Clinical Manifestations and Hematological Profiles of Pediatric Acute Myeloblastic Leukemia Patients: 3 Years Observational Study in A West Java Tertiary Hospital, Indonesia

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Abstract

Objective: To determine and describe the clinical manifestations and hematological profiles of pediatric Acute Myeloblastic Leukemia (AML) in Dr. Hasan Sadikin General Hospital (RSHS), Bandung as a tertiary hospital in West Java, Indonesia.

Methods: A retrospective cross-sectional study using the total sampling method was performed on the medical records of pediatric patients (0-18 years old)who were diagnosed as AML for the first time through bone marrow examination during the period of January 1, 2015–December 31, 2017.

Results: Of the 54 subjects who met the inclusion criteria, 42.6% were AML patients in the age group 6-12 years with male patients comprised 59.3% of the total number of subjects. Patients generally experienced pallor (83.3%), fever (75.9%), and decreased appetite (70.4%). The hematological profiles showed that 35.2% of patients had Hb <6.5 g/dL and 44.4% had a leukocyte count of >50,000 cells/mm^3. The majority of the subjects had a platelet count of <50,000 cells/mm^3 (83.3%) and almost half of them had a peripheral blasts count of >50% (46.3%).

Conclusions: Clinical manifestations and hematological profiles are important to diagnose AML, especially in pediatric patients. By assessing the manifestations and profiles, it is feasible to access and detect suspected cases of AML.

Received:
October 12, 2018

Revised:
September 09, 2019

Accepted:
October 19, 2019

Keywords: Acute myeloblastic leukemia, clinical manifestation, hematological profile, pediatric

pISSN: 2302-1381; eISSN: 2338-4506; http://doi.org/10.15850/ijihs.v7n2.1480
IJIHS. 2019;7(2):61–6

Introduction

Acute Myeloblastic Leukemia (AML) is a type of acute leukemia with rapid and progressive infiltrations of myeloid/myeloblast cells to the bone marrow, blood, and other organs.[1] In United States, 350 new cases of AML in pediatric are identified annuallya.[2] Approximately 15–20% of leukemia cases in children ≤15 years old are AML.[2, 3] In Indonesia, acute leukemia is the most common type of cancer in children.[4] Data from a department of pediatrics in a tertiary hospital in Jakarta demonstrated that 21.8% of acute leukemia in 2007-2010 are AML.[5] Another study in a tertiary hospital in Yogyakarta also showed that 27.7% of acute leukemia are AML, which is higher than in western countries.[6]

To be able to improve the survival rate of pediatric AML patients, it is necessary to understand the characteristics of clinical and hematological profiles of the patients to facilitate early diagnosis. Pediatric AML have various clinical manifestations, with anemia (pale, weak, decreased in appetite and body weight), bleeding, and infection as the most common. In addition, cancer cells can migrate

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and cause manifestations in other organs such as in the liver, spleen, and lymph nodes.[7, 8]

Based on the hematological examination, AML patients generally experience anemia, leukocytosis, thrombocytopenia, and increased number of blast cells.[9] A study in Dharmais Cancer Hospital Jakarta showed that 83% of AML patients have a hemoglobin level of <12 g/dL, 61% have a leukocyte count of ≥50,000 cells/mm^3, and 57% have a platelet count of <30,000 cells/mm^3.[4] Data from a tertiary hospital in Jakarta (2007–2009) revealed that AML patients that male patients with hepatomegaly and a platelet count of <20,000 cells/mm^3 tend to experience failure to achieve remission.[5]

Reports on clinical and hematological profiles of pediatric AML patients in tertiary hospitals are still lacking. Therefore, this study aimed to gather information on clinical manifestations and hematological profiles of pediatric AML patients in a tertiary hospital in West Java Province, Indonesia.

Methods

This was a cross-sectional study on all inpatient medical records of AML pediatric patients treated in Dr. Hasan Sadikin General Hospital Bandung, West Java, Indonesia during the period of January 1, 2015 to December 31, 2017 using the total sampling approach. The study was performed from June to July 2018 The inclusion criteria of this study was all medical records of pediatric (0–18 years old) patients who were diagnosed as AML in Dr. Hasan Sadikin General Hospital (*Rumah Sakit Hasan Sadikin,* RSHS) for the first time based on the results of the bone marrow examination. Medical records were excluded if they were incomplete, lost, or contained inaccessible data. Medical records of patients who who did not come to RSHS for the first time, refused to undergo bone marrow examination, and diagnosed as non-AML were also excluded.

This study had been approved by the Research Ethical Committee of Universitas Padjadjaran, Bandung through issuance of the ethical clearance Number 202/UN6.KEP/EC/2018 and by the Medical Research Ethical Committee of Dr. Hasan Sadikin General Hospital, Bandung with the issuance of ethical clearance Number LB.02.01/X.2.2.1/9375/2018. This study was also acknowledged and approved by the Pediatrics Department and Clinical Pathology Department of Dr. Hasan Sadikin General Hospital Bandung, Indonesia.

Variables of this study were patient demographics (including age and sex), clinical manifestations of AML, and hematological profiles (hemoglobin level, leukocyte count, thrombocyte count and peripheral blast count). Hemoglobin level was categorized into <6.5, 6.5–7.9, 8.0–9.4, 9.5–10.9 and ≥11 g/dL. Leukocyte count was classified into <10,000, 10,000–50,000, and >50,000 cells/mm^3. Platelet count was grouped into <50,000, 50,000-99,999, 100,000–149,999, 150,000–450,000, and >450,000 cells/mm^3 while peripheral blast count was categorized into <20, 20–50, and >50%.

Data were then selected and sorted based on the inclusion criteria and analyzed using descriptive statistics and processed using Microsoft® Excel 2016 and IBM® SPSS® version 20. Tables, percentages, and charts were used to present patient demographics, clinical manifestations, and hematological profiles.

Results

Of the seventy-three medical records retrieved, 54 met the inclusion criteria of this study. The flow diagram used for the selection process is presented in Figure 1.

The age and gender distribution of the AML pediatric patients in RSHS from 2015–2017 were depicted in Figure 2. Most patients were in the age group 6–12 years old (42.6%) and males (59.3%).

Figure 3 displays the clinical manifestations of pediatric AML patients in RSHS during the period of 2015–2017. The most frequently observed clinical manifestations were pallor (83.3%), followed by fever (75.9%), loss of appetite (70.4%), as well as weight loss and hepatomegaly (each 59.3%).

Table 1 illustrates the hematological profiles of pediatric AML patients in RSHS. Most subjects had a hemoglobin level of <6.5 g/dL (35.2%) whereas the leukocyte and platelet counts were mostly in the category of >50,000 cells/mm^3 (44.4%) and <50,000 cells/mm^3 (83.3%), respectively. The number of blast cells on peripheral blood examination were mostly in the category >50% (46.3%).

Discussion

This study demonstrated that 42.6% of children with AML in RSHS from 2015-2017 belonged to the age group 6–12 years old and most of the patients were males (59.3%). This finding is similar to the finding of a study

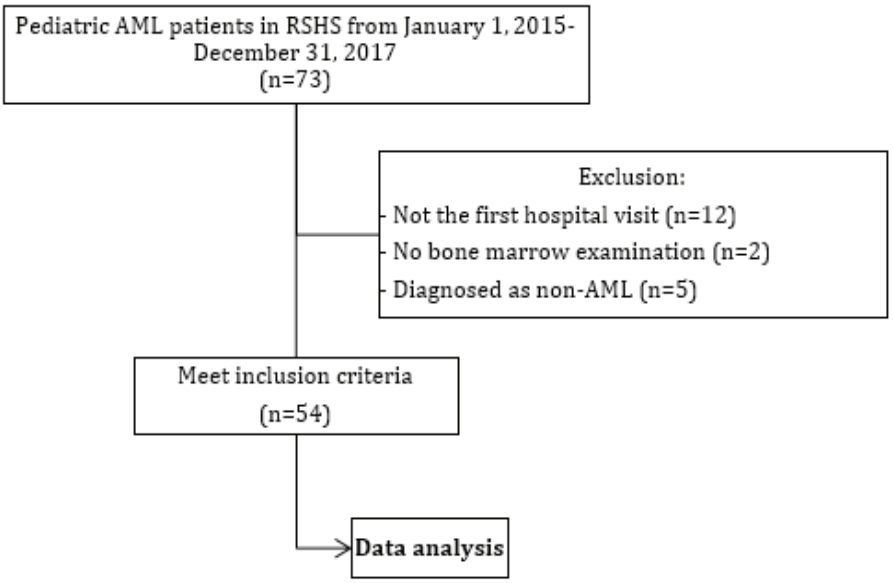

Figure 1 Flow Diagram for Medical Record Selection Process

Table 1 Hematological Profiles of Pediatric AML Patients

Hematological Profiles	(n=54)	%
Hemoglobin level (g/dL)		
<6.5	19	35.2
6.5–7.9	17	31.5
8.0–9.4	9	16.7
9.5–10.9	8	14.8
≥11	1	1.9
Leukocyte count (cells/mm^3)		
<10,000	15	27.8
10,000–50,000	15	27.8
>50,000	24	44.4
Platelet count (cells/mm^3)		
<50,000	45	83.3
50,000–99,999	4	7.4
100,000-149,999	1	1.9
150,000–450,000	3	5.6
>450,000 cells/mm^3	1	1.9
Peripheral blast count (%)		
<20	16	29.6
20–50	13	24.1
>50	25	46.3

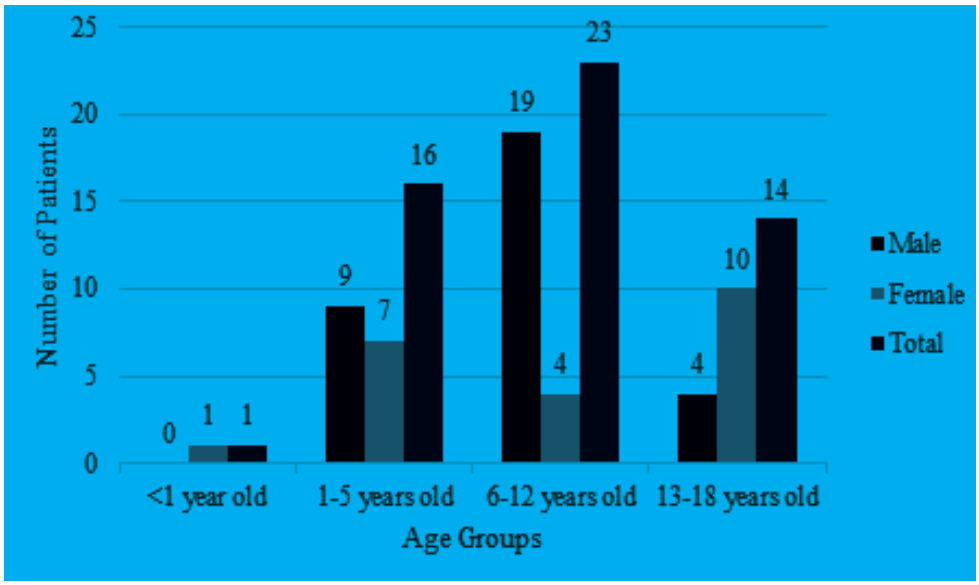

Figure 2 Age and Gender of Pediatric AML Patients

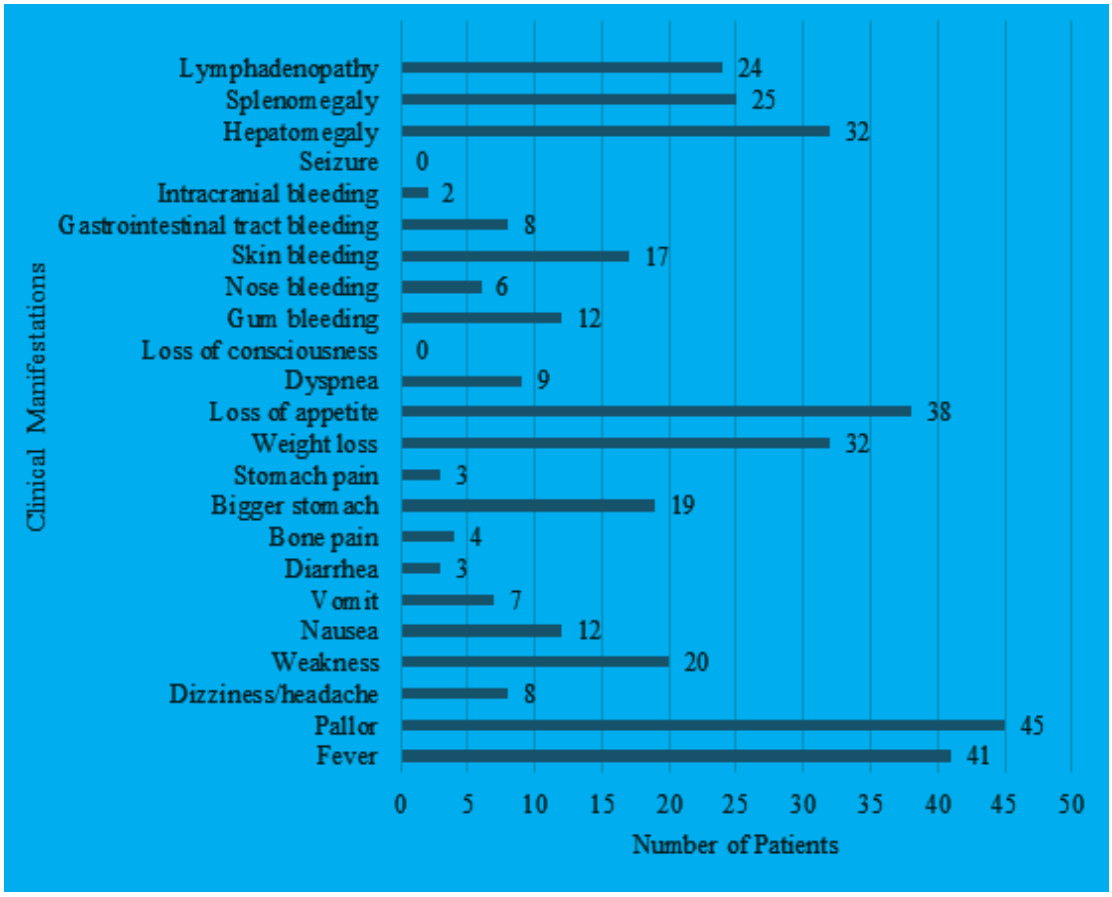

Figure 3 Clinical Manifestations in Pediatric AML Patients

by Supriyadi E et al. stating 41.4% of the pediatric AML patients were 6–12 years old when diagnosed.[10] Another study conducted by Rahadiyanto *et al*.[11] and Sjakti HA et al. also stated that AML in children is more frequent in males (52.4% and 61.3% respectively).[5]

Most of the pediatric AML patients had more than one clinical manifestation. Results showed that pallor was the clinical manifestation with the highest frequency that was seen in 83.3% of the patients, followed by fever (75.9%), decreased appetite (70.4%), as well as weight loss and hepatomegaly (each 59.3%). These data resemble the results of a study by Hu *et al*.[12] which concluded that the most common manifestations of pediatric AML patients are pallor (60.3%), fever (40.5%), and mucosal bleeding (15.5%). Another study from Asif and Hassan[13] in Pakistan also stated that pallor is the most common manifestations (86.6%), followed by fever (82.9%) and bleeding (52.4%), while hepatomegaly is found in 38 of 82 patients (46.3%).

Hematopoietic disorders of AML cause several clinical manifestations such as symptoms of anemia (most commonly paleness, weakness, and decreased appetite), infection, and an increased probability to bleed.[13] In AML, the cancer cells do not only accumulate in the bone marrow, but also in other organs, such as liver, spleen, lymph nodes, central nervous system, and skin, which were also identified in this study.[14]

The hemoglobin level of this study was mostly found in the category of <6.5 g/dL (35.2%). This was in line with a study by Chang *et al*.[15] Most patients in were in the category of <8 g/dL (45.8% of 107).Similar findings are presented by Rahmadin *et al*.[8] who reported that 48.57% of AML patients had a hemoglobin level of <6 g/dL. Anemia is usually caused by inadequate hematopoiesis triggered by abundant proliferation of leukocytes in bone marrow.[7,8]

Most patients in this study had a leukocyte count in the category of >50,000 cells/mm^3 (44.4%). This is similar to the findings of Johnston *et al.*[16] which revealed that 50.7% of their patients had 10,000-99,999 cells/mm^3 leukocytes.It is concluded that the majority of pediatric AML patients in this study experienced hyperleukocytosis caused by blocked leukocyte maturation leading to the accumulation of myeloid cells in bone marrow and vessels.[7, 8]

In this study, the platelet count was predominantly in the category of <50,000 cells/mm^3, which reflects severe thrombocytopenia (83.3%). This is supported by a finding from Mehta *et al.*[17] stating that 88.9% of the patients have thrombocytopenia (<150,000 cells/mm^3). Thrombocytopenia can be caused by bone marrow infiltration, disseminated intravascular coagulation, immunological reactions or secondary hypersplenism due to an enlarged spleen.[18]

In this study, 46.3% of the patients had >50% blast cells on peripheral blood examination, which is similar to a previous study by Rendra *et al*.[19] with 41.02% of their patients had 50–59% blasts.This condition is a result of disturbed myeloid cell development that leads to blast accumulation in bone marrow and blood.[8] The initial suspicion of AML may arise when the blasts count is >20% on bone marrow or peripheral blood examination, when bone marrow is not possible.[7]

This study also has limitations. One of them is the difficulty in reading and accessing patient medical records. In addition, researchers were not able to collect data other than those from 2015 to 2017 due to limited time for data collection and incomplete medical records from before 2015.

It is recommended that this type of study is performed in a longer period of time and with a larger sample size or other variables that have not been studied yet. Subsequent studies can also explore the links between variables discovered in this study.

In conclusion, clinical manifestations and hematological profiles are important for diagnosing AML, especially in pediatric patients, to make it feasible to detect AML cases earlier.

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