

DOI: 10.217672576-3903.100011

The Association between Red Cell Distribution Width and Mortality in Pediatric Acute Lymphoblastic Leukemia

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Rec Date: Apr 19, 2017, **Acc Date:** Apr 29, 2017, **Pub Date:** May 05, 2017

Citation: Rafsanjani KA, Falahati V, Kiumarsi A, et al. The Association between Red Cell Distribution Width and Mortality in Pediatric Acute Lymphoblastic Leukemia. J Neoplasm. 2017, 2:2

Abstract

Background: Red cell distribution width (RDW) is one of the standard parameters with blood cell counts. Studies have revealed that RDW could be used as a predictor of mortality in different contexts. However, data about the relation of RDW with hematologic malignancies is limited. In this research, we evaluated the relation of RDW with mortality in pediatric acute lymphoblastic leukemia (ALL).

Materials and methods: In the oncology department of a tertiary care children hospital, between years of 2010 to 2013, we had 83 registered cases of acute lymphoblastic leukemia (ALL) whose data was collected and analyzed retrospectively. RDW, mean corpuscular volume (MCV), hemoglobin (Hgb) and platelet (Plt) measurements were recorded and their relation with mortality, leukemia relapses and treatment cessation was examined.

Results: A total 83 patients were enrolled in the study. The mean age was 5.5 years and 50 (60.2%) were male. The mean baseline RDW level was 16.0%, and it ranged from 11.2% to 23.2%. During the study period, 12(14.5%) cases had died. The rate of mortality did not significantly correlate with RDW level.

Conclusions: Although a relationship between elevated RDW and mortality has been reported in several contexts, we did not find any significant correlation between the RDW level and the rate of mortality and relapse in pediatric patients with acute lymphoblastic leukemia (ALL).

Keywords: Cancer; Red Cell Distribution Width (RDW); Acute Lymphoblastic Leukemia (ALL); Prognosis; Mortality

Introduction

Red cell distribution width (RDW) is a laboratory parameter which expresses the variability in red blood cell size and is calculated as the standard deviation in red blood cell (RBC) size divided by the mean corpuscular volume (MCV). Clinically, it is a widely available and low-cost test. Its normal range is between 11.5% to 14.5%. Elevated RDW on complete blood count reflects impairment in erythropoiesis and abnormal red blood cell survival which can be caused by any disease involving red blood cell destruction or production [1]. In recent years, several studies have demonstrated that elevation of this simple parameter is associated with increased risk of mortality in different contexts including sepsis, cardiovascular disease, cancer, and chronic lower respiratory tract disease [2-10]. It is established that inflammation and oxidative stress affect RDW and it has been shown that RDW elevation is associated with raise in the cytokines such as IL6, TNF- α [11,12]. On the other hand, cancer is characterized with increased inflammation. However, few reports have focused on RDW in the area of oncology especially in pediatric patients. In view of that, the aim of this study is to evaluate the correlation between RDW and mortality in pediatric acute lymphoblastic leukemia patients.

Material and Methods

We retrospectively reviewed the medical records of all pediatric patients diagnosed with ALL between the ages of 1 and 15 years, registered at our hospital, between years 2010 to 2013. The diagnosis of ALL at presentation was made according to bone marrow morphology and immunophenotyping. Our patients were treated in accordance with the ALL IC-BFM [13]. From the complete blood counts of the patients at the time of diagnosis, the mean cell volume (MCV), hemoglobin (hgb), platelet (plt) and RDW values were recorded.

RDW is reported as a coefficient of variation (percentage) of red blood cell volume. Patients were categorized in to four

RDW quartiles based on previously published a priori cut-points (RDW < 13.4, 13.4–14.3, 14.4–15.7 and >15.7) [8,9].

The records of all patients were followed for at least 3 years after diagnosis and events including disease relapse, death or treatment termination were documented.

SPSS version 16.0 program was used for statistical analysis. All parameters were reported as mean and \pm S.D. Chi-square was used for comparing categorical variables. $P < 0.05$ level was considered statistically significant.

Table 1: The characteristics of patients

Characteristics		RDW	<13.4	13.4-14.3	14.4-15.7	>15.7	p-value
		All patients					
Number (%)		83	16(19.3%)	8(9.6%)	16(19.3%)	43(51.8%)	0.5
Mean Age(years)		5.5	6.1	3.5	6	5.5	0.9
Gender	Male	50(60.2%)	14	4	8	24	--
	Female	33(39.8%)	2	4	8	19	
Mean WBC		19798	13881	5125	42512	17674	0.5
Mean Hgb (mg/dl)		8.4	10.2	8.9	7.7	8	0.4
Mean Plt		93659	119562	111125	55438	88513	0.2
Mean MCV		83.6	82	83	84	84	0.5
Death		12	5	0	1	6	0.09
Relapse		12	7	1	0	4	0.2
Treatment termination		73	37	15	8	13	0.4

During the study period, 12(14.5%) cases had died. The rate of mortality did not significantly correlate with RDW level. The same percent of patients had experienced disease relapse and the rate of relapse did not correlate with RDW level either. In 88% of patients treatment had reached the termination time but this rate did not also correlate with RDW level in our patients.

Discussion

Acute Lymphoblastic Leukemia (ALL) is the most common childhood malignancy, comprising 19% of cancers occurring before age 20 years [14]. Due to the development of active chemotherapeutic agents and significant advances in supportive care, overall cure rates for pediatric ALL have improved to the current Event Free Survival (EFS) rates of 75% to 85% [15]. Certain clinical and laboratory features exhibited at diagnosis have prognostic value but the relative value of these features as prognostic indicators varies. The identification of valuable prognostic factors has become essential in the design and analysis of modern therapeutic trials.

Hematological tumors are associated with disturbance in erythropoiesis and also inflammation [16,17]. In view of the fact that RDW level is indicative of abnormal red blood cell survival and that it correlates with the presence of

Results

A total 83 patients were enrolled in the study. The mean age was 5.5 years and 50 (60.2%) were male. The mean baseline RDW level was 16.0%, and it ranged from 11.2% to 23.2%. Among these, 43(51.8%) patients presented an RDW higher than 15.7%. Characteristics of the patients stratified according to RDW quartiles are presented in Table 1. Baseline RDW level did not correlate with initial WBC, hemoglobin, MCV and platelet count.

inflammatory states [18,19], this parameter has been investigated as prognostic factor in hematological malignancies [20-26]. Some recent studies and a meta-analysis have demonstrated that RDW is a potent predictor of all-cause mortality, including cancer-related deaths [4,11]. In a prospective cohort study including patients with solid and hematological cancer, high RDW was associated with an increased risk of mortality [27].

Lee et al. demonstrated that multiple myeloma patients who had RDW >14.5% at diagnosis were associated with higher risk of mortality [20]. In a study by Iriyama et al. CML associated deaths were more common in the high-RDW group [22].

Conclusion

Nearly all of these studies have investigated the relationship between RDW and cancer among elderly populations in whom RDW could also reflect comorbidities such as age, risk of cardiovascular complications, and severity of renal impairment [28]. In our study, which was conducted among the pediatric age group, RDW level did not have significant correlation with neither mortality nor relapse rate. These results seem to be supporting the fact that the connection between RDW and cancer merely is a reflection of inflammation and oxidative stress which are inevitably seen in cancer [29].

The limitations of this study were the potential inaccuracy in retrospective data collection, the small size of the study population, undetermined etiology and timing of death and also timing and type of relapse. Despite these limitations, to our knowledge, this is the first documentation on the prognostic value of RDW in patients with acute lymphoblastic leukemia in a pediatric population. Further prospective studies are required to affirm that RDW could or could not be useful in adding prognostic information in oncology patients.

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