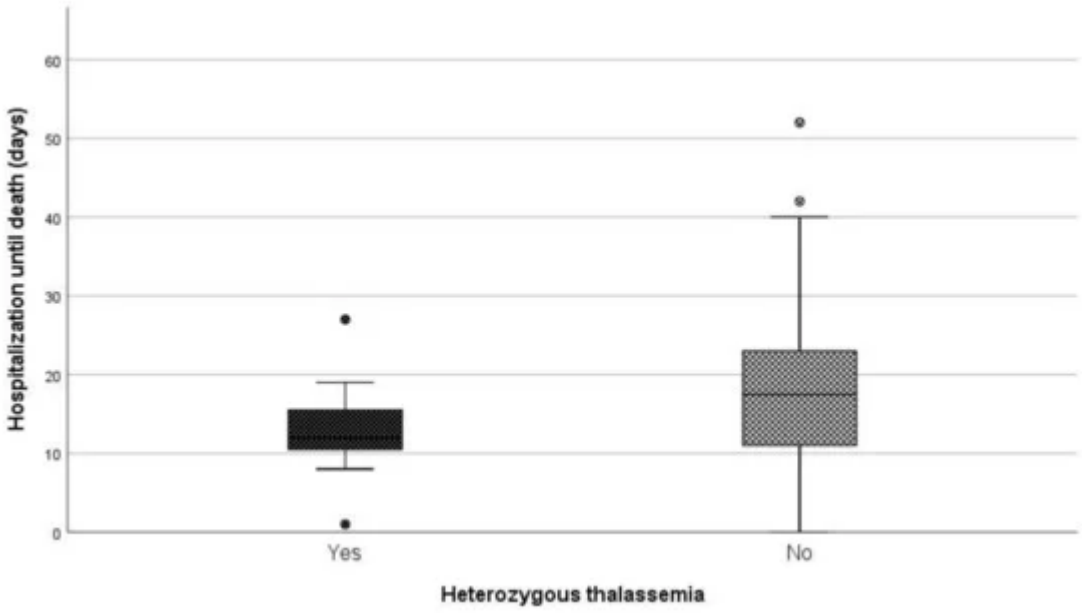

Figure 3. Days of hospitalization until death between carries and non-carriers.

2.4. Length of Hospitalization among Patients Who Survived

Regarding days of hospitalization among patients that survived COVID-19, the median duration was eight days for patients that were heterozygous for thalassemia and six days for non-carriers ($p = 0.014$) (**Figure 4**).

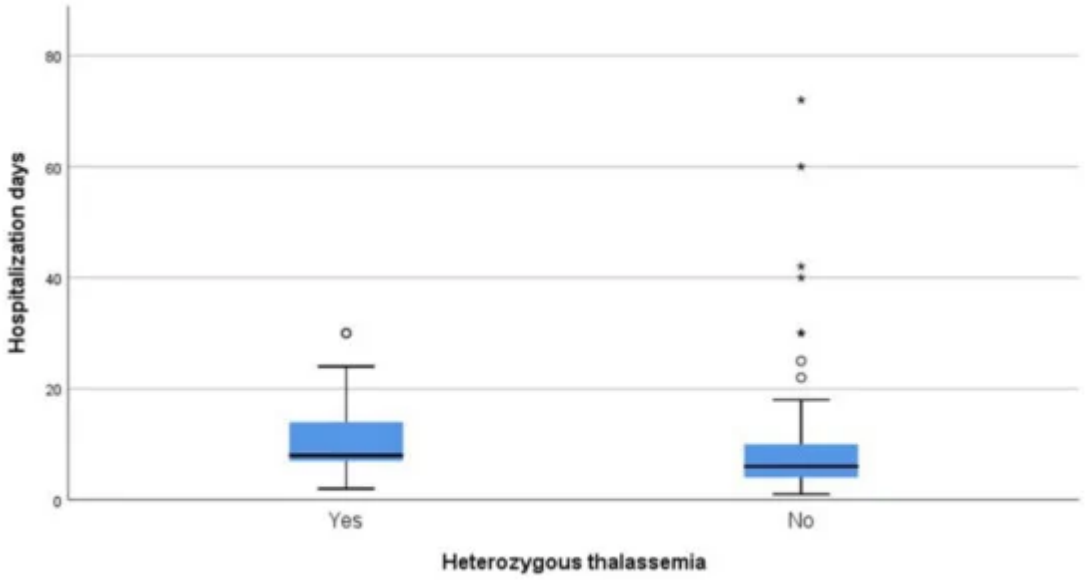

Figure 4. Days of hospitalization between carries and non-carriers that survived.

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