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Original Research Article

Association between thrombocyte and neutrophyl count with cutaneous manifestations in children with acute lymphocytic leukemia and acute myelocytic leukemia

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ABSTRACT

Background: Acute leukemia is a hematopoietic stem cell malignant disease, with abnormal proliferation of leukemic and immature cells that suppress the production of normal blood cell and extensively invade peripheral tissues organs including skin. Homeostatic abnormalities that occur in leukemia e.g. thrombocytopenia and neutropenia. Various cutaneous manifestations can be observed in leukemia but the etiology is usually unknown, because many factors are responsible for this cutaneous manifestation. The aim of the present study was to determine association between thrombocyte and neutrophyl count with cutaneous manifestations in children with Acute Lymphocytic Leukemia (ALL) and Acute Myelocytic Leukemia (AML).
Methods: This is an observational analytical cross-sectional study involving 51 children with acute leukemia (ALL and AML) were hospitalized in H. Adam Malik General Hospital Medan during April – September 2018. Interview, dermatology examination and recording thrombocyte and neutrophil count were performed to the subjects. Differences between thrombocyte and neutrophyl count with cutaneous manifestations were analyzed using Mann Whitney test. Association between thrombocyte and neutrophyl count with cutaneous manifestations were analyzed using Kolmogorov Smirnov test.
Results: Children with Acute Leukemia in this study most of them were girls (51.0%), age between 0 - 5years old (39.2%). There were no significant differences between thrombocyte and neutrophyl count with cutaneous manifestations in children with acute leukemia (p value 0.692 and 0.814). There was no significant association between thrombocyte and neutrophyl count with cutaneous manifestations in children with acute leukemia (p value 0.490 and 0.803).
Conclusions: There is no significant association between thrombocyte and neutrophyl count with cutaneous manifestations in children with acute leukemia.

Keywords: Acute leukemia, Cutaneous manifestation, Neutrophyl, Thrombocyte

INTRODUCTION

Leukemia is a group of diseases characterized by immature white blood cells accumulation in the bone marrow and peripheral blood. These abnormal cells cause symptoms due to bone marrow failure (anemia, neutropenia, thrombocytopenia) and organ infiltration (liver, spleen, lymph nodes, meningens, brain, gingiva, testis including skin). Acute leukemia is the common malignancy that occur in children especially Acute

Lymphoblastic Leukemia (ALL) and Acute Myeloblastic Leukemia (AML).[1,2]

In blood examination, leukemia patients may have anemia, abnormalities leukocyte count and thrombocytopenia. Clinical symptoms that are often found are fever, weakness, fatigue and pallor. Anemia can cause pallor, fatigue, tachycardia and dyspnea. Neutropenia causes fever, buccal mucosa ulceration and infection. While thrombocytopenia can cause infection, purpura, and other bleeding.[1,3]

Cutaneous manifestations are common in patients with leukemia. However, the cause is not always immediately clear, as there are often numerous potential etiologies. Cutaneous manifestations of leukemia can be divided into specific and non-specific lessions. Unspecific lessions have been associated with leukemia and which develop on the basis of abnormal hematopoiesis or as expression of a cutaneous paraneoplastic disorder. While thrombocytopenia may give rise to hemorrhagic skin diseases and inadequate granulocytopoiesis can lead to opportunistic.[4-6]

METHODS

This research is a cross sectional study with observational analytic design. All pastients who have diagnosed as Acute Lymphoblastic Leukemia (ALL) and Acute Myeloblastic Leukemia (AML), observed from April to September 2018 at Department of Pediatrics Haji Adam Malik General Hospital Medan, were considered for the study.

Inclusion criteria

- ALL and AML patients aged 0 -18years old
- And who have undergone routine blood test included thrombocyte and neutrophyl count.

Exclusion criteria

ALL and AML patients who did not have blood test results for thrombocyte and neutrophyl count.

All research samples were evaluated for skin manifestations. Clinical details including age, sex, type of leukemia was recorded. Laboratory results thrombocyte and neutrophyl count of patient using secondary data based on medical record.

Statistical analysis

Descriptive analysis was performed to determine patients' characteristics. Kolmogorov Smirnov test was used to test the normality of the data obtained. Differences between thrombocyte and neutrophyl count with cutaneous manifestations were analyzed using Mann Whitney test and association between thrombocyte and neutrophyl count with cutaneous manifestations were analyzed using Kolmogorov Smirnov test. P value <0.05 were considered to be significant.

Ethics

Ethical clearance was given by Health Research Etchical Committee, Faculty of Medicine, University of Sumatera Utara, and we obtained written informed consent from all patients.

RESULTS

During the study period, total of 51 pediatric patients with Acute Leukemia (ALL and AML) at Department of Pediatrics Haji Adam Malik General Hospital Medan were registered.

Table 1: Distribution of research subjects based on their characteristic.

Characteristic	ALL		AML	
Age group (year)	**n**	**%**	**n**	**%**
0 - 5	20	44.4	0	0
6 - 10	13	28.9	3	50
11 - 15	12	26.7	3	50
Gender	**n**	**%**	**n**	**%**
Boy	21	46.7	4	66.7
Girl	24	53.3	2	33.3
Cutaneus manifestation	**n**	**%**	**n**	**%**
Positive	23	51.1	2	33.3
Negative	22	48.9	4	66.7

Table 1 shows children with acute leukemia (ALL and AML) in this study most of them were age between 0 - 5years old (39.2%). Most of children with ALL were age between 0 - 5years old (44.4%). And children with AML were age between 6 - 10years old same as age between 11-15years old (50%). Median age of ALL children was 6 year (range 1 to 15 year) and group AML children median age was 10,5 year (range 7 to 13 year). Acute Leukemia children in this study most of them were girls, 26 patients (51.0%) and boys 25 patients (49%). And most of them did not have skin manifestation, 26 patients (51%).

Table 2 shows higher thrombocyte count in group with cutaneous manifestation (78,000.00/mL) than group without cutaneous manifestation (68,500.00/mL), but the differences was not statistically significant.

Result of this study that shows in Table 3, authors found that both group acute leukemia children with cutaneous manifestation and without cutaneous manifestation mostly with thrombocytopenia. Statistically there is no association between thrombocyte count with cutaneous manifestations.

From Table 4, this study showed higher median neutrophyl count in group with cutaneous manifestations (2.14/mL) than group without cutaneous manifestation (1.11/mL) in children with acute leukemia (ALL and AML), but the differences was not statistically significant.

Table 5 shows acute leukemia children with cutaneous manifestations in this study mostly have normal neutrophyl count and without cutaneous manifestation mostly with neutropenia. Statistically there is no association between neutophyl count with cutaneous manifestations.

DISCUSSION

Leukemia is a malignancy mostly occur in children age <15years old. Leukemia (76% of which are lymphoid leukemias) accounts for 30% of all childhood cancer. Leukemia affecting the hematopoietic system following a generalization phase in the bone marrow and subsequent appearance of leukemic cells in peripheral blood, extramedullary manifestation can occur in various organ of the body including skin. The clinical symptom of acute leukemia is caused by the often rapidly developing bone marrow insufficiency.[6,7]

Table 2: Differences thrombocyte count with cutaneous manifestations in children with acute leukemia (ALL and AML).

Cutaneous manifestation	Mean	Median	SD	Min	Max	p
Positive	157,952.00	78,000.00	158,091.77	4,000.00	408,000.00	0.692
Negative	113,538.46	68,500.00	106,795.59	4,000.00	363,000.00	

Table 3: Association thrombocyte count with cutaneous manifestations in children with acute leukemia (ALL and AML).

Thrombocyte	Cutaneous manifestation						p
	Positive		negative		Total		
Thrombocytopenia	15	45.5%	18	54.5%	33	100.0%	0.490
Normal	10	55.6%	8	44.4%	18	100.0%	

Table 4: Differences neutrophyl count with cutaneous manifestations in children with acute leukemia (ALL and AML).

Cutaneous manifestation	Mean	Median	SD	Min	Max	p
Positive	4.17	2.14	6.75	0.05	30.11	0.814
Negative	8.30	1.11	23.25	0.04	118.71	

Table 5: Association neutrophyl count with cutaneous manifestations in children with acute leukemia (ALL and AML).

Neutrophyl count	Cutaneous manifestation						P
	Positive		Negative		Total		
Neutropenia	8	38.1%	13	61.9%	21	100.0%	
Normal	14	63.6%	8	36.4%	22	100.0%	0.803
Neutrophilia	3	37.5%	5	62.5%	8	100.0%	

The evaluation of skin manifestation in the leukemia patient is confounded by potential cutaneous infiltration of leukemic cells, infection, bone marrow suppression, chemotherapeutic regimens and other factors. Among many types of nonspecific skin manifestations, the most frequently encountered are pruritus, prurigo, urticaria, erythema multiforme like lessions, papulovesicles, subcutaneous nodules, petechiae and hemorhages. In about 5% to 10% patients with leukemia, the cutaneous lessions precede the diagnosis, in about 35% to 45% they are simultaneous and in about 55% they appear afterward, usually months later.[1,4,5]

Blood smears of acute leukemia patients typically reveals decreased red cells and thrombocyte, with the white count varying from leukopenia to marked leukocytosis. A decrease in the number of mature neutrophyl is common. In this study showed no significant differences between thrombocyte and neutrophyl count with cutaneous manifestations in children with acute leukemia (ALL and AML). The results accordance with the research of Agis

et al, which found there is no significant differences between thrombocyte count with leukemia cutis and without leukemia cutis in AML patients.[5,8]

Thrombocytopenia in leukemia patients can manifest epistaxis or skin bleeding such as purpura. Neutropenia in malignant patients or undergoing chemotherapy can result in fever, oral mucous ulceration and infection. Research of Bakhshi et al, found most location of infections in pediatric patients with acute lymphoblastic leukemia is the lungs, HEENT (head, ear, eyes, nose, throat), gastrointestinal tract, urinary tract blood, cellulitis and skin. Psaila et al, found, 14 thrombocytopenic patients with AML (70%) experienced skin and oral bleeding.[5,9-11] In this study authors only assessed the presence of infections in the skin and mucosa, and authors did not find any infection skin or mucosa. Results of this study showed there is no significant association between thrombocyte and neutrophyl count with cutaneous manifestations in children with acute leukemia.

Cutaneous manifestations in leukemia are divided into specific and non-specific based on clinical and histopathological criteria. But this study does not distinguish whether cutaneous manifestations specific or non-specific. Non-specific skin lessions in leukemia are usually caused by abnormalities of the hematopoiesis system or due to the appearance of skin abnormalities associated with malignancy.[4,6] Cutaneous manifestation in this study including purpura, alopecia, prurigo, miliaria, hiperpigmentation, striae, echimosis, intertrigo and cheilitis. Among the many types of nonspecific skin manifestations, the most frequently encountered are pruritus, prurigo, urticaria, erythema multiforme like lessions, papulovesicles, subcutaneous nodules, petechie, and hemorrhages. Research of Millot et al, demonstrates that cutaneous involvement can be an early manifestation of acute lymphoblastic leukemia or lymphoblastic lymphoma.[12,13]

CONCLUSION

There is no significant association between thrombocyte and neutrophyl count with cutaneous manifestations in children with acute leukemia.

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