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Pulmonary Hypertension and Its Determinants in β-thalassemia Major and Intermedia Considering Left Ventricular Functional State

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Abstract

Introduction: Pulmonary hypertension (PHT) is a common complication in β-thalassemia. We aimed to determine the prevalence of PHT and its main indicators in patients with β thalassemia Major (TM) and β-thalassemia Intermedia (TI), considering left ventricular function.

Methods: Pulmonary hypertension (PHT) is a common complication in β-thalassemia. We aimed to determine the prevalence of PHT and its main indicators in patients with β thalassemia Major (TM) and β-thalassemia Intermedia (TI), considering left ventricular function.

Results: The overall prevalence of PHT in TM and TI group was estimated to be 35.2% and 29.3%, respectively; while reduced LVEF was evident in 22.7% and 10.1% of patients with TM and TI, respectively. No significant correlation was observed between mean PAP and LVEF in the patients with TI (Pearson coefficient = -0.096, P value = 0.345); while, an adverse association was revealed between mean PAP and LVEF in patients with TM (Pearson coefficient = -0.227, P value = 0.033). Upon univariate analysis, the only significant association was observed between LVEF and pulmonary hypertension among TM patients (P value = 0.001).Our results did not indicate that male gender and aging may affect the development of PHT.

Conclusions: According to our findings, a considerable proportion of patients with TM and TI may have PHT. We detected an adverse association between mean PAP and LVEF in patients with TM. Left ventricular function was reduced in patients with PHT among TM group.

INTRODUCTION

β-thalassemia is an inherited hemoglobin disorder which results in chronic hemolytic anemia. Depending on the clinical severity, two forms are distinguished, including β-thalassemia Major (TM) and β-thalassemia Intermedia (TI) [1]. While TM is characterized by severe anemia starting from the first year of life and therefore requiring lifelong transfusion therapy for survival, the TI form has a later clinical onset with a milder anemia that permits survival without regular transfusions and a longer life expectancy [2-4]. The diverse clinical severity of TM and TI and the different therapeutic approaches lead to a wide variety of clinical phenotypes. Findings regarding cardiac

status in these types of β-thalassemia are not completely comparable in both forms [5, 6].

With regard to the cardiac complications of β-thalassemia, Pulmonary Hypertension (PHT) is a common complication, especially among patients with TI [7]. It is considered to be the primary cause of congestive heart failure in such patients [8]. However, the majority of patients with increased Pulmonary Arterial Pressure (PAP) are asymptomatic [9]. Even, most of the patients may have normal left ventricular function in spite of severe PHT. Therefore, this condition is often unrecognized until patients develop heart failure and/or hypoxemia [10-12].

There is paucity of data regarding the prevalence of PHT in both forms of β-thalassemia and also its main determinants. In this line, the present study aimed to determine the prevalence of PHT and identify its main indicators in patients with TM or TI, considering normal or reduced left ventricular function.

METHODS

In this cross-sectional study performed at Firoozgar Hospital and Zafar Thalassemia Center in Tehran, patients with TM or TI referred between January 2009 and May 2009 were selected by simple sequential non-random sampling and enrolled into the study. In general, 187 consecutive patients without previous history of any cardiovascular or pulmonary disease (i.e. chronic obstructive pulmonary disease or ischemic heart disease) were selected. The Institutional Review Board (IRB) of Iran University of Medical Sciences (IUMS) approved the study protocol and patients provided informed written consent. Baseline characteristics including demographics and disease duration were collected by interviewing or reviewing medical records. Then, all participants were referred to Firoozgar Hospital for echocardiography evaluation in order to determine Pulmonary Artery Pressure (PAP) and Left Ventricular Ejection Fraction (LVEF). In this regard, PHT was defined as mean PAP higher than 25 mmHg. Also LVEF less than 50% was considered as left ventricular dysfunction in β-thalassemia patients. Echocardiography was performed by the same physician for all of the patients. Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's t-test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. Association between the quantitative variables was examined by the Pearson's correlation coefficient test. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13.0 (SPSS Inc. Released 2005. SPSS for Windows, Version 13.0. Chicago, SPSS Inc.).

RESULTS

In the present study, 187 patients -88 in TM group and 99 in TI group - were studied among whom 46.6% and 50.5% were male, respectively. Patients in the TM group were significantly younger compared to the TI group (P value < 0.001). Table 1 shows some of the demographic and clinical characteristics of the patients in both groups. The overall prevalence of PHT in TM and TI groups was 35.2% and 29.3%, respectively. Left ventricular dysfunction based on reduced LVEF was also evident in 22.7% and 10.1% of patients with TM and TI, respectively. In patients with TI, prevalence of PHT in the subgroup with normal LVEF was 21.3% and in those with reduced ventricular function was 20.0% (P value = 0.921). In fact, the linear correlation between PAP and LVEF was not significant (Pearson coefficient = -0.096, P value = 0.345). In TM group, the overall prevalence of PHT in normal left ventricular function group was 13.2% and in left ventricular dysfunction group was 25% (P value = 0.294); while, an inverse correlation was revealed between mean PAP and LVEF in this group of patients (Pearson coefficient = -0.227, P value = 0.033). Table 2 shows the univariate association of PHT with gender, age and LVEF among both TM and TI patients. In this regard, the only significant association was observed between LVEF and PHT among TM patients (P value = 0.001).

Table 1: Comparison of demographics as well as pulmonary artery pressure (PAP) and left ventricular ejection fraction among thalassemia major (TM) and thalassemia intermedia (TI) groups (TM: thalassemia major, TI: thalassemia intermedia, PAP: pulmonary artery pressure, LVEF: left ventricular ejection fraction).

Variable	TM	TI	P value
Sex			0.66
Male	41 (46.6)	50 (50.5)	
Female	47 (53.4)	49 (49.5)	
Age (y)	24.93 ± 5.56	33.28 ± 11.23	0.001
PAP (mmHg)	31.4 ± 11.08	34.26 ± 18.08	0.20
LVEF (%)	55.81 ± 13.21	58.85 ± 9.53	0.07

Data are presented as mean SD and No. (%).

TM: Beta-thalassemia major; TI: Thalassaemia intermedia; PAP: Pulmonary Artery Pressure; LVEF: Left ventricular ejection fraction

Table 2: The Univariate associations between Pulmonary Hypertension (defined as PAP>25 mmHg) and Gender, Age and LVEF among thalassemia major (TM) and thalassemia intermedia (TI) patients (TM: thalassemia major, TI: thalassemia intermedia, LVEF: left ventricular ejection fraction, PAP: pulmonary artery pressure).

	TM			TI		
	PAP > 25 mmHg	**PAP < 25 mmHg**	**P value**	**PAP > 25 mmHg**	**PAP < 25 mmHg**	**P value**
Sex			0.84			0.55
Male	14	27		16	34	
Female	17	30		13	36	
Age(y)	24.1 ± 5.2	25.4 ± 7.2	0.42	30.5 ± 11.4	34.5 ± 10.9	0.13
LVEF (%)	53.0 ± 14.9	60.8 ± 7.0	0.001	54.9 ± 9.8	58.6 ± 9.4	0.67

Data are presented as mean SD and No. (%).
TM: Beta-thalassemia major; TI: Thalassaemia intermedia; LVEF: Left ventricular ejection fraction

DISCUSSION

In this study, the prevalence of PHT in the TM group was 35.2% and in the TI group was 29.3%, which was not significantly different. The obtained prevalence of PHT in our survey was in the range published in most of the previous reports. In a study by Vlahos et al. [13], PHT was observed in 18.5% of TM patients and in another study by Aessopos et al. [14], PHT prevalence was estimated to be 23% in patients with TI. Generally speaking, it could be concluded that PHT is a partially common finding in both forms of thalassemia, even more frequent in TI patients.

Another important finding of our study was that PAP and LVEF were not associated in our patients. Also, the prevalence of PHT is independent to left ventricular function state in both types of β-thalassemia. Thus, prevalence of PHT in patients with normal left ventricular function and those with impaired ventricular function is not different that is consistent with most of the previous studies. Vlahos et al. [13] similarly showed that despite normal systolic and diastolic ventricular function, 18.5% of TM patients had PHT. In another study by Aessopos et al. [14], despite the high prevalence of PHT 60%, right heart failure was detected in only 5% of patients and left ventricular dysfunction was reported in none. Aessopos also indicated no cases of left ventricular dysfunction in thalassemia patients with PHT [4]. Also, upon univariate analysis of our data, the only significant association was observed between LVEF and pulmonary hypertension among TM patients. Our results did not indicate that male gender and aging may affect the development of PHT.

In summary, our obtained prevalence of PHT is reported in most of the previous observations and a considerable proportion of patients in both TM and TI groups had PHT that was more prevalent in the former group. We detected an adverse association between mean PAP and LVEF in patients with TM. Left ventricular function was reduced in patients with PHT among TM group.

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CONFLICTS OF INTEREST

Authors declare that they have no conflict of interest.

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