# Blast Cells Count Influences Bleeding Incidence in Acute Leukemia: Preliminary Study in South Kalimantan, Indonesia

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Abstract

BACKGROUND: Acute leukemia is a malignant disease involving hematopoietic tissue, characterized by abnormal blood cells in bone marrow or called blast cells. The most common complications of acute leukemia are bleeding. A high percentage of blasts have been reported to increase the risk of bleeding in acute leukemia.

AIM: Preliminary study was needed to investigate relationship between blast cells count and bleeding incidence in acute leukemia.

METHODS: A cross-sectional study with observational analytic in 38 adult subjects was conducted from November 2019 to May 2021 in Ulin Hospital, Banjarmasin, South Kalimantan. The data were taken from medical records of acute leukemia patients who met inclusion and exclusion criteria. Data analysis was using Fisher's exact test.

RESULTS: This study enrolled 17 men and 21 women. Blast cells count in peripheral with cutoff <50% was 20 (52.6%) and ≥50% was 18 (47.4%) and otherwise in bone marrow. Both of women and men mostly have bleeding in acute leukemia, and bleeding incidence in women is higher than men. Bleeding condition was happened both in peripheral and bone marrow blast cells count with cutoff <50% and ≥50%. Significance of relationship between blast cells count and bleeding incidence was 0.669.

CONCLUSION: There is no significant relationship between blast cells count and bleeding incidence in acute leukemia. Another parameters that could influence bleeding incidence need to be investigated in acute leukemia.

Introduction

Acute leukemia is a malignant disease characterized by the displacement of normal bone marrow components by abnormal blood cells or called blast cells [1]. Acute leukemia is divided into two types, namely, acute myeloid leukemia (AML) that attacks myeloid cells and acute lymphoblastic leukemia that attacks lymphoid cells [2]. The American Cancer Society states the incidence of leukemia in the United States in 2020 reached 19,940 new cases occurring in AML with a mortality rate of 11,180 cases due to AML [3]. The clinical manifestation features in acute leukemia include bone marrow failure in forming normal blood cells because of the accumulated blast also accompanied by infiltration of organs [4]. Blast cell presentations more than 30% in the bone marrow are found during clinical examination of acute leukemia [5].

One of the most common complications of acute leukemia is bleeding caused by various hemostatic disorders [1]. A high percentage of blasts have been reported to increase the risk of bleeding in acute leukemia, which is one of the complications of acute leukemia which can increase the risk of death [6]. Mucosal bleeding or bleeding under the skin is common manifestations of acute leukemia and is usually associated with platelet deficiency [7]. The study of relationship between blast count and bleeding incidence is still limited, especially in Indonesia. This is preliminary study to investigate their relationship in South Kalimantan. This area has many factories that contribute air pollution as one of the antigens to promote acute leukemia.

Methods

An observational study with cross-sectional approach was conducted in Ulin Hospital, Banjarmasin, South Kalimantan, from November 2019 to May 2021.

The subjects of the study were 38 acute leukemia patients who met inclusion and exclusion criteria by consecutive sampling. The inclusion criteria were >15 years old, 1st time diagnosis of leukemia, men and women, normal body temperature, steroid free, menstruation was normal according to age for women, drug free causes coagulation/anticoagulant abnormalities, while the exclusion criteria were patients with history or were suffering autoimmune disease, coronary heart disease and stroke or other blood vessel abnormalities, kidney abnormalities, liver abnormalities, and malignancies other than leukemia and trauma.

Data were taken from medical records in Ulin Hospital, including name, age, sex, activity, current symptoms, history of previous hematological diseases, and results of laboratory data (complete blood count and bone marrow aspiration). Complete blood count was performed by Sysmex XN-1000. Bone marrow aspiration was done and interpreted by clinical pathologist. Data analysis was performed by statistical program computer. Fisher's exact test was conducted to examine the relationship between the number of blast cells with the incidence of bleeding in acute leukemia. The result of statistical test is significant if $p < 0.05$ was considered. Ethical clearance was obtained from the Medical and Health Research Ethics Commission of the Dr. Kariadi Hospital Semarang, number 417/EC/KEPK-RSDK/2019.

Table 1: Characteristics of subjects

Variable	F	%	Median (min-max)
Age			34.5 (16–67)
Adolescence (13–18 years)	7		
Adult (19–59 years)	26		
Senior adult (60 years and above)	5		
Gender			
Men	17	44.7	
Women	21	55.3	
Activity			
Housewife	12	31.6	
Farmer	7	18.4	
College student	4	10.6	
Civil servants	6	15.8	
Construction laborer	1	2.6	
Student	7	18.4	
Retirement	1	2.6	
Weight (kg)			54 (38–68)
Height (cm)			160 (150–173)
Hemoglobin (g/dL)			8.6 (3.3–13.2)
Hematocrit (%)			26.5 (10.7–42.0)
Erythrocytes (x 10^6/μL)			3.00 (1.09–5.22)
MCV (fl)			87 (79.0–105)
MCH (pg)			29 (25–34)
MCHC (g/dL)			33 (30–37)
Leukocyte count (cells/μL)			16,950 (351–118,200)
Platelet count (cells/μL)			43,500 (6000–256,000)
Peripheral blast cells count			
< 50%	20	52.6	
≥ 50%	18	47.4	
Bone marrow blast cells count			
< 50%	18	47.4	
≥ 50%	20	52.6	

F: Frequency, Min: Lowest value, max: Highest value.

Results

The characteristic data of subjects are shown in Table 1. Hematology profile showed that some subjects were normocytic normochromic anemia, leukopenia, leukocytosis, thrombocytopenia, and also thrombocytosis.

The cutoff blast cells count in this study is <50% and ≥50%. It was found that there were 18 subjects (47.4%) who had bone marrow blast cells count <50% and 20 subjects (52.6%) who had number of bone marrow blast cells count >50%. Peripheral blast cells count showed otherwise. There were 20 subjects (52.6%) who had peripheral blast cells count <50% and 18 subjects (47.4%) who had peripheral blast cells count >50%.

Table 2: Bleeding incidence related to sex

Bleeding	Sex (person)		Total
	Men	Women	
Yes	9	8	17
No	8	13	21
Total	17	21	38

Table 2 shows that both of women and men mostly have bleeding in acute leukemia, and bleeding incidence in women is higher than men. Table 3 shows that bone marrow blast cells count with cutoff ≥50% has slightly more bleeding incidence, while in peripheral blast cell count with cutoff ≥50% has slightly lesser bleeding incidence. Bleeding condition could be happened in acute leukemia with low blast cells count, even high blast cells count.

Table 3: Bleeding incidence related to peripheral and bone marrow blast count

Bleeding	Peripheral blast cells count		Total	Bone marrow blast cells count		Total
	< 50%	≥ 50%		< 50%	≥ 50%	
Yes	8	9	17	8	9	17
No	12	9	21	10	11	21
Total	20	18	38	18	20	38

Data were analyzed by Fisher's exact test to examine the relationship between blast cells count and bleeding incidence in acute leukemia. Based on the Fisher's exact test, the result showed that there was no significant correlation between blast cells count and bleeding incidence in acute leukemia, as shown in Table 4.

Table 4: Fisher's exact test results

Variable	Bleeding incidence
	p
Blast cells count	0.669

Discussion

The result of Fisher's test between blast cells count and bleeding incidence showed that there was no significant correlation. The study has same result with Kim *et al.* (2006) and Balmages *et al.* (2018) found that there were no significant relationship blast cells count and bleeding incidence in acute leukemia [6], [8].

An unsignificant relationship between blast cells count and bleeding incidence can be caused by several factors. One of them is state of cytopenia. The results showed that patients had decreased levels of hemoglobin, hematocrit, erythrocytes, and platelets. In patients with AML, there is a blockade of maturity that causes the process of differentiation of myeloid series cells stops in young cells (blast), resulting in accumulation of blast cells in the bone marrow [9]. Thrombocytopenia is a major risk factor for bleeding in acute leukemia [10]. Webert (2006) found that there was a relationship between bleeding incidence and thrombocytopenia in acute leukemia patient that more influence the bleeding state [11].

Another factor is age, acute leukemia can affect all ages [12]. The incidence of AML increases with age and this disease is more common in men than women that reversely happened in this study. Gender can also affect the incidence of bleeding in patients with acute leukemia. Kelton *et al.* (2011) found that sex was associated with differences in sensitivity in terms of platelet aggregation between men and women [13]. The agregation of thrombocytes in male is easier to happen than female. Bleeding incidence that occurs in female patients can be associated with the use of oral contraceptives and hormone replacement therapy in women [14]. In addition, female sex hormones can increase the risk of coagulopathy in acute leukemia [6].

This study has analyzed blast cells count only. Based on theory, bleeding could be occurred in thrombocytopenia than high blast cell count. Another parameters such as hemostasis parameters and biomolecular parameters related to leukemia cells also host cells were not examined in this preliminary study. Future studies need to perform those parameters correlate with bleeding incidence.

Conclusion

There is no significant relationship between blast cells count and the bleeding incidence in acute leukemia. Another parameters that could be influenced bleeding incidence need to be investigated in acute leukemia.

Acknowledgment

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