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Short Report

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Prevalence and Risk Factors of Pulmonary Arterial Hypertension in Thalassemia Major Patients of Ilam, 2014

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Abstract

Pulmonary arterial hypertension (PAH) is a progressive disease with high morbidity and mortality rates. Research has shown that PAH has a prevalence rate of 10-79% in thalassemia major patients. This cross-sectional study was carried out in 2014 to determine the prevalence and risk factors of PAH in all thalassemia major patients of over 18 years of age in Ilam, Iran. A cardiologist measured systolic pulmonary artery pressure (SPAP) by using Doppler echocardiography. SPAP of higher than 25 mm Hg was defined as PAH criterion. The obtained data was analyzed using SPSS, version 17. Of the 36 studied patients, 17 (47.2%) were male and 19 (52.8%) were female. The mean age of the patients was 26.0±5.6 years. The prevalence of PAH in the thalassemia major patients was estimated to be 47.2% and the mean SPAP was determined to be 26.2±14.6 mm Hg. Among the examined PAH risk factors, only the history of pulmonary disease (0.02) and transfusion (0.03) was found to be significant.

Keywords: Echocardiography, Pulmonary hypertension, Thalassemia major

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Introduction

Pulmonary arterial hypertension (PAH) is a progressive disease induced by cardiovascular, pulmonary, or systemic conditions. Regardless of its etiology, PAH is associated with high rates of morbidity and mortality, as well as systolic pulmonary arterial pressure (SPAP) of more than 25 mm Hg (1-2).

Hemoglobinopathies including thalassemia are widely regarded as the most common causes of PAH (3). Pathophysiology of PAH is multifactorial and includes chronic hemolysis, splenectomy, coagulation, vascular inflammation, hepatic dysfunction, hypoxemia, hemochromatosis, left ventricular dysfunction, and increased cardiac output (4-6).

Various studies have reported the prevalence of PAH in thalassemia major patients to range between 10% and 79% (7-11). The National Institutes of Health has reported that the median survival of these patients is 2.8 years after diagnosis. Survival is associated with increased severity of New York Heart Association functional class, which is as low as six months for Class IV patients (12-14). There is also evidence suggesting the significant role of PAH in cardiogenic death in these patients (1).

Clinical symptoms of PAH are usually blinded by its underlying etiology, and definitive diagnosis is often established after the onset of right ventricular failure (15). Today, SPAP can be diagnosed accurately by Doppler echocardiography, which is a non-invasive procedure (16). PAH is normally progressive and leads to right ventricular overload, right ventricular failure, and ultimately, premature death (17). The increased pulmonary vascular resistance is due to the large number of progressive changes associated with pulmonary arterioles including vasoconstriction, inflammation, in-situ thrombosis, and proliferative remodeling of the pulmonary vessel wall (18).

Research on PAH in thalassemia major patients in Iran is limited, and studies in other countries reported various PAH prevalence rates among these patients (7-11). This study was conducted in 2014, Ilam, Iran, to determine the prevalence and risk factors of PAH in thalassemia major patients.

Methods

This was an observational, cross-sectional study. Prior to initiation of this study, the study protocol was reviewed and approved by the Ethics Committee of the Medical University of Ilam. The objective of the study was explained to the patients and oral informed consent was obtained from the subjects. Clinical and demographic information were collected using questionnaires, physical examination, and echocardiography. Participants who refrained from echocardiography or whose image had a poor quality were excluded from the study.

The participants were the entire population of thalassemia major patients aged at least 18 years old, who visited the special diseases clinic of Mostafa Khomeini Hospital in Ilam during one year from March 21, 2014. Thalassemia major diagnosis was inquired and confirmed by a review of medical records. A multi-part questionnaire consisting of items on demographic information, as well as history of transfusion (age at onset, duration, and frequency), desferal treatment (age at onset, duration, and frequency), splenectomy, and other diseases was distributed among the participants.

The patients were referred to a cardiologist to measure their SPAP by a VIVID4 echocardiography machine (USA). Two-dimensional color Doppler echocardiography images of patients were obtained, and the systolic tricuspid regurgitation velocity was measured via an apical or parasternal view. SPAP was then calculated; PAH criterion was considered as SPAP of higher than 25 mm Hg (19).

T-test (for comparison of the quantitative variables) and Chi-square test (for qualitative variables) were performed, using SPSS version 17. A p-value less than 0.05 was considered statistically significantly.

Results

We studied a total of 36 thalassemia major patients consisting of 17 (47.2%) men and 19 (52.8%) women, with a mean age of 26.0±5.6 years. The prevalence of PAH in thalassemia major patients was estimated to be 47.22%, and mean SPAP of all the participants was determined to be 26.2±14.6 mm Hg.

Out of the 36 patients participating in the study, 29 (80.55%) patients were receiving iron chelation therapy (with desferal) and 32 (88.9%) had a history of blood transfusion; in addition, 52.8% of the

patients (8 males and 11 females) had a splenectomy. The demographic characteristics of the patients are presented in Table 1.

Table 1: Demographic and clinical characteristics of subjects

Variable		Frequency (Percentage)
Gender	Male	17 (47.2%)
	Female	19 (51.7%)
Smoking	Yes	1 (2.8%)
	No	35 (97.2%)
History of lung disease	Yes	4 (11.1%)
	No	32 (88.9%)
History of heart disease	Yes	4 (11.1%)
	No	32 (88.9%)
History of diabetes	Yes	3 (8.3%)
	No	33 (91.7%)
History of splenectomy	Yes	19 (52.8%)
	No	17 (47.2%)
		Mean ± SD
Age (years)		26.08±5.6
Body mass index (BMI)		19.21±2.51
Age at the first transfusion (in 32 patients who were undergoing transfusion)		72.3±79.9 months.
Transfusion intervals (in 32 patients who were undergoing transfusion)		33.6±30.0 days
Age at the start of desferal treatment (in 29 patients who were receiving such treatment)		13.7±7.3 years
Desferal injection frequency (days per week)		5.6±2.6
Desferal injection duration (years)		11.7±5.7
Mean systolic pulmonary artery pressure (SPAP)		26.6±14.9

Groups of patients with and without pulmonary hypertension were compared in terms of demographic data (Table 2), which reflected significant differences between the two groups in terms of the history of transfusion and pulmonary disease, as well as mean SPAP.

Table 2: Comparison of Risk Factors in patients with pulmonary hypertension (group I) and without pulmonary hypertension (group II)

Risk Factor		Group I Frequency (percentage) 17 (47.22%)	Group II Frequency (percentage) 19 (52.77%)	Chi-square test
Gender	Male	9 (52.9%)	8 (42.1%)	0.51
	Female	8 (47.1%)	9 (57.9%)	
Smoking		0 (0%)	1 (5.3%)	0.33
History of lung disease		4 (23.5%)	0 (0%)	0.02
History of heart disease		2 (11.8%)	1 (5.3%)	0.09
History of diabetes		2 (8.1%)	1 (5.3%)	0.48
History of splenectomy		11(64.7)	8(42.1)	0.17
History of transfusion		13 (76.5%)	17 (89.5%)	0.03
Under Iron chelation therapy		15 (88.2%)	14 (73.7%)	0.79
			Mean ± SD	**T-Test**
Age (years)		27.1±4.6	25.15±6.3	0.51
Body mass index (BMI)		19.3±2.0	19.0±2.9	0.72
Age at the first transfusion (months)		59.9±45.6	78.3±98.5	0.48
Transfusion intervals (days)		24.23±6.72	40±37.67	0.09
Age at the start of desferal treatment (years)		13.2±7.0	13.9±7.5	0.80
Desferal injection frequency (days a week)		5.2±1.6	5.2±1.9	0.98
Desferal injection duration (years)		12.28±4.7	11.2±6.6	0.56
Mean systolic pulmonary artery pressure (SPAP)		38.1±12.4	15.5±4.9	<0.001

Implications for Practice

In general, this study showed that PAH is highly prevalent in thalassemia major patients; thus, PAH screening of the thalassemia patients of over 18 years of age seems necessary. Future studies are recommended to investigate the relationship of the prevalence of pulmonary hypertension in thalassemia major patients with other factors including blood pressure, ejection fraction, systolic and diastolic heart function, cardiomegaly, and the levels of liver enzymes, ferritin, hematocrit, and hemoglobin.

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Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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