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FREQUENCY OF PULMONARY HYPERTENSION IN NON-TRANSFUSION DEPENDENT THALASSEMIAS

Original Research

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ABSTRACT

Introduction: One of the main cardiac complications in non-transfusion-dependent thalassemia (NTDT) is pulmonary hypertension. It has been demonstrated that the occurrence of pulmonary hypertension positively correlates with a number of clinical and laboratory indicators, including iron overload.

Objective: The objective of this study was to determine the frequency of pulmonary hypertension in non-transfusion dependent thalassemia (NTDT).

Study Design: Cross-sectional study as carried out in Thalassemia centre of sir Ganga Ram Hospital Lahore.

Methodology: Following the ethical committee's acceptance letter, 170 patients who met the inclusion and exclusion criteria and visited the thalassemia center at Sir Ganga Ram Hospital Lahore (SGRH) were added to the study. Every enrolled patient had an echocardiogram performed in the hospital to check for TRV and ejection fraction. According to the operational definition, pulmonary hypertension was identified. In accordance with hospital practice, treatment was provided. Age is displayed as the mean standard deviation.

Results: Of the 170 cases in our study, 61.18% (n=104) were between the ages of 5 and 9 and 38.82% (n=66) were between the ages of 10 and 12. The mean age was 5.82+2.30 years, and 71.76% (n=122) of the cases were male and 28.24% (n=48) were female. Of the cases with non-transfusion dependent thalassemia (NTDT), 6.47% (n=11) had pulmonary hypertension, while 93.53% (n=159) did not show. any signs of this morbidity.

Conclusion: We came to the conclusion that pulmonary hypertension is not significantly more common in non-transfusion dependent thalassemia (NTDT). However, as it is the major data, we believe that smoother multicenter local trials could validate it.

Keywords: Children, Non-transfusion dependent thalassemia, pulmonary hypertension

INTRODUCTION

Thalassemia syndromes pose a serious threat to world health, especially in underdeveloped nations. Globally, β-thalassemia is the most common of the thalassemia syndromes, which affect about 68,000 newborns annually. Globally, an estimated 80–90 million people—or 1.5% of the population—are carriers[1]. With a carrier incidence of 5–8% and around 6,000 new cases diagnosed each year, the illness is very common in Pakistan[2].

Thalassemia was divided into two categories by the Thalassemia International Federation in 2013: transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT). Hemoglobin H illness, mild/moderate hemoglobin E/β-thalassemia, and β-thalassemia intermedia are all included in NTDT. Pulmonary hypertension (PH) has become a major issue among the several disease-related problems that NTDT patients still face, even if they do not need frequent transfusions to survive[3].

The echocardiographic diagnosis of pulmonary hypertension is usually predicated on a tricuspid regurgitant jet velocity (TRV) >2.5–2.8 m/s, which corresponds to a pulmonary artery systolic pressure >30–35 mmHg. Pulmonary hypertension is defined as a mean pulmonary artery pressure >25 mmHg. Research has indicated that the prevalence of PH in patients with thalassemia ranges from 10% to 78.8%, with greater rates typically seen in NTDT as opposed to TDT. Reduced exercise tolerance, functional restriction, right ventricular dysfunction, and elevated morbidity are all linked to PH in NTDT[4,5].

In NTDT, the pathophysiology of PH is intricate and multifaceted. Chronic hemolysis and nitric oxide depletion cause pulmonary arterial hypertension; myocardial iron overload causes left heart disease; chronic anemia causes high cardiac output; chronic thromboembolic events cause pulmonary fibrosis; and so on. The risk of vascular and cardiac problems is increased by these pathways, which frequently overlap. Crucially, data suggests that transfusion treatment in NTDT patients is linked to a decreased incidence of PH, suggesting a possible preventive function[6,7].

The burden of PH in NTDT has not been the subject of any local studies in Pakistan, despite evidence from around the world. Early detection is essential because prompt treatment can increase survival and stop the development of right heart failure. For NTDT patients, routine echocardiographic evaluation of TRV may be a useful screening method in clinical practice[8].

The purpose of the proposed study is to ascertain the prevalence of pulmonary hypertension in a local population of NTDT patients. The study aims to highlight the significance of routine screening and early intervention by measuring its burden. Evaluating the relationships between PH and clinical factors such age, disease duration, history of transfusions, and splenectomy status are secondary goals.

To wrap it up, pulmonary hypertension is a severe and little-known side effect of NTDT. By determining its incidence in Pakistan, important evidence will be gathered to support the inclusion of routine echocardiographic screening in thalassemia care regimens. This will enable early discovery, prompt intervention, and better patient outcomes.

METHODOLOGY

Cross-sectional study conducted at Sir Ganga Ram Hospital's Thalassemia Center in Lahore. Following the ethical committee's acceptance letter, 170 patients who met the inclusion and exclusion criteria and visited the thalassemia center at Sir Ganga Ram Hospital Lahore (SGRH) were added to the study. Every enrolled patient had an echocardiogram performed in the hospital to check for TRV and ejection fraction. According to the operational definition, pulmonary hypertension was identified. In accordance with hospital practice, treatment was provided. The mean standard deviation of age is displayed.

DATA ANALYSIS

SPSS program 20 was used to enter and evaluate the data. For categorical factors such as pulmonary hypertension and gender, frequency and percentages were calculated. To determine the effect modifier, pulmonary hypertension was categorized by age, gender, and

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thalassemia type. The significance between the stratified groups was examined using the chi square test. A P value of less than 0.05 was deemed significant.

RESULTS

To ascertain the prevalence of pulmonary hypertension in non-transfusion dependent thalassemia (NTDT), 170 cases that met the inclusion/exclusion criteria were enrolled.

The patients' age and gender distribution revealed that the majority of cases (61.18%, or 104 cases) were between the ages of 5 and 9 while the remaining 38.82%, or 66 cases, were between the ages of 10 and 12. The mean+sd was 38.82% (n=66). However, the gender distribution reveals that 28.24% (n=48) were female and 71.76% (n=122) were male. (Table No. 1) Figure 1 displays the gender distribution graphically.

Table 1: Age and Gender distribution (n=170)

Age (in years)	**No. of patients (n)**	**Percentage %**
5-9	104	61.18
10-12	66	38.82
Mean±sd	**5.82±2.30**	
Gender	**No. of Patients (n)**	**Percentage %**
Male	122	71.76
Female	48	28.24

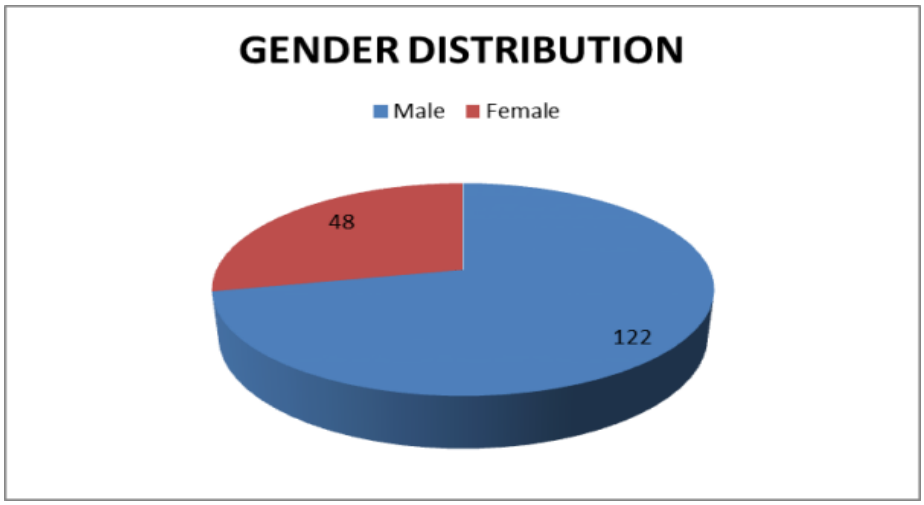

Figure 1Gender Distribution

6.47% (n=11) of patients with non-transfusion dependent thalassemia (NTDT) had pulmonary hypertension, while 93.53% (n=159) did not have this complication. (Table No. 2)

Table 2: Frequency Of Pulmonary Hypertension in Non-Transfusion Dependent Thalassemia (n=170)

Pulmonary hypertension	No. of patients	Percentage%
Yes	11	6.47
No	159	93.53

After adjusting for patient gender and age, we found that 5 out of 104 cases were between the ages of 5 and 9, whereas 6 out of 66 cases were between the ages of 10 and 12. The p-value was 0.26. According to stratified data, 3 out of 48 cases were female, whereas 8 out of 122 cases were male; the p-value was 0.96. (Table no. 3a, b)

Table No. 3a Stratification for Frequency of Pulmonary Hypertension in Non-Transfusion Dependent Thalassemia (NTDT) With Regards to Age (n=170)

Age (in years)	Pulmonary hypertension		P value
	Yes	No	
5-9	5	99	0.26
10-12	6	60	

Table No. 3b Stratification For Frequency of Pulmonary Hypertension in Non-Transfusion Dependent Thalassemia (NTDT) With Regards To Gender (n=170)

Gender	Pulmonary hypertension		P value
	Yes	No	
Male	8	114	0.96
Female	3	45	

Seven out of 128 instances had thalassemia intermedia, two out of ten had sickle cell disease, one out of 23 had HBE, one out of eight had HBH, and there were no cases of alpha thalassemia. (Table No. 4)

Table 4: Stratification For Frequency Of Pulmonary Hypertension In Non-Transfusion Dependent Thalassemias (NTDT) With Regards To Type Of Thalassemia (N=170)

Type of thalassemia		Pulmonary hypertension		P value
		Yes	No	
Alpha thalassemia	Yes	0	1	0.79
	No	11	158	
HBE	Yes	1	22	0.65
	No	10	137	
HBH	Yes	1	7	0.47
	No	10	152	
Sickle cell	Yes	2	8	0.07
	No	9	151	
Thalassemia intermedia	Yes	7	121	0.35
	No	4	38	

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DISCUSSION

One known and dangerous cardiac consequence in people with non-transfusion-dependent thalassemia (NTDT) is pulmonary hypertension (PH). Iron overload is the most notable clinical and laboratory parameter that has been connected to its occurrence. One circulating form of free plasma iron that is thought to be a good sign of iron overload and a key predictor of illness consequences is non-transferrin-bound iron (NTBI)[9].

The purpose of this study was to ascertain the prevalence of PH in a pediatric population because there is a lack of local data on the burden of PH in NTDT. Early detection is essential because it may help stop or slow the growth of the disease. Timely identification and treatment may be possible if routine echocardiographic evaluation of tricuspid regurgitant jet velocity (TRV) is incorporated into therapeutic practices.

170 NTDT cases were examined in this investigation. With a mean age of 5.82±2.30 years, the majority (61.18%, n=104) were between the ages of 5 and 9, while 38.82% (n=66) were between the ages of 10 and 12. 71.76% (n=122) of the patients were male, whereas 28.24% (n=48) were female. While 93.53% of patients (n=159) had no echocardiographic evidence of PH, the total prevalence of the disorder was 6.47% (n=11).

According to international research that mostly rely on echocardiographic measures, the prevalence of PH in thalassemia ranges from 10% to 78.8%, with NTDT continuously having higher rates than transfusion-dependent thalassemia (TDT)[10]. When TRV surpasses 2.5–2.8 m/s, which corresponds to a pulmonary arterial systolic pressure of 30–35 mmHg, the diagnosis is typically made. The impact of chronic anemia was highlighted by a large Italian study that included more than 1,000 patients and confirmed that β-thalassemia intermedia is linked to a five-fold higher prevalence of PH compared to β-thalassemia major (5.7% vs. 1.2%)[11,12].

Although our results indicate a lower prevalence of PH than those from other countries, they nevertheless emphasize the significance of local surveillance. Better long-term results, prompt treatment, and early identification may be facilitated by integrating TRV testing into NTDT management procedures.

LIMITATIONS

Small sample size, lack of time and funding constrains are the limitations of this study.

CONCLUSION

We came to the conclusion that non-transfusion dependent thalassemia (NTDT) does not have a significantly greater incidence of pulmonary hypertension. However, as it is the major result, we believe that more multicenter local trials could validate it.

AUTHOR CONTRIBUTION

Author	Contribution
Abnas Batool*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published

REFERENCES

1. Colah R, Gorakshakar A, Nadkarni A. Global burden, distribution and prevention of beta-thalassemias and hemoglobin E disorders. Expert Rev Hematol 2010;3(1):103-117.

2. Ahmed S, Saleem M, Sultana N, Raashid Y. Prenatal diagnosis of β-thalassemia in Pakistan: Experience in a Muslim country. Prenatdiagn. 2000;20:378-83.
3. Musallam KM, Rivella S, Vichinsky E, Rachmilewitz EA. Non-transfusion-dependent thalassemias. Haematologica 2013;98(1): 833-844.
4. Derchi G, Galanello R, Bina P, Cappellini MD, Piga A, Lai ME, Quarta A, Casu G, Perrotta S, Musallam KM, Forni GL. Estimation of the prevalence of pulmonary artery hypertension in a large group of β-thalassemia patients using right heart catheterization. Blood 2012;120(21):3262.
5. Taher A, Isma'eel H, Cappellini MD. Thalassemia intermedia: revisited. Blood Cells Mol Dis 2006;37(1):12-20.
6. Amoozgar H, Farhani N, Karimi M. Early echocardiographic findings in beta-thalassemia intermedia patients usingstandard and tissue Doppler methods. PediatrCardiol 2011;32(2):154-159.
7. Yeager ME, Nguyen CM, Belchenko DD. Circulating fibrocytes are increased in children and young adults with pulmonary hypertension. Eur Respir J. 2012;39(1):104–111.
8. Chueamuangphan N, Wongtheptien W, Nawarawong W, Sukornthasarn A, Chuncharunee S, Tawichasri C, Patumanond J. Clinical indicators for pulmonary arterial hypertension in thalassemia. J Med Assoc Thai 2012;95(1):16-21.
9. Farmakis D, Aessopos A. Pulmonary hypertension associated with hemoglobinopathies: prevalent but overlooked. Circulation. 2011;123(11):1227–32
10. Levin C, Koren A. Healing of refractory leg ulcer in a patient with thalassemia intermedia and hypercoagulability after 14 years of unresponsive therapy. Isr Med Assoc J. 2011;13(5):316–8
11. Badesch DB, Champion HC, Sanchez MA. Diagnosis and assessment of pulmonary arterial hypertension. J Am Coll Cardiol. 2009;54(1, Suppl):S55–S66.
12. Beghetti M, Galiè N. Eisenmenger syndrome a clinical perspective in a new therapeutic era of pulmonary arterial hypertension. J Am Coll Cardiol. 2009;53(9):733–740.