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Value of Red Cell Distribution Width in Children with Congenital Heart Disease Associated- Pulmonary Arterial Hypertension

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Pulmonary arterial hypertension (PAH) commonly occurs as a consequence following untreated congenital heart disease (CHD). It's often related to high morbidity and mortality rates. The work was aimed at assessing the RDW measurements in children who had PAH-CHD.
Methods: Thirty children who have PAH-CHD took part in this study. Electrocardiography and echocardiographic evaluation were applied to all participants. RDW, a parameter included in complete blood count, was measured.
Results: Our study involved thirty children. Up to 53.3% of them were males, whose age varied between three months and twelve months with median of 5 months. The optimal cutoff RDW measurement reached 17.0% (mean); a significant relation between RDW level and low oxygen

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saturation was reported (p=0.02), right ventricular fractional area change (p=0.023), and left ventricular ejection fraction (p=0.13).
Conclusion: RDW, a parameter included in the standard complete blood count, showed a sagnificant elevation in children who had PAH-CHD children. In addition, it was significantly correlated with hypoxia and right ventricular fractional area change and left ventricular ejection fraction.

Keywords: Pulmonary hypertension; congenital heart disease; RDW; Echocardiography.

1. INTRODUCTION

Pulmonary arterial hypertension (PAH) is a serious and progressive disorder affecting the blood vessels of the lungs, resulting in elevated resistance in the pulmonary blood vessels, failure of the right ventricle, and ultimately, death. The predominant form observed in pediatrics is PAH-CHD [1].

Pediatric pulmonary hypertension (PH) has a mean pulmonary artery pressure (mPAP) of at least ≥25 mmHg after three months of age. This definition takes into account the fluctuations in pulmonary hemodynamics that occur during the postnatal transition [2]. As per the 6th World Symposium on Pulmonary Hypertension (WSPH) in 2018, Pulmonary Hypertension (PH) has a mean pulmonary artery pressure (mPAP) of above 20 mm Hg, which is determined using cardiac catheterization while the patient is at rest [3].

For assessing the pulmonary vascular disease in pediatrics, particularly those having congenital heart defects, utilizing pulmonary vascular resistance (PVR) indexed to body surface area (PVRI) is recommended [2].

Unlike idiopathic PAH and hereditable PAH, PAH-CHD is prevalent in children and often correlates with post-tricuspid left-to-right circulatory shunts, thus producing a rise in pulmonary vascular resistance (PVR) [4].

The Red Cell Distribution Width (RDW) is a parameter included in the Complete Blood Count (CBC) that estimates variation in the RBCs size or volume (anisocytosis). Anemia is the primary reason for high RDW. High red cell distribution width (RDW) is identified as an indicator for a poor clinical course in numerous pediatric disorders [5].

An increased RDW implies a pathological or abnormal process impacting the production of red blood cells. In addition, it could be a sign of inflammation, nutritional deficiencies, impaired lung function, or heart failure [6,7].

The work was aimed at assessing the RDW measurements in children who had PAH-CHD.

2. PATIENTS AND METHODS

This prospective cohort study took place in Cardiology Unit, Pediatric department, Tanta University Hospital. 30 childrens who had PAH-CHD were enrolled in this study during the period from April 2022 to Mars 2023. Study approval was obtained by the ethical committee of Faculty of Medicine, Tanta University. Patients' guardians were asked to fill in an informed consent. Inclusion criteria included children younger than eighteen years who had PAH-CHD. While the exclusion criteria were children with PH secondary to other causes rather than CHD such as persistent pulmonary hypertension of neonate, chronic lung diseases, or thromboembolism. Children with Eisenmenger syndrome, sepsis, malignancy, or chronic inflammation, autoimmune, and liver or renal disease. All children underwent medical history, a detailed clinical assessment, and cardiac investigation.

2.1 Cardiac Assessment

Two-dimensional echocardiography was applied to participants utilizing Vivid 7 ultrasound machine (GE Medical System, Horten, Norway) with 7 and 4s MHz multi- frequency transducers. Mean pulmonary artery pressure was determined based on the peak pulmonary resurge (PR) Doppler signal. RV diameter, RV systolic and diastolic function, RV fractional area change (FAC) was assessed using apical four chamber 2-D echocardiography.

2.2 Statistical Analysis

The study underwent a statistical analysis utilizing SPSS V20 program (IBM, Chicago, IL). Shapiro-Walk test was utilized to evaluate the normality of the data. The quantitative data were displayed as the mean and standard deviation

(SD) if normally distributed while skewed quantitative data were displayed as median and interquartile range (IQR). Qualitative data were displayed as number and percentages. We used Student't test during comparing normally distributed data. P-value ≤ 0.05 revealed significance.

3. RESULTS

Tables 1 and 2 show the baseline characteristics of our cohort with CHD-PAH. Thirty children were enrolled in the study. Up to 53.3% of them were males, whose age varied between three and twelve months with median of 5 months.

Laboratory findings showed high RDW in the patients' group with mean 17.0 ± 2.33 which is higher when compared to the reference value in children with the same age (mean 13.7± 0.9) (8).

The most common diagnosis of CHD-PAH was VSD which represented 30% of cases, followed by combined PDA and ASD in 23.0% of patients, and the least type was combined VSD and ASD in 3.3% of patients (Table 3).

As regard the ECG finding, sinus tachycardia was the most predominant observation present in 93.3% of the cases. As regard axis deviation, right and left axis deviation were present in 43.3%, 30.0% respectively (Table 3).

As regard the echocardiographic data, the results showed high value of RV diameter, low value of RV FAC and normal value of RV E/A ratio (Table 3).

The research assessed the association between RDW and various laboratory and echo parameters as shown in Table 4. The optimal cutoff value of RDW reached 17.0% (mean); a significant relation between RDW level and low oxygen saturation was documented(p=0.02), right ventricular fractional area change (p=0.023) and left ventricular ejection fraction (p=0.13). However, no significant relation between other parameters and RDW level was observed as shown in Table 4.

Table 1. Demographic, clinical, and outcome findings of the patients

		PAH-CHD group (n=30)
Age (month) Median (IQR)		5.0 (3.0 – 12.0)
Sex		
	▪ Male	▪ 16 (53.3%)
	▪ Female	▪ 14 (46.7%)
Weight (kg.) Mean ± SD		6.4 ± 2.01
Clinical manifestations		
	▪ Cyanosis	▪ 12 (40.0%)
	▪ Dyspnea	▪ 30 (100%)
	▪ Fever	▪ 11 (36.7%)
	▪ Refusal of feeding	▪ 10 (33.3%)
	▪ Cough	▪ 4 (13.3%)
	▪ Failure to thrive	▪ 14 (46.7%)
Association		
	▪ Down facies	▪ 3 (10.0%)
	▪ Abnormal facies	▪ 3 (10.0%)
HR (beat/min) Median (IQR)		155.0 (138.75 – 160.0)
RR (cycle/min) Median (IQR)		60.0 (55.0 – 62.75)
O2 saturation % Median (IQR)		92.0 (82.0 – 95.0)
Prognosis		
	▪ Died	▪ 8 (26.7%)
	▪ Improved	▪ 22 (73.3%)

PAH-CHD: pulmonary arterial hypertension-congenital heart diseases, IQR: interquartile range, SD: standard deviation, HR: heart rate, RR: respiratory rate, O2: oxygen.

Table 2. Laboratory findings of the studied patients

	PAH-CHD (n=30)
Hb (g/dl)	
Mean ± SD	10.7 ± 1.58
Hematocrit %	
Mean ± SD	32.9 ± 3.90
MCV (fl)	
Mean ± SD	77.7 ± 7.42
MCH (pg)	
Mean ± SD	26.9 ± 3.95
RDW %	
Mean ± SD	17.0 ± 2.33
Platelet (10^3/ µL)	
Median (IQR)	215000 (174000 – 299250)
TLC (10^3/ µL)	
Median (IQR)	13400 (11825 – 15650)
Neutrophil %	
Median (IQR)	65.0 (43.5 – 70.25)
Lymphocytes %	
Median (IQR)	30.0 (22.8 – 50.5)
CRP (mg/L)	
Median (IQR)	48.0 (10.5 – 96.0)

PAH-CHD: pulmonary arterial hypertension-congenital heart diseases, IQR: interquartile range, SD: standard deviation, Hb: hemoglobin, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, RDW: red cell distribution width, TLC: total leucocytic count, CRP: C-reactive protein.

Table 3. Electrocardiographic and Echocardiographic parameters of the patients

		PAH-CHD group (n=30)
Type of congenital heart defect		
ASD	▪	2 (6.7%)
PDA	▪	5 (16.6%)
VSD	▪	9 (30.0%)
PDA,ASD	▪	7 (23.0%)
PDA, VSD	▪	2 (6.7%)
VSD, ASD, PDA	▪	2 (6.7%)
VSD, ASD	▪	1 (3.3%)
Common A-V canal	▪	2 (6.7%)
ECG findings		
Rhythm		
Sinus tachycardia	▪	28 (93.3%)
SVT	▪	2 (6.7%)
Axis deviation		
Right axis deviation	▪	13 (43.3%)
Left axis deviation	▪	9 (30.0%)
mPAP		
Median (IQR)		47.5 (35.75 – 56.25)
RVD		
Median (IQR)		18.0 (14.825 – 22.25)
RV systolic function (FAC)		
Median (IQR)		33.0 (31.0 – 35.0)
RV diastolic function (E/A ratio)		
Mean ± SD		1.0 ± 0.10
LV EF		
Median (IQR)		70.5 (64.0 – 74.25)

PAH-CHD: pulmonary arterial hypertension-congenital heart diseases, IQR: interquartile range, SD: standard deviation, mPAP: mean pulmonary artery pressure, RVD: right ventricular diameter, RV: right ventricle, FAC: functional area change, E/A: early/ late, LVEF: left ventricular ejection fraction.

Table 4. Laboratory and echocardiographic parameters stratified by RDW value

	≤ 17.0	>17.0	t-test	
	Mean± SD	Mean± SD	t	P-value
Age (m)	6.53±7.27	8.10±13.24	-0.402	0.691
HR (beat/min)	141±14.74	145.93±6.96	-0.815	0.422
RR (breath/min)	55.47±5.89	58.40±6.96	-1.246	0.223
O2 sat %	91.73±5.89	85.47±7.90	2.460	0.020*
Hb (g/dl)	10.30±1.10	11.06±1.90	-1.336	0.192
Hematocrit %	32.64±4.01	33.23±3.89	-0.402	0.691
MCV (fl)	76.06±8.56	79.38±5.88	-1.237	0.226
MCH (pg)	26.26±3.17	27.56±4.62	-0.898	0.377
Platelets (10^3/L)	245.2±116.07	256.66±106.81	-0.503	0.619
TLC (10^3/lL)	10.92±3.05	11.90±3.03	-0.882	0.385
mPAP	48.07±13.67	49.53±14.58	-0.284	0.778
RVD	17.36±4.49	19.47±5.02	-1.215	0.235
RV (FAC)	35.33±4.19	32.47±1.92	2.410	0.023*
RV diastolic function (E/A ratio)	1.04±0.08	0.99±0.11	1.478	0.150
LV EF	72.53±5.17	64.61±10.29	2.664	0.013*

P-value ≤ 0.05 revealed significance. RDW: red cell distribution width, HR: heart rate, RR: respiratory rate, O2: oxygen, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, TLC: total leucocytic count, CRP: C-reactive protein, mPAP: mean pulmonary artery pressure, RVD: right ventricular diameter, FAC: functional area change, E/A: early/ late, LVEF: left ventricular ejection fraction.

4. DISCUSSION

The assessment of routine laboratory measurements as an indicator for PAH-CHD) has not received the optimum attention. Red cell distribution width (RDW), which refers to variations in RBCs size, has been studied as a potential indicator for heart diseases [8]. It is easily accessible with routine complete blood count (CBC) tests. The elevation of RDW can be attributed to either a decrease in the generation of erythrocytes or an increase in their destruction.

The current study observed elevated levels of HR and RR for patients having PAH-CHD. The elevated heart rate observed in these patients can be attributed to the increased right ventriclar afterload, resulting in a reduced volume of blood pumped per heartbeat. This reduction in stroke volume triggers sympathetic activation, which in turn increases the heart rate. This mechanism ensures that the cardiac output remains sufficient to deliver an adequate supply of oxygen to the body, particularly during physical exertion [9].

This is in agreement with other studies conducted by Ploegstra and Berger [10], Hildenbrand et al. [11] and Chemla et al. [12] addressing tachycardia in patients having PAH-CHD. Moreover, this is in line with study conducted by Goetze et al. [13] who observed tachypnea and tachycardia in their patients with PAH, especially when HF develops.

The study revealed also low value of O_2 saturation in PAH-CHD patients, hypoxemia in PAH depends on various factors, including ventilation-perfusion mismatch, decreased diffusing capacity, admixture of venous blood with low oxygen saturation due to reduced cardiac output, and the opening of an intrapulmonary or intra- cardiac shunt [14,15].

This is in agreement with a study conducted by Porteous and Fritz [16] who revealed that PAH is often linked to variable degrees of hypoxemia even in absence of anatomic shunt. PH is often linked to mild to moderate hypoxemia; advanced hypoxemia must encourage further investigations of another reason for PH, identifying any accompanying pulmonary or cardiac impairment, or existence of an intra-cardiac or intrapulmonary shunt.

The present study showed the predominance of VSD (30% of cases) among other types of congenital heart defect associated with PH, which aligned with the findings of Sharmin et al. [17] demonstrating that the commonest CHD lesion was VSD (42.6%) followed by TOF (18.3%), ASD (14.8%), and PDA (7.8%).

This is in contrast with study demonstrated by Alsuwayfee et al. [18] who reported that PH is commonly associated with CAVC and PDA. However, their study was conducted among children with Down syndrome.

Our findings revealed a marked elevation in values of RDW in patient with PAH-CHD, which comes in consistency with prior research carried out by by Thayer et al and Zuk et al. [19,20] who demonstrated that patients with PH with different etiologies including CHD usually associated with higher values of RDW.

Higher erythropoiesis as a result of hypoxia may cause a rise in RDW. When it comes to the present study, high RDW was significantly correlated to low oxygen saturation which aligns with a prior study carried out by Ycas et al [21].

5. LIMITATIONS

They involve a modest sample size, and an insufficient follow-up timeframe. In addition, we didn't assess the RDW prognostic value, that helps predict treatment's response in children who have PAH-CHD.

6. CONCLUSIONS

RDW, a parameter included in the standard complete blood count, showed a significant elevation in children who had PAH-CHD children. In addition, it was significantly correlated with hypoxia and right ventricular fractional area change and left ventricular ejection fraction.

ETHICAL APPROVAL

Study approval was obtained by the ethical committee of Faculty of Medicine, Tanta University.

CONSENT

As per international standards, parental written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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