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The Role of Bleeding History: Mortality Risk Acute Leukimia

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Acute leukemia is a malignant hematological disease with a low survival rate. The survival rate of acute leukemia patients is influenced by several factors, one of which is a history of bleeding. This study aimed to evaluate whether a history of bleeding constitutes an independent risk factor for mortality in patients diagnosed with acute leukemia at Dr. Moewardi Regional General Hospital, Surakarta. This study employed an observational and analytical retrospective cohort design. The subjects were patients diagnosed for the first time with acute leukemia by bone marrow puncture (BMP) and immunophenotyping from January to December 2023. The data was analyzed using chi-square for bivariate analysis and multivariate logistic regression. Survival analysis was performed using the Kaplan-Meier test. A total of 124 patients were included in the analysis. Bivariate analysis demonstrated that both history of bleeding ($p = 0.008$) and leukocyte count ($p = 0.001$) were significantly associated with mortality. Multivariate logistic regression confirmed that a history of bleeding ($p = 0.027$; relative risk [RR] = 3.45) and leukocyte count exceeding 50,000 cells/µL ($p = 0.002$; RR = 5.10) were independently associated with reduced survival. Kaplan-Meier survival curves showed lower cumulative survival among patients with a history of bleeding and those with elevated leukocyte counts. A history of bleeding is an independent risk factor for decreased survival in patients with acute leukemia at Dr. Moewardi Regional General Hospital. Additionally, leukocyte counts exceeding 50,000 cells/µL are associated with significantly worse survival outcomes.

Keywords: Bleeding History, Acute Leukimia, Survival

INTRODUCTION

Leukemia is a hematological malignancy characterized by the transformation of hematopoietic progenitor cells and diffuse infiltration of the bone marrow. It is broadly classified into two major lineages: myeloid and lymphoid. These include acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML). Leukemia accounts for approximately 2.5% to 3.1% of all cancer cases, with an incidence rate of 5.4 per 100,000 individuals (Du et al., 2019; Huang et al., 2022). Over the past two decades, the incidence of leukemia has shown a notable increase. Leukemia is the fifth leading cause of cancer-related mortality in Indonesia, accounting for 11,314 reported deaths.

Among the leukemia subtypes, acute leukemia is associated with a significantly lower survival rate compared to chronic forms. The prognosis of patients with acute leukemia is influenced by a range of factors, including epidemiological characteristics, laboratory findings, and clinical presentation at diagnosis (Dong et al., 2020; Balta et al., 2023). The clinical condition of patients plays a significant role in determining the survival outcomes in acute leukemia (Du et al., 2019). A study conducted by Versluis et al. (2020) reported that bleeding complications during the induction phase of AML treatment are associated with increased mortality (Versluis et al., 2020). A history of bleeding, including intracranial hemorrhage, gastrointestinal bleeding, and epistaxis, is associated with poor outcomes in patients with acute leukemia (Demir et al., 2020).

Bleeding episodes are often linked to underlying conditions such as leukocytosis, disseminated intravascular coagulation (DIC), and platelet dysfunction (Corea et al., 2020; Ladikou et al., 2020). While the mechanism by which bleeding contributes to mortality remains unclear, clinical studies consistently demonstrate a significant correlation between bleeding and increased mortality in patients with acute leukemia

(Intusoma et al., 2019; Koschade et al., 2022). This study aims to investigate the relationship between bleeding history at the time of diagnosis and the survival rate of patients with acute leukemia. Unlike prior studies that focused predominantly on bleeding during treatment, we investigated bleeding history specifically at the time of initial diagnosis and observed all subtypes of acute leukemia.

By providing a comprehensive understanding of the relationship between bleeding history and survival in acute leukemia patients, this study aims to support clinicians in identifying individuals at risk of bleeding-related mortality. Furthermore, improved recognition of this risk is anticipated to enhance clinical vigilance and guide the provision of optimal treatment for acute leukemia patients, particularly those presenting with clinical bleeding.

METHODS

This study employed an observational and analytical retrospective cohort design to evaluate the association between a history of bleeding and survival outcomes in acute leukemia patients at Dr. Moewardi General Regional Hospital. The study population comprised patients who were newly diagnosed with acute leukemia between January and December 2023, based on bone marrow puncture (BMP) findings and immunophenotyping results. Patients who were lost to follow-up or referred to other healthcare facilities were excluded from the analysis.

A total of 124 subjects were included using total sampling. The study parameters assessed included gender, history of infection and bleeding (epistaxis, gum bleeding, hemoptysis, gastrointestinal bleeding, and hemorrhagic stroke) reported by the patient, body mass index (underweight, overweight, or obesity), hemoglobin levels, leukocyte counts, platelet counts, and aberrant phenotypes, all assessed at the time of initial diagnosis. Research data were collected from the electronic medical records and laboratory information system (LIS) of Dr. Moewardi General Regional Hospital in Surakarta.

Descriptive statistics were used to summarize the characteristics of study subjects. Bivariate analysis using the chi-square test was conducted to examine associations between independent variables and patient outcomes. Independent variables that were statistically significant were further analyzed using multivariate logistic regression. Survival analysis was performed using the Kaplan-Meier method. Data analysis was carried out in June 2024 using the Statistical Package for the Social Sciences (SPSS) version 29.0. The study protocol received approval from the Indonesian Institutional Review Board (Protocol ID 1.722/VII/HREC/2024).

RESULTS AND DISCUSSION

A total of 124 subjects were included in this study. Of these, 61 (49.2%) were male and 63 (50.8%) were female. The most frequently diagnosed subtype was acute myeloid leukemia (AML), which was observed in 66 subjects (53.2%). At the time of initial diagnosis, 57 subjects had documented infections. Regarding nutritional status, 83 subjects (66.9%) had a body mass index (BMI) within the normal range. Bleeding manifestations at diagnosis, such as intracranial hemorrhage, gastrointestinal bleeding, and epistaxis, were present in 42 subjects (33.9%). The distribution of laboratory parameters was assessed using the Kolmogorov– Smirnov test, which yielded p-values <0.05, indicating that the data were not normally distributed. The characteristics of the subjects are summarized in Table 1.

Table 1
Characteristics of research subjects

Variables	Died (n=84)	Survived (n=40)
Gender		
Male (n=61)	38 (62.3%)	23 (37.7%)
Female (n=63)	46 (73%)	17 (27%)
Age	37.09 (31.5-42.6)	21.5 (14.7-28.3)
Leukemia Diagnosis		
AML (n=66)	48 (72.7%)	18 (27.3%)
ALL (n=51)	36 (70.6%)	15 (29.4%)
MPAL (n=7)	3 (42.9%)	4 (57.1%)
Infection (n=57)	43 (75.4%)	14 (24.6%)
Body mass index		
BMI (underweight, overweight, obese)	32 (78%)	9 (22%)
(n=41)		
Normoweight (n=83)	52 (62.7%)	31 (37.3%)
Bleeding (n=42)	35 (83.3%)	7 (16.7%)
Hemoglobin Level (g/dl)	9.1 (7.1-11.1)	9.5 (7.5-11.5)
Leukocyte Level (10^3/ ul)	78.2 (0.9-196.2)	37.9 (0.2-117.1)
Platelet Level (^{109} / ul)	42.2 (7.8-76.6)	37 (1.21-72.8)
Phenotype aberrant (n=50)	36 (72%)	14 (28%)
CD3 (n=30)	21 (70%)	9 (30%)
CD7 (n=25)	17 (68%)	8 (32%)
CD19 (n=8)	7 (87.5%)	1 (12.5%)
Variable	**n**	**%**
Age		
17-25 years	4	10
26-35 years	33	82,5
36-45 years	3	7,5
Blood pressure		
Normotension	18	45
Hypertension	22	55
Blood pressure		

Variables	Died (n=84)	Survived (n=40)
Normotension	34	8.0 %
Hypotension	6	15.0 %

Description: Data are presented as mean ± SD or median, AML = acute myeloblastic leukemia, ALL= acute lymphoblastic leukemia, MPAL= mixed phenotype leukemia, BMI: body mass index, CD = cluster of differentiation.

Chi-square test was performed to determine factors that influence the mortality of acute leukemia patients (Table 2). We found that a history of bleeding (p = 0.008) and leukocyte count (p = 0.001) have a significant effect on survival outcomes in acute leukemia.

Table 2
Bivariate analysis of independent variables with mortality of acute leukemia patients

Variables	Died (n=84)	N	Alive (n=40)	RR	95% IK	p
Gender						
Man	38		21	0.611	0.29–1.31	0.278
Woman	46		16	1,154	0.90–1.47	0.337
Infection						
Yes	45		17			
No	39		23	1.25	0.99–1.57	0.128^
IMT						
Underweight, overweight, and obese		32	9			
Normal BMI		52	31			
Bleeding						
Yes	35		7	3.37	1.34–8.48	0.008*^
No	49		33	1.49	0.68–3.26	0.320
Aberrant Phenotype						
Yes	36		14			
No	48		26	1.49	0.68–3.26	0.428
Hemoglobin Level						
Less than 10 g/dL	58		24			
More from 10 g/dL	26		16	5.00	1.78–	0.001 *^
Leukocyte Levels						
More from $50x10^3/\mu L$	49		35		14.04	
Less than $50x10^3/\mu L$ Platelet Level	35		5	1.18	0.55–2.54	0.670
Less than $30x10^9/\mu L$	37		16			
More from $30x10^9/\mu L$	47		24			

Description: RR: relative risk ; g/dL: gram/ deciliter , * significant , ^ analysis multivariate

A multivariate analysis was performed using logistic regression to evaluate the simultaneous influence of body mass index (BMI), bleeding history, leukocyte count, and platelet count on clinical outcomes in patients with acute leukemia (Table 3). The analysis identified bleeding (RR 3.45 (95% CI 1.33–8.97); p = 0.011) and leukocyte levels (RR 5.10 (95% CI 1.78–14.62); p = 0.002) as independent predictors of mortality.

Table 3
Multivariate analysis of independent variables with mortality of acute leukemia patients

Variables	RR (CI 95%)	p
BMI	0.69 (0.296–1.620)	0.396
Bleeding	3.45 (1.326–8.970)	0.011*
Leukocyte Levels	5.10 (1.780 – 14.620)	0.002*

Description: BMI: body mass index, RR: relative risk ; CI = confidence interval

Survival analysis was performed using Kaplan-Meier test. As shown in Figure 1, subjects with leukocyte levels of over 50×10³ cells/µL demonstrated a lower cumulative survival. The mean survival period for acute leukemia patients with leukocyte levels of over 50×10³ cells/µL was 400 days, lower than that of patients with lower leukocyte count. Figure 2 illustrates that patients presenting with a history of bleeding at the time of acute leukemia diagnosis had a lower cumulative survival compared to those without.

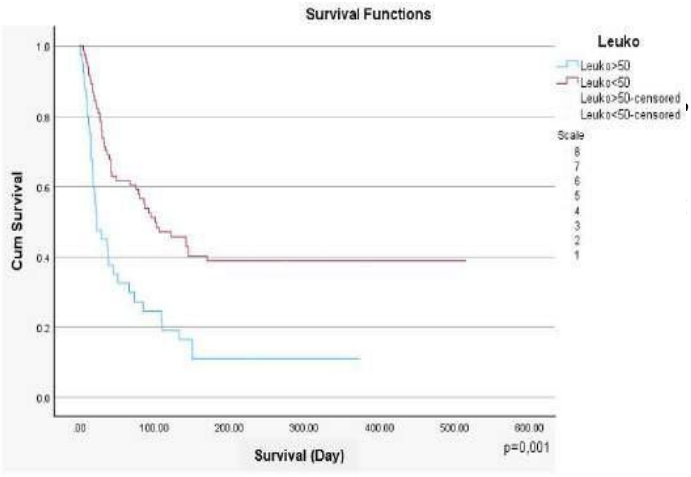

Figure 1. Kaplan-Meier curve of acute leukemia patients based on leukocyte levels

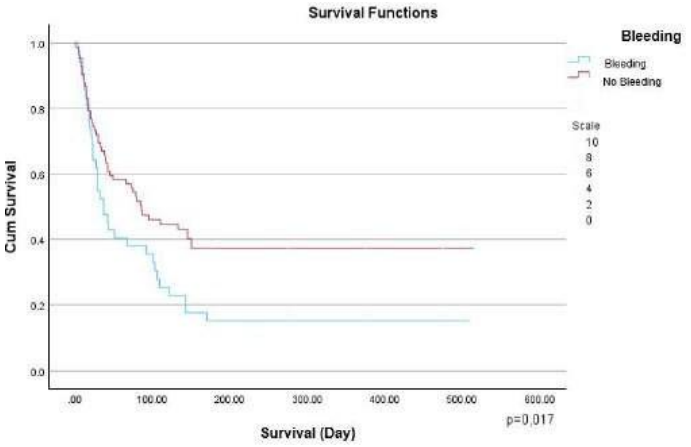

Figure 2. Kaplan-Meier curve of acute leukemia patients based onhistory of bleeding

This study demonstrates that clinical bleeding is associated with increased mortality in patients with acute leukemia, as supported by previous findings (Veresluis et al., 2020). Bleeding complications in malignancy are linked to both intrinsic and extrinsic factors, including anemia, thrombocytopenia, vascular integrity, coagulopathy, and infection. In acute leukemia, bleeding is most commonly associated with hyperleukocytosis, disseminated intravascular coagulation (DIC), and platelet dysfunction (Wilson et al., 2020). Hyperleukocytosis contributes to bleding through leukocytosis, wherein leukimia cells cell proliferation obstructs capillaries, leading to vessel damage and potential organ failure.

The proliferation of leukemia cells also activates the coagulation system, which may result in thrombosis and bleeding (Fero dan infante, 2021). Cancer cells activate monocytes, releasing extracellular vesicles that express procoagulant phospholipids and tissue factor (TF), initiators of the coagulation cascade. In addition to TF, young cells release cell-free DNA, which activates factor XII (FXII), leading to excessive coagulation and coagulopathy. These hemostatic disturbances are major contributors to mortality in patients with acute leukemia (Hisada et al., 2024; Wang et al., 2020).

Leukemia cells promote hyperfibrinolysis by increasing the levels of urokinase-type plasminogen activator receptor levels and decreasing the levels of plasminogen activator inhibitor-1 (PAI-1), which leads to bleeding (Teruya et al., 2021). Studies have shown that bleeding in acute leukemia can elevate the mortality rate by up to 10%. Bleeding in these patients is often accompanied by thrombocytopenia, although no specific platelet level has been established to predict bleeding risk. While some studies suggest increased bleeding risk at platelet counts ≤5 × 10⁹/L (Petros, 2021), our findings did not reveal a statistically significant association between platelet count and mortality. This is inconsistent with previous studies suggesting that platelet levels <50 × 10⁹/L are associated with increased bleeding risk and mortality (Hermsen & Hambley, 2023; Zhang et al., 2022). The discrepancy may be attributable to prior transfusions or variations in patient care across institutions. Furthermore, our study's relatively short six-month observation period may limit comparability with studies that have assessed long-term outcomes over several years. The incidence of bleeding in acute leukemia is not solely attributable to coagulopathy.

Previous research has indicated that high blast cell counts, common in acute leukemias, can exacerbate bleeding risks. For instance, Limijadi et al. found a correlation between increased blast counts and the frequency of bleeding events in a cohort of acute leukemia patients (Limijadi et al., 2021). This is particularly notable since mucosal bleeding and skin hemorrhages are serious complications of the disease, often tied to periods of thrombocytopenia (Limijadi et al., 2021). Thrombotic events, while less frequent, can also occur and complicate clinical management, highlighting the risk profiles associated with various leukemia subtypes like acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) (Cate & Leader, 2021). In terms of nutritional status, we did not find a statistically significant association between body mass index (BMI) and mortality.

This contrasts with previous studies suggesting that both underweight and obesity are linked to relapse and mortality in acute leukemia (Dong et al., 2024;

Paviglianiti, 2020). Obesity affects cancer progression, although the exact relationship to leukemia relapse is unclear. The lack of significance in our study may stem from the comprehensive nature of the observations across all acute leukemia subtypes and the fact that BMI was calculated without considering fat and muscle mass (Saenz et al., 2018; Tsilingiris et al., 2024). Similarly, although infection is widely recognized as a major contributor to morbidity and mortality in hematologic malignancies, this study did not identify infection at diagnosis as a statistically significant predictor of mortality.

Previous research has established that infections adversely affect survival, prolong hospitalization, reduce quality of life, and increase healthcare costs (Carlesse et al., 2024; Torres et al., 2020). This may be because infections identified at diagnosis might not have been caused directly by leukemia itself, but rather by neutropenia or other comorbidities (Jain et al., 2020; Zajac et al., 2019). A longer observation period would be beneficial in capturing the full impact of infection- related mortality, which varies depending on the treatment phase, occurring in 48% of cases during induction, 9.3% during consolidation, 22.6% during late intensification, and 20% during maintenance therapy (Bharucha et al., 2021; Natukunda et al., 2023).

Leukocyte levels at the time of diagnosis were found to be an independent predictor of mortality in acute leukemia. Patients with leukocyte counts exceeding 50,000 cells/µL had a fivefold higher risk of death compared to those with lower counts. Elevated leukocyte levels are associated with viscosity, circulatory stasis, and inflammation, contributing to tissue damage (Ramadhan et al., 2024). The Kaplan-Meier survival analysis further supported these findings by confirming that patients with leukocyte levels ≤50,000 cells/µL had higher survival rates than those with higher leukocyte counts. Other laboratory parameters, including hemoglobin levels at the time of diagnosis, also affect mortality in acute leukemia. Decreased erythropoiesis and erythrocyte lifespan due to bone marrow hypoplasia and leukemia cell infiltration can contribute to anemia, which increases the risk of infection (Bawersdorf, 2020; Oakley et al., 2020).

However, we found no association between hemoglobin values and mortality, possibly because the data reflected post-transfusion levels, not initial levels at diagnosis. Phenotype aberrations did not significantly impact mortality in this study, in contrast with previous studies linking certain aberrant phenotypes (CD3, CD7, CD56, CD2, CD90 low, CD123 high, CD117 high, CD15) with poor prognosis (Yin et al., 2023). In this study, CD3 and CD7 were associated with worse outcomes, while CD19 was associated with better prognosis. The lack of statistical significance in this study could be due to the absence of cytogenetic examinations and the relatively short observation period. Cytogenetic abnormalities such as BCR-ABL1, KMT2A-r, and high hyperdiploidy significantly impact prognosis and patient mortality.

This study is limited by its retrospective design, short follow-up period of six months, and the absence of comprehensive cytogenetic data. These limitations may have reduced the ability to detect long-term survival patterns and identify more nuanced prognostic indicators. Longer observation periods and more comprehensive genetic profiling are recommended for future research.

CONCLUSION

A history of bleeding increases the mortality of acute leukemia patients at Dr. Moewardi Regional General Hospital. In addition to bleeding, leukocyte levels of over 50,000 cells/µL were associated with lower survival rates. It is recommended that future research be conducted with a larger sample size, a longer observation period, complete laboratory and clinical data, as well as analysis based on the risk classification of acute leukemia patients.

REFERENCE

Arsunan, A. A., Elisafitri, R., Wahyu, A., & Aisyah, A. (2020). Prognostic factors and survival rate of childhood acute lymphoblastic leukemia in eastern Indonesia: Kaplan–Meier and COX regression approach. Open Access Maced J Med Sci, 8(T2), 204–9. [Crossref] [Publisher]

Balta, B., Gebreyohannis, T., & Tachbele, E. (2023). Survival and predictors of mortality among acute leukemia patients on follow-up in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A 5-year retrospective cohort study. Cancer Rep, 6(10), 1–11. [Crossref] [Publisher]

Bewersdorf, J. P., & Zeidan, A. M. (2020). Hyperleukocytosis and Leukostasis in Acute Myeloid Leukemia: Can a Better Understanding of the Underlying Molecular Pathophysiology Lead to Novel Treatments? Cells, 9(10). [Crossref] [Publisher]

Bharucha, J., Cao, Q., Sachs, Z., Smith, A., Williams, S., Amin, K., et al. (2021). Prognostic factors for clinical outcomes of patients with central nervous system leukemia. Hematol Oncol Stem Cell Ther, 14(3), 240–5. [Crossref] [Publisher]

Carlesse, F., & Lopes de Sousa, A. V. (2024). Infections in children and adolescents with Acute Leukemia. EJC Paediatr Oncol, 3(January), 100142. [Crossref] [Publisher]

Cate, H. and Leader, A. (2021). Management of disseminated intravascular coagulation in acute leukemias. Hämostaseologie, 41(02), 120-126. [Crossref] [Publisher]

Corrêa, L. C., Teles, D., Silva, O. B. da, Trindade-Filho, G. H., Loureiro, P., & Cavalcati, M. do S. M. (2020). Predictors of mortality among patients with acute leukemia admitted to an intensive care unit specialized in patients with hematological disease

at a Brazilian hospital. Hematol Transfus Cell Ther, 42(1), 33–9. [Crossref] [Publisher]

Demir, M. K. (2020). A diagnostic dilemma in the emergency room: intracranial hemorrhages in acute myeloblastic leukemia with hyperleukocytosis. Acta Neurol Belg, 120(2), 487–9. [Crossref] [Publisher]

Dong, L., Dai, G., & Zhao, J. (2024). Impact of body mass index at diagnosis on outcomes of pediatric acute leukemia: A systematic review and meta-analysis. PLoS One, 19(5). [Crossref] [Publisher]

Dong, Y., Shi, O., Zeng, Q., Lu, X., Wang, W., Li, Y., et al. (2020). Leukemia incidence trends at the global, regional, and national level between 1990 and 2017. Exp Hematol Oncol, 9(1), 1–11. [Crossref] [Publisher]

Du, M., Chen, W., Liu, K., Wang, L., Hu, Y., Mao, Y., et al. (2022). The Global Burden of Leukemia and Its Attributable Factors in 204 Countries and Territories: Findings from the Global Burden of Disease 2019 Study and Projections to 2030. J Oncol, 2022. [Crossref] [Publisher]

Ferro, J. M., & Infante, J. (2021). Cerebrovascular manifestations in hematological diseases: 291 an update. J Neurol, 268(9), 3480–92. [Crossref] [Publisher]

Hermsen, J., & Hambley, B. (2023). The Coagulopathy of Acute Promyelocytic Leukemia: An Updated Review of Pathophysiology, Risk Stratification, and Clinical Management. Cancers (Basel), 15(13), 1–21. [Crossref] [Publisher]

Hisada, Y., Archibald, S. J., Bansal, K., Chen, Y., Dai, C., Dwarampudi, S., et al. (2024). Biomarkers of bleeding and venous thromboembolism in patients with acute leukemia. J Thromb Haemost, 22(7), 1984–96. [Crossref] [Publisher]

Ho, C., Lo, Y. Y., & Crawford, J. R. (2022). Intracerebral hemorrhage as an initial manifestation of T-cell acute lymphoblastic leukemia in a pediatric patient. BMJ Case Rep, 15(9), 1–2 [Crossref] [Publisher]

Huang, J., Chan, S. C., Ngai, C. H., Lok, V., Zhang, L., Lucero-Prisno, D. E., et al. (2022). Disease Burden, Risk Factors, and Trends of Leukaemia: A Global Analysis. Front Oncol, 12, 1–8. [Crossref] [Publisher]

Intusoma, U., Nakorn, C. N., & Chotsampancharoen, T. (2019). Intracranial Hemorrhage in Childhood Acute Leukemia: Incidence, Characteristics, and Contributing Factors. Pediatr Neurol, 99, 23–30. [Crossref] [Publisher]

Jain, H., Rengaraj, K., Sharma, V., Bonda, A., Chanana, R., Thorat, J., et al. (2020). Infection Prevalence in Adolescents and Adults With Acute Myeloid Leukemia Treated in an Indian Tertiary Care Center. JCO Glob Oncol, 6, 1684–95. [Crossref] [Publisher]

Koschade, S. E., Stratmann, J. A., Miesbach, W., Steffen, B., Serve, H., Finkelmeier, F., et al. (2022). Intracranial hemorrhage in newly diagnosed non-promyelocytic acute myeloid leukemia patients admitted for intensive induction chemotherapy. Eur J Haematol, 108(2), 125–32. [Crossref] [Publisher]

Ladikou, E. E., Ashworth, I., Seviar, D., & Chevassut, T. (2022). Acute leukemia: no reason to panic. Clin Med JR Coll Physicians London, 22(3), 221–4. [Crossref] [Publisher]

Limijadi, E., Ismail, Q., Retnoningrum, D., Devi, W., & Riansari, A. (2021). Blast cells count influences bleeding incidence in acute leukemia: preliminary study in south kalimantan, indonesia. Open Access Macedonian Journal of Medical Sciences, 9(B), 900-902. [Crossref] [Publisher]

Natukunda, B., Omoding, A., Bongomin, F., Mubiru, K. R., Ddungu, H., Sekaggya-Wiltshire, C., et al. (2023). One-Year Survival and Prognosticators of Adults With Acute Leukemia at the Uganda Cancer Institute. JCO Glob Oncol, 9, 1–10. [Crossref] [Publisher]

Oakley, J., Williams, E. K., Caruso, C., Sakurai, Y., Tran, R., Lew, G., et al. (2020). Incorporating Hemoglobin Levels to Map Leukostasis Risk in Acute Leukemia Using Microvasculature-on-Chip Technologies. Blood, 136(Supplement 1), 9–10. [Crossref] [Publisher]

Paviglianiti, A. (2020). A review on the impact of body mass index on outcomes in pediatric leukemia. J Blood Med, 11, 205–12. [Crossref] [Publisher]

Petros, S. (2021). Pathophysiology of bleeding. Medizinische Klin - Intensivmed und 329 Notfallmedizin, 116(6), 475–81. [Crossref] [Publisher]

Pinheiro, L. H. S., Trindade, L. D., Costa, A. F. de O., Silva, N. de L., Sandes, A. F., Nunes, M. A. P., et al. (2020). Aberrant phenotypes in acute myeloid leukemia and their relationship with prognosis and survival: A systematic review and meta-analysis. Int J Hematol Stem Cell Res, 14(4), 274–88. [Crossref] [Publisher]

Ramadhan, M. H., Sari, N. M., Peryoga, S. U., & Susanah, S. (2024). Survival and Treatment Outcomes of Childhood Acute Lymphoblastic Leukemia in a Low-Middle Income Country: A Single-Center Experience in West Java, Indonesia. J Blood Med, 15(January), 77–85. [Crossref] [Publisher]

Saenz, A. M., Stapleton, S., Hernandez, R. G., Hale, G. A., Goldenberg, N. A., Schwartz, S., et al. (2018). Body mass index at pediatric leukemia diagnosis and the risks of relapse and mortality: Findings from a Single Institution and Meta-analysis. J Obese, 2018. [Crossref] [Publisher]

Smith, E. C., & Stevens, E. A. (2022). Fatal intracranial hemorrhage as the presenting sign of acute promyelocytic leukemia: A case report. Radiol Case Reports, 17(6), 2123–8. [Crossref] [Publisher]

Teruya, J. (Ed.). (2021). Management of Bleeding Patients (2nd ed.). Houston: Springer. pp. 344 3–11. [Publisher]

Torres-Flores, J., Espinoza-Zamora, R., Garcia-Mendez, J., Cervera-Ceballos, E., Sosa- Espinoza, A., & Zapata-Canto, N. (2020). Treatment-Related Mortality From Infectious Complications in an Acute Leukemia Clinic. J Hematol, 9(4), 123–31. [Crossref] [Publisher]

Tsilingiris, D., Vallianou, N. G., Spyrou, N., Kounatidis, D., Christodoulatos, G. S., Karampela, I., et al. (2024). Obesity and Leukemia: Biological Mechanisms, Perspectives, and Challenges. Curr Obesity Rep, 13, 1–34. [Crossref] [Publisher]

Versluis, J., Flamand, Y., Haydu, E. J., Vedula, R. S., Charles, A., Copson, K., et al. (2020). Incidence and Risk Factors for Bleeding in Patients with Acute Myeloid Leukemia Receiving Intensive Induction Chemotherapy. Blood, 136 (Supplement 1), 12–3. [Crossref] [Publisher]

Versluis, J., Pandey, M., Flamand, Y., Haydu, E. J., Belizaire, R., Faber, M., et al. (2022). Prediction of life-threatening and disabling bleeding in patients with AML receiving intensive induction chemotherapy. Blood Adv, 6(9), 2835–46. [Crossref] [Publisher]

Wang, T. F., Makar, R. S., Antic, D., Levy, J. H., Douketis, J. D., Connors, J. M., et al. (2020). Management of hemostatic complications in acute leukemia: Guidance from the SSC of the ISTH. J Thromb Haemost, 18(12), 3174–83. [Crossref] [Publisher]

Wilson, N. R., Khan, M., Cox, T. M., Nassif, M., Qiao, W., Garg, N., et al. (2020). Bleeding outcomes in thrombocytopenic acute leukemia patients with venous thromboembolism. Br J Haematol, 1(2), 448–56. [Crossref] [Publisher]

Yin, T., Han, J., Hao, J., Yu, H., Qiu, Y., Xu, J., et al. (2023). Clinical characteristics and risk factors of acute lymphoblastic leukemia in children with severe infection during maintenance treatment. Cancer Med, 12(19), 19372–82 [Crossref] [Publisher]

Zając-Spychała, O., Skalska-Sadowska, J., Wachowiak, J., Szmydki-Baran, A., Hutnik, Ł., Matysiak, M., et al. (2019). Infections in children with acute myeloid leukemia: increased mortality in relapsed/refractory patients. Leuk Lymphoma, 60(12), 3028–35. [Crossref] [Publisher]

Zhang, L., Liu, J., Qin, X., & Liu, W. (2022). Platelet–Acute Leukemia Interactions. Clin Chim 372 Acta, 536, 29–38. [Crossref] [Publisher]