Bali
Medical Journal
www.BaliMedicalJournal.org

Characteristics of patients with acute lymphoblastic leukemia in 2016-2020 at Sanglah General Hospital, Bali

CrossMark

Evelin Vianetha Prima Snak[1*], Ni Nyoman Mahartini[2], Sianny Herawati[2], Ni Kadek Mulyantari[2], Anak Agung Wiradewi Lestari[2]

ABSTRACT

Background: Acute lymphoblastic leukemia (ALL) is a bone marrow malignancy that is the most common cause of death in children. This study aims to determine the characteristics of ALL patients in 2016-2020 at Sanglah Hospital Denpasar, Bali.
Methods: This study used a retrospective descriptive study with secondary data from 166 patients. Variables assessed in this study included: demographic characteristics (age, gender, place of origin), complete blood count results include of hemoglobin levels, leukocyte (white blood cell) count, absolute neutrophil count, absolute lymphocyte count, thrombocyte count, and morphology subtype of ALL based on FAB classification from bone marrow aspiration (BMA).
Results: From demographic characteristics: most patients' age was in school-age children (>6 - ≤18 years) about 59.7%, dominated by male (60.2%), place of origin from Bali (71.7%) which is from Denpasar city (23.5%). From the laboratory results, complete blood count found that the most results are moderate anemia in children (54.7%), in adult female (70%), and in adult male (52.9%); leukocytosis in children (41%), in adult (77.8%); neutropenia in children (61.2%), in adult (59.3%); lymphocytosis in children (43.2%), in adult (81.5%); thrombocytopenia in children (97.1%), in adult (100%). From the results of the BMA examination, based on the FAB (French, American, and British) classification, the most common morphology of ALL was L2 subtype (78.9%).
Conclusion: Characteristics of patients with ALL at Sanglah General Hospital are dominated by children, male, from Denpasar, Bali, with laboratory results showing moderate anemia, leukocytosis, neutropenia, lymphocytosis, thrombocytopenia, and the most common morphological variants are ALL-L2 subtype.

[1]Clinical Pathology Resident, Faculty of Medicine, Universitas Udayana, Sanglah General Hospital, Bali, Indonesia;
[2]Department of Clinical Pathology, Faculty of Medicine, Universitas Udayana, Sanglah General Hospital, Bali, Indonesia;

*Corresponding author:
Evelin Vianetha Prima Snak;
Clinical Pathology Resident, Faculty of Medicine, Universitas Udayana University, Sanglah General Hospital, Bali, Indonesia;
evelynsnak@gmail.com

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a malignant disease of the bone marrow which is characterized by the proliferation of precursors of the lymphoid pathway, causing changes in normal hematopoietic cells in the bone marrow to become neoplastic. These changes cause a deficiency of normal bone marrow products such as erythrocytes, leukocytes (except lymphocytes), and thrombocytes. This malignancy originated from B lymphocytes (85% in adults) or T lymphocytes. Patients with suspected ALL should undergo laboratory examinations to establish the diagnosis, determine the classification, prognosis, and determine the type of therapy. Examinations used to establish the diagnosis of ALL include

complete blood count showed an increase in leukocytes, decrease of absolute neutrophil count, erythrocyte, and thrombocyte. Bone marrow aspiration (BMA) is necessary to establish the diagnosis and determine the classification of ALL. Classification of ALL is important to determine the management and prognosis.[1-3] Bone marrow aspiration showed increased hypercellularity, with an increase in lymphoblast cells of approximately >20%.[4]

The American Cancer Society in 2017 reported that there were 5,970 new cases of ALL in adults and children, consisting of 3,350 male and 2,620 female. The National Cancer Institute estimates that in 2018 as many as 60,300 people were living with ALL, and about 1,440 deaths from this disease.[5] ALL has a high incidence rate

and is the most common cause of death in children.[6] However, not much data have been reported about the characteristics of patients with ALL.

This study aims to determine the characteristics of ALL patients in 2016-2020 at Sanglah Hospital Denpasar based on patient demographics (age, sex, and place of origin), laboratory examinations include hemoglobin levels, leukocyte count, absolute neutrophil, absolute lymphocyte, thrombocyte count, and morphology of ALL.

METHODS

This research is a retrospective descriptive study. Samples were obtained from secondary data based on medical records of pediatric and adult patients diagnosed

with ALL in 2016-2020 at Sanglah General Hospital Denpasar, Bali. The inclusion criteria of this study were ALL patients who had complete demographic data, complete blood count result, morphology of ALL, and had not received chemotherapy. Data was analyzed using IBM SPSS Statistics 20.0.

RESULTS

166 subjects with ALL met the inclusion criteria. The mean age of patients with ALL was 13.9 ± 13.4 years. Based on demographic characteristics (Table 1), dominated by children, as many as 139 patients (83.7%), most of them school-aged (>6 to ≤18 years), about 83 subjects (59.7%). Gender is dominated by male, with about 100 patients (60.2%). From the place of origin, dominant from Bali, with about 119 patients (71.7%), most of them from Denpasar city, about 23.5%. Moreover, 47 patients (28.3%) came from outside Bali.

Complete blood count results were obtained before the patient received chemotherapy, can be seen in Table 2. From hemoglobin levels, the most results in children were between 7 – 9.9 g/dL about 76 patients (54.7%), in adult female patients were between 8 – 10.9 g/dL about 7 patients (70%), in adult male patients were between 8 – 10.9 g/dL about 9 patients (52.9%). From leukocyte count, the most results in children were >13.5×10³/μL about 57 patients (41.0%), while in adult patients were >10.6×10³/μL about 21 patients (77.8%). From absolute neutrophil count, the most results in children were <1.2×10³/μL about 85 patients (61.2%), while in adult patients were <1.7×10³/μL about 16 patients (59.3%). From absolute lymphocyte count, the most results in children patients were >7.2×10³/μL in 60 patients (43.2%), while in adult patient were >3.2×10³/μL in 22 patients (81.5%). Thrombocyte count, the most results in children were <150×10³/μL in 135 patients (97.1%), while in adult patients were <150×10³/μL in 27 patients (100%).

The most common morphology of ALL from BMA examination results based on French – American - British (FAB) classification in this study was ALL-L2 subtype, about 131 patients (78.9%), can

be seen in Table 3.

DISCUSSION

Most of patients with ALL in this study are children (83.7%), dominated by school-aged children >6 to ≤18 years (59.7%). Similar results have been reported by Reddy et al who reported that from 204 ALL patients, about 68.6% are children, and Silva et al., from 92 ALL patients, about 53.26% are children aged between 6-11 years (53.26%).[7,8] No subjects were found in the infant aged group (0 - <1 year). According to some literature, the incidence of ALL in the infant is very rare.[9] Males were predominant (60.2%) in our study, similar to a previous study by Saleh et al. and Saikia et al.[10,11] ALL is more common in males but remains unexplained, gender may affect the prognosis. Males with ALL have a worse prognosis than females because testicular involvement can occur in 10 – 23% of cases.[12] Based on the place of origin, mostly from Bali (71.7%), which is from Denpasar city (23.5%). Meanwhile, 28.3% of total patients came from outside Bali, which is from the eastern part of Indonesia, e.g. West and East Nusa

Tenggara, because Sanglah Hospital is also a referral hospital for the eastern part of Indonesia.

We found that the most results of the hemoglobin level were between 7 – 9.9 g/dL in 76 children (54.7%), between 8 – 10.9 g/dL in 7 adult females (70%) and also in 9 adult males (52.9%), all of that classified as moderate anemia. In a previous study by Putri et al., from 50 ALL patients, 33 patients (66%) had hemoglobin level of 5 – 10 g/dL.[5] Another study by Tarigan et al showed 40 patients (48%) had hemoglobin level <7.0 g/dL.[6] Anemia in ALL caused by loss of bone marrow hematopoietic function due to progressive infiltration of malignant leukemia cells.[5] Leukocyte count in ALL can be found increased, normal, or decreased.[6] In our study, most children and adults showed an increase in leukocyte count (leukocytosis). According to Pahloosye et al., from 100 ALL patients, about 38% with leukocytosis, and Saikia et al., from 52 of ALL patients, about 33 patients (63%) with leukocytosis.[11,13] An excessive increase of leukocyte count occurs due to impaired of proliferation and regulation in the release of leukocytes

Table 1. Baseline characteristics of patients with ALL.

Variables	n (%)	Average ± SD
Age		13.9 ± 13.4
Children (0 - ≤ 18 years)	**139 (83.7)**	
Infant (0 - ≤1 years)	0 (0.0)	
Toddler (>1 - ≤5 years)	34 (24.5)	
Preschool-aged (>5 - ≤6 years)	22 (15.8)	
School aged(>6 - ≤18 years)	83 (59.7)	
Adult (> 18 years)	**27 (16.3)**	
Gender		
Male	**100 (60.2)**	
Female	**66 (39.8)**	
Place of origin		
Bali	**119 (71.7)**	
Denpasar	39(23.5)	
Jembrana	12 (7.2)	
Tabanan	8 (4.8)	
Badung	15 (9.0)	
Gianyar	12 (7.2)	
Klungkung	7 (4.2)	
Bangli	6 (3.6)	
Karangasem	4 (2.4)	
Buleleng	16 (9.6)	
Others	**47 (28.3)**	

from bone marrow.[14] The results of the absolute neutrophil count in this study, both in children (61.2%) and in adults (59.3%), showed a decrease in neutrophil count (neutropenia). A previous study by Tarigan et al. reported that 84 ALL patients had neutropenia in 34 patients (40%).[6] Neutropenia caused by bone marrow suppression and infiltrations of malignant leukemic cells results in hematopoiesis dysfunction. So can lead to disturbances in neutrophil production. Patients with

Table 2. Complete blood count results.

Variable	Results		n (%)
Hemoglobin (g/dL)	**Children (n=139)**		
	≥ 11	(Normal)	32 (23.0)
	10 - 10.9	(Mild Anemia)	28 (20.1)
	7 - 9.9	(Moderate Anemia)	76 (54.7)
	<7	(Severe anemia)	3 (2.2)
	Adult Female (n=10)		
	≥ 12	(Normal)	0 (0.0)
	11-11.9	(Mild Anemia)	0 (0.0)
	8-10.9	(Moderate Anemia)	7 (70)
	<8	(Severe anemia)	3 (30)
	Adult male (n=17)		
	≥ 13	(Normal)	1 (5.9)
	11-12.9	(Mild Anemia)	1 (5.9)
	8-10.9	(Moderate Anemia)	9 (52.9)
	<8	(Severe anemia)	6 (35.3)
Leukocyte count (10³/µL)	**Children (n=139)**		
	<6	(Leukopenia)	53 (38.1)
	6 - 13.5	(Normal)	29 (20.9)
	>13.5	(Leukocytosis)	57 (41.0)
	Adult (n=27)		
	<3.6	(Leukopenia)	4 (14.8)
	3.6 - 10.6	(Normal)	2 (7.4)
	>10.6	(Leukocytosis)	21 (77.8)
Absolute neutrophil (10³/µL)	**Children (n=139)**		
	<1.2	(Neutropenia)	85 (61.2)
	1.2-9.5	(Normal)	50 (36.0)
	>9.5	(Neutrophilia)	4 (2.9)
	Adult (n=27)		
	<1.7	(Neutropenia)	16 (59.3)
	1.7-7.5	(Normal)	9 (33.3)
	>7.5	(Neutrophilia)	2 (7.4)
Absolute lymphocyte (10³/µL)	**Children (n=139)**		
	<2.5	(Lymphopenia)	35 (25.2)
	2.5-7.2	(Normal)	44 (31.7)
	>7.2	(Lymphocytosis)	60 (43.2)
	Adult (n=27)		
	<1.0	(Lymphopenia)	1 (3.7)
	1.0-3.2	(Normal)	4 (14.8)
	>3.2	(Lymphocytosis)	22 (81.5)
Thrombocyte (x10³/µL)	**Children (n=139)**		
	<150	(Thrombocytopenia)	135 (97.1)
	150 – 450	(Normal)	4 (2.9)
	>450	(Thrombocytosis)	0 (0.0)
	Adult (n=27)		
	<150	(Thrombocytopenia)	27 (100)
	150 – 450	(Normal)	0 (0.0)
	>450	(Thrombocytosis)	0 (0.0)

prolonged severe neutropenia have a higher risk of infection, increasing the mortality rate in ALL patients.[15,16] From absolute lymphocyte count, both in children (43.2%) and in adults (81.5%), most of them showed an increase of lymphocyte count (lymphocytosis). Lymphocytosis is caused by the proliferation of lymphoid precursor pathway resulting in changes in the regulatory process of cell division, leading to increased self-renewal capacity. Suppression of the hematopoietic differentiation process and increased cell resistance to apoptotic signals.[1] On the other hand, gene mutation in ALL causes the processes of clonal expansion, differentiation, cell proliferation, and apoptosis to become dysregulated. The results are the replacement of normal lymphoid cells with malignant cells.[17] From thrombocyte count, both in children (97.1%) and in adults (100%), most of them showed a decrease of thrombocyte count (thrombocytopenia). Similarly, Previous studies showed that from 50 patients with ALL, 42 patients (66%) were found with thrombocytopenia, and from 189 patients with ALL patients, 162 found with thrombocytopenia.[5,18] Thrombocytopenia can occur as one of the hematopoietic dysfunction results.[5]

The result of the bone marrow aspiration (BMA) examination, based on the FAB classification (Table 3), showed that the most common morphology of ALL was L2 subtype/ALL-L2 (78.9%). Similarly, Tarigan et al., from 84 patients with ALL, 61 patients (72%) was L2 subtype.[6] But, Sousa et al., found that L1 subtype is more frequent than L2 subtype (ALL-L2).[19] ALL-L2 subtype was more severe than ALL-L1. The prevalence ratio show that ALL-L2 is more at risk of relapse than ALL-L1 and ALL-L3, so that there is a relationship between severity based on the morphological classification of ALL with the incidence of relapse.[20]

CONCLUSION

Characteristics of patients with ALL in 2016-2020 at Sanglah General Hospital were dominated by children with ages >6 - ≤18 years, male, from Denpasar, Bali. Most of complete blood count result showed moderate anemia, leukocytosis, neutropenia, lymphocytosis, and

Table 3. Morphology of ALL from BMA results based on FAB Classification*

Morphology	n (%)
L1	30 (18.1)
L2	131 (78.9)
L3	5 (3.0)

*The French – American - British (FAB) Classification

thrombocytopenia. From the bone marrow aspiration result, ALL-L2 subtype was the most common morphological variants of ALL.

DISCLOSURE

Conflict of Interest

The author declares no conflict of interest related to material presented in this article.

Ethical Consideration

Ethical research has approved by Research Ethics Committee Faculty of Medicine Universitas Udayana/Sanglah General Hospital Denpasar, with letter number: 763/UN14.2.2.VII.14/LT/2021.

Author Contribution

All authors contributed equally contribute to the study.

ACKNOWLEDGEMENT

REFERENCES

1. Pambudi B, Agustiani, C. Buku saku hematologi, leukosit dan kelainannya: Leukemia Limfoblastik Akut. In: Lembar S, Dony Y, Aprilia A, Tjahyadi CA, editors. 2nd Ed. Jakarta: Universitas Katolik Indonesia Atma Jaya; 2017.
2. Coutre SE. Wintrobe's clinical hematology: Acute lymphoblastic leukemia in adults. In: Greer JP, Rodger GM, Glader B, Arber DA, Means RT, List AF, et al, editors. 14th Ed. Philadelphia: Wolters Kluwer; 2019.
3. Leclair SJ, Bentley G. Clinical laboratory hematology: Precursor Lymphoid Neoplasms. In: McKenzie SB, Williams JL, Piwowar KL, editors. 3rd Ed. New Jersey: Pearson Education; 2015.
4. Hoffbrand AV, Moss PAH. Hoffbrand's essential haematology: Acute lymphoblastic leukaemia. 7th Ed. UK: John Wiley & Son Ltd; 2016.
5. Putri KW, Ugrasena IDG, Hernaningsih Y. Epidemiological study of clinical and laboratory profiles of patients with acute lymphoblastic leukemia at dr. soetomo hospital Surabaya. Biomolecular and Health Science Journal. 2019;02(01):48-52.
6. Tarigan ADT, Ariawati K, Widnyana P. Prevalensi dan karakteristik anak dengan leukemia limfoblastik akut tahun 2011-2015 di RSUP Sanglah Denpasar. Medicina. 2019;50(2):391-5.
7. Reddy P, Shankar R, Koshy T, Radhakrishnan V, Ganesan P, Jayachandran PK, et al. Evaluation of cytogenetic abnormalities in patients with acute lymphoblastic leukemia. Indian J Hematol Blood Transfus. 2019;35(4):640-8.
8. Silva N, Masria S, Roekmantara T. Characteristic of patients with acute lymphoblastic leukemia (ALL) at al islam bandung hospital in 2017. Proseding Pendidikan Dokter. 2019;5(1):634-9.
9. Kakaje A, Alhalabi MM, Ghareeb A, Karam B, Mansour B, Zahra B, et al. Rates and trends of childhood acute lymphoblastic leukaemia: an epidemiology study. Scientific Reports Nature Research. 2020;10:6756.
10. Saleh R, Musa HH, Hamid GA. Epidemiological study of acute lymphoblastic leukemia in yemen. European Journal of Biomedical and Pharmaceutical Sciences. 2017;4(10):794-7.
11. Saikia BJ, Roy PS, Kumar G, Mishra RK, Sarma A. Clinico-epidemiological features and response in childhood acute lymphoblastic leukemia at regional cancer center of northeast india. South Asian Journal of Cancer. 2019;8(4):241-3.
12. Adinatha Y, Ariawati K. Gambaran karakteristik kanker anak di RSUP Sanglah, Bali, Indonesia periode 2008-2017. Intisari Sains Medis. 2020;11(2):575-581.
13. Pahloosye A, Hashemi A, Mirmohammadi SJ, Atefi A. Presenting clinical and laboratory data of childhood acute lymphoblastic leukemia. Iranian Journal of Pediatric Hematology Oncology. 2011;1(3):71-7.
14. Windiastuti E, Mulawi C. Gangguan metabolik pada leukemia limfositik akut dengan hiperleukositosis. Sari Pediatri. 2002;4(1):31-5.
15. Biswal S, Godnaik C. Incidence and management of infections in patients with acute leukemia following chemotherapy in general wards. Ecancermedicalscience. 2013;7(310):1-16.
16. Utami AAIAYT, Niruri R, Ariawati K. Pola kuman dan sensitivitas antibiotika pada anak dengan leukemia limfoblastik akut yang mengalami demam neutropenia. Jurnal Farmasi Udayana. 2013;2(3):67-72.
17. Huang FL, Liao EC, Li CL, Yen CY, Yu SJ. Pathogenesis of pediatric b-cell acute lymphoblastic leukemia: Molecular pathway

and disease treatments. Oncology Letters. 2020;20:448-454.

18. Zuckerman T, Rowe JM. Pathogenesis and prognostication in acute lymphoblastic leukemia. Prime Reports. 2014;6(59):1-5.

19. Sousa DWLD, Ferreira FVDA, Felix FHC, Lopes MVDO. Acute lymphoblastic leukemia in children and adolescent: prognostic factors and analysis of survival. Brazilian Journal of Hematology and Hemotherapy. 2015;37(4):223-9.

20. Juniasari C, Fitriyani S, Afgani A, Yuniarti L, Triyani, Y. Klasifikasi morfologi leukemia limfoblastik akut berhubungan dengan kejadian relaps pada pasien anak. Jurnal Integrasi Kesehatan dan Sains. 2020;2(1):1-5.