



# Prevalence of acute myeloid leukemia and its associated risk factors at a tertiary care center: a retrospective cross-sectional study

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**Background:** Acute myeloid leukemia (AML) is a common malignant disorder of the bone marrow, accounting for 23.1% of total leukemia cases globally in 2017. This study aimed to know the prevalence of AML in a tertiary hospital center in Nepal and assess the associated etiological factors in the causation of AML.

**Materials and methods:** A hospital-based retrospective cross-sectional study was conducted among patients with acute leukemia admitted to a tertiary care center in Kathmandu from 1 April 2021 to 30 April 2022. Three hundred and ten participants with acute leukemia were selected via a convenience sampling technique. The data were entered into Microsoft Excel 365 and then analyzed using Statistical Packages for Social Sciences version 22.0.

**Results:** One hundred and forty five (46.7%) out of 310 acute leukemia patients had AML. Most of the cases were male (104, 71.7%) and aged 40–49 years (36, 24.8%). The most common signs and symptoms were pallor (115, 79.3%), fever ( $n = 92$ , 63.4%), and lethargy/weakness (78, 53.8%). Ninety one (62.8%) patients underwent multiple cycles of chemotherapy while 51 (35.2%) had supportive care only, and 3 (2.1%) went bone marrow transplants.

**Conclusion:** The prevalence of AML was higher as compared to AML in other studies done in a similar setting. Early diagnosis and treatment are key to a good prognosis and cure in most cases.

**Keywords:** acute myeloid leukemia, cross-sectional study, Nepal, prevalence

## Introduction

Acute myeloid leukemia (AML) is one of the most common subtypes of acute leukemia. It is a malignant disorder of the bone marrow characterized by the clonal expansion and differentiation arrest of myeloid progenitor cells. The common symptoms of AML are fever, bone pain, lethargy and fatigue, shortness of breath, pale skin, frequent infections, easy bruising, and unusual bleeding<sup>[1]</sup>. Although most cases of AML remain without a clear etiology, prior exposure to therapeutic, occupational, or environmental DNA-damaging agents is implicated in some patients<sup>[2]</sup>. However, previous studies have shown important differences in geographic, racial/ethnic, and age trend patterns for different leukemia subtypes<sup>[3]</sup>.

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## HIGHLIGHTS

- Acute myeloid leukemia is a malignant disorder of the bone marrow.
- It presents with pallor, fever, lethargy, bone pain, infections, and bleeding.
- It commonly affects adults.

It is the most common form of leukemia among adults and accounts for about 80% of all cases<sup>[4]</sup>. AML accounted for 23.1% of total leukemia cases worldwide in 2017<sup>[5]</sup>. Based on the Global Burden of Disease 2017 database, AML incidence cases increased by 87.3% while AML-related deaths increased remarkably by 93% from 1990 to 2017, and geography-wise analysis showed that Western Europe and South Asia had the most incidence cases<sup>[6]</sup>. AML accounted for 28.11% of deaths due to leukemia globally in 2019<sup>[7]</sup>. However, the lack of a proper cancer registry in Nepal makes it difficult to know the nationwide incidence of AML cases.

Our study primarily aimed to study the prevalence of AML in a tertiary hospital center in Nepal. Apart from that, the objective of the study was also to assess the role of associated etiological factors in the causation of AML and to know its most common presentations.

## Methods

### Study design and setting

This is a hospital-based retrospective cross-sectional study conducted among patients with acute leukemia admitted to the tertiary care center in Kathmandu.

### Study participants

Acute leukemia (myeloid and lymphoblastic) patients admitted to the hematology subunit of a tertiary care center from 1st April 2021 to 30th April 2022 were included. Patients with other coexisting hematologic disorders and those with incomplete data entry were excluded from the study.

### Study instruments

The data were collected by reviewing hospital records. The collected data were demographic variables (name, age, sex, residence, ethnicity, and, consanguinity) and clinical variables like common signs and symptoms related to AML (pallor, fever, lethargy/weakness, recurrent infections, shortness of breath, easy bruising, unusual bleeding, hepatosplenomegaly, and bone pain) and management of AML (chemotherapy or bone marrow transplantation or supportive measures only).

### Sampling methods and sample size

Hospital records were reviewed for the selection of acute leukemia cases via a convenience sampling technique.

A hospital-based study done in Nepal by Kulshrestha and Sah<sup>[3]</sup> found that 28.57% of acute leukemia patients belonged to AML. Considering an infinite population proportion of AML (28.6%);  $P = 0.28$ ;  $q = 0.72$ ; alpha 5% level of significance; with the allowable error of ( $e$ ) = 5%, the sample size calculated was 310.

The detailed elaboration is as follows:

$$n = z^2 \times (p \times q) / e^2$$

$$= 3.8416 \times (0.28 \times 0.72) / 0.0025$$

$$= 310$$

where,

$n$  = required sample size

$z = 1.96$  at alpha 5% level of significance

$P$  = prevalence = 0.28;  $q$  (compliment of prevalence) = 0.72

$e$  = allowable error, 5%

### Statistical analysis

The data were entered into an Excel sheet (Microsoft Excel 365) and then analyzed using Statistical Packages for Social Sciences (SPSS) version-22. Frequency, percentage, mean, and SDs were used to express descriptive statistics as applicable. We described the categorical data as frequency and proportions while continuous data as mean  $\pm$  SD and interquartile range. The binary logistic regression was used to identify the association of AML with the background characteristics of patients. For binary logistic regression analysis, odds ratios (OR) and 95% CI were calculated, and significance was established.

### Ethical consideration

Ethical approval was taken from the Institutional Review Committee (IRC) of the hospital (Reference no. 17/ 2022) after submitting a proposal letter to the board.

The manuscript has been reported in line with the strengthening the reporting of cohort, cross-sectional, and case-control studies in surgery (STROCSS) criteria<sup>[8]</sup>.

### Results

Out of 310 acute leukemia patients, 145 (46.7%) had AML. The mean age of acute leukemia cases was  $34.25 \pm 17.0$  years, while that of AML was  $35 \pm 18.82$  years.

Around two-thirds of the AML patients belonged to the 20–49 age group (101, 69.6%) whereas only 14 (9.6%) were less than 20 years. Sex-wise, AML predominates in males (104, 71.7%). The residence distribution revealed that province three has the highest burden of the disease (59, 40.7%) followed by province two (28, 19.3%), while province six (5, 3.4%) had the lowest cases. Regarding ethnic distribution, the Janajati subclass had the highest number of cases (46, 31.7%) followed by Brahmin (43, 29.6%) and Chhetri (23, 15.9%). A total of 60 (41.4%) AML patients were found to have been born after consanguineous marriage (Table 1).

More than three-fourths of the patients had pallor ( $n = 115$ , 79.3%) on the conjunctiva, while more than half of the patients had fever during admission ( $n = 92$ , 63.4%), and lethargy/weakness ( $n = 78$ , 53.8%). Recurrent infections and shortness of breath were noted in more than one-third ( $n = 56$ , 38.6%) and one-fourth ( $n = 43$ , 29.7%) of the cases, respectively. Nearly one-fourth of the cases had bruising ( $n = 36$ , 24.8%) and abnormal mucosal bleeding ( $n = 34$ , 23.4%). During the examination, hepatosplenomegaly was present in 17.9% ( $n = 26$ ) of patients. Only 16.6% ( $n = 24$ ) of AML patients complained of bone pain (Table 2).

**Table 1**

**Demographic variables of AML patients**

Characteristics	Frequency (%)
Age group	
< 10	6 (4.1)
10–19	8 (5.5)
20–29	30 (20.6)
30–39	35 (24.1)
40–49	36 (24.8)
50–59	18 (12.4)
60–69	12 (8.2)
Sex	
Male	104 (71.7)
Female	41 (28.3)
Residence	
Province one	19 (13.1)
Province two	28 (19.3)
Province three	59 (40.7)
Province four	6 (4.1)
Province five	20 (13.8)
Province six	5 (3.4)
Province seven	8 (5.5)
Ethnicity	
Brahmin	43 (29.6)
Chhetri	23 (15.9)
Madheshi	14 (9.7)
Dalit	16 (11.0)
Janajati	46 (31.7)
Other	3 (2.1)
Consanguinity	
No	85 (58.6)
Yes	60 (41.4)

AML, Acute myeloid leukemia.

**Table 2**  
Symptoms and signs of AML patients

Signs and symptoms	Frequency (%)
Pallor	115 (79.3)
Fever	92 (63.4)
Lethargy/weakness	78 (53.8)
Recurrent infections	56 (38.6)
Shortness of breath	43 (29.7)
Bruising	36 (24.8)
Bleeding	34 (23.4)
Hepatosplenomegaly	26 (17.9)
Bone Pain	24 (16.6)

AML, Acute myeloid leukemia.

More than half ( $n = 91$ , 62.8%) of AML patients underwent multiple cycles of chemotherapy. On the other hand, more than one-third ( $n = 51$ , 35.2%) of the cases had supportive care only. Bone marrow transplant was done in just 2.1% ( $n = 3$ ) patients (Table 3).

The factors associated with AML patients were analyzed using the binary logistic regression model. A  $\chi^2$ -test has been performed to test association. A CI containing the null value, that is 1, indicates a statistically insignificant association. Age groups 40–49 were found to be significantly associated with AML cases (OR 3.5, 95% CI: 1.27–9.61) as compared to other age groups (Table 4).

**Discussion**

AML is a common subtype of leukemia with a poor prognosis and a significantly greater incidence in countries with higher sociodemographic indexes, probably due to better cancer diagnosis and registry systems<sup>[6]</sup>. However, in countries like Nepal where there is a lack of a proper cancer registry, the data that we see regarding AML cases might be just the tip of the iceberg.

Our study demonstrates the prevalence of AML among all acute leukemia patients was 46.7%, which is higher than the study performed in Nepal by Kulshrestha and Sah<sup>[3]</sup> (28.57%) and Shrestha *et al.*<sup>[9]</sup> ( $n = 16$ , 14.5%). The mean age of AML patients in our study was  $35 \pm 18.82$  years. This is similar to a cross-sectional study from Pakistan, which shows a mean age to be  $37 \pm 17.19$  years<sup>[10]</sup>. However, results from the Global Burden of Disease 2017 database showed most incidences were seen in cases aged 50 years and older<sup>[6]</sup>. Our study showed that more than two-thirds of the AML cases were male (71.7%). A cross-sectional study from Pakistan also revealed that 59% ( $n = 33$ ) of AML patients were male<sup>[10]</sup>. The geographic pattern of leukemia varies widely. According to our present study, province number three which incorporated the capital city of Nepal accounts for the highest number of cases (40.7%). This may be because the hospital is the nearest referral center with the hemato-oncologic

**Table 3**  
Management of AML patients

Treatment modality	Frequency (%)
Chemotherapy only	91 (62.8)
Supportive treatment only	51 (35.2)
Bone marrow transplant	3 (2.1)

AML, Acute myeloid leukemia.

**Table 4**  
Factors affecting AML

Risk factors	Total (%)	AML		Binary logistic regression	
		No (%)	Yes (%)	OR (odd ratio)	CI
Age group					
< 10	12 (100)	6 (50)	6 (50)	1.167	0.297–4.588
10–19	25 (100)	17 (68)	8 (32)	0.549	0.176–1.717
20–29	84 (100)	54 (64)	30 (36)	0.648	0.266–1.580
30–39	82 (100)	47 (57.3)	35 (42.7)	0.869	0.358–2.108
40–49	48 (100)	12 (25)	36 (75)	<b>3.500</b>	1.274–9.616
50–59	33 (100)	15 (45)	18 (55)	1.400	0.499–3.927
60–69	26 (100)	14 (53.8)	12 (46.2)	1 Ref	
Sex					
Male	203 (100)	99 (48.8)	104 (51.2)	<b>1.691</b>	1.049–2.725
Female	107 (100)	66 (61.7)	41 (38.3)	1 Ref	
Residence					
Province number 1	42 (100)	23 (54.7)	19 (45.3)	1.033	0.340–3.135
Province number 2	43 (100)	15 (34.8)	28 (65.2)	2.333	0.760–7.162
Province number 3	140 (100)	81 (57.8)	59 (42.2)	0.910	0.339–2.446
Province number 4	16 (100)	10 (62.5)	6 (37.5)	0.750	0.190–2.964
Province number 5	33 (100)	13 (39.3)	20 (60.7)	1.923	0.601–6.151
Province number 6	18 (100)	13 (72.2)	5 (27.8)	0.481	0.120–1.927
Province number 7	18 (100)	10 (55.5)	8 (44.5)	1 Ref	
Ethnicity					
Brahmin	86 (100)	43 (50)	43 (50)	1.667	0.375–7.413
Chhetri	50 (100)	27 (54)	23 (46)	1.420	0.306–6.594
Madheshi	21 (100)	7 (33.3)	14 (66.7)	3.333	0.612–18.150
Dalit	33 (100)	17 (51.5)	16 (48.5)	1.569	0.321–7.660
Janajati	112 (100)	66 (58.9)	46 (41.1)	1.162	0.264–5.103
Other	8 (100)	5 (62.5)	3 (37.5)	1 Ref	
Consanguinity					
Yes	194 (100)	109 (56.2)	85 (43.8)	1.374	0.866–2.180
No	116 (100)	56 (48.3)	60 (51.7)	1 Ref	

AML, Acute myeloid leukemia.

service for people living in province number three. Regarding ethnicity, Janajati followed by Brahmin accounted for the highest AML cases. This is partly explained by more such castes living in province number three. The current study demonstrated that 41.4% of AML cases had a family history of consanguineous marriage. But a study based in the UAE showed that 80% of families were consanguineous among 69 acute lymphoblastic leukemia cases (ALL), which is closely related to AML<sup>[11]</sup>.

Pallor (79.3%), fever (63.4%), and lethargy/weakness (53.8%) were the most common presenting features in AML patients in our study. A study from Pakistan also showed similar results, where fever (80.4%), pallor (46.4%), and weakness (46.4%) were the most common clinical features in AML patients<sup>[10]</sup>. However, in one study conducted in Kanti Children Hospital, Nepal, the most common presenting features in ALL, closely related to AML, were fever (89.2%), followed by splenomegaly (89.1%), hepatomegaly (69.2%), and lymphadenopathy (58.4%)<sup>[12]</sup>.

The classical treatment for AML patients consists of cytarabine and anthracycline (7 + 3) based chemotherapy for induction and those in remission would proceed to consolidation therapy consisting of high-dose cytarabine while those with intermediate risk features would undergo hematopoietic stem cell transplant<sup>[6,13]</sup>. More than half of the cases (62.8%) in our study also were treated with chemotherapy alone while 2.1% went through bone marrow transplants. Currently, there is an emerging role of target-based therapy such as Venetoclax, a BCL-2 inhibitor that can be used solely or in combination with other chemotherapeutic agents along with potential roles of CAR-T cells in the treatment of AML<sup>[14]</sup>.

Binary logistic regression was applied for risk assessment. The study demonstrates age group 40–49 is greater than three times more susceptible (OR = 3.5, CI = 1.2–9.6) to AML as compared to the 60–69 age group. Similarly, the male is slightly more at risk of developing AML (OR = 1.69, CI = 1.04–2.72) which is statistically significant. A cross-sectional study in southwest Ethiopia concluded that being older age ( $P=0.019$ ) and male sex ( $P=0.047$ ) were significantly associated with having leukemia, at a 95% CI<sup>[15]</sup>.

The sample was taken from the study population visiting the tertiary center. Therefore, its findings cannot be generalized to other places. Many data available were incomplete so the convenience sampling method was applied, which affects the representative study sample. Our study design is cross-sectional, thus different AML-associated factors could not establish its causation. These were the limiting factors found during the study.

## Conclusion

We found out that the prevalence of AML was 46.7% which is higher compared to AML in other studies done in a similar setting. The most affected age group was 40–49 years, and males were most affected. Pallor, fever, and lethargy/weakness were the most common clinical presentations, which help in the early diagnosis and treatment of the cases for a good prognosis. The results from our study can serve as a helpful guide to government and voluntary institutions like nongovernmental organizations (NGOs) and international nongovernmental organizations (INGOs) to plan suitable health programs for leukemic patients regarding early diagnosis and treatment.

## Ethical approval

The study was approved by the Institutional Review Committee (IRC) of the Civil Service Hospital (Reference no. 17/ 2022).

## Consent

Not applicable.

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This study did not receive any grant from any funding agencies in public or organizations.

## Author contribution

P.S.C.: literature review, conceptualization, methodology, data collection, formal analysis, writing – original draft, review and edit; D.K.L.: literature review, conceptualization, methodology, data collection, writing – original draft, review and edit; A.K.: literature review, conceptualization, methodology, data collection, writing – original draft, review and edit, supervision; A.P.: literature review, conceptualization, methodology, data collection, writing –original draft, review and edit; P.R.S.: literature review, conceptualization, methodology, data collection, writing – original draft, review and edit; L.A.: literature review, conceptualization, methodology, data collection, writing – original draft, review and edit; S.P.: literature review, conceptualization, methodology, data collection, writing – original draft, review and edit; S.G.: literature review, methodology, data interpretation, writing – original draft, review and edit. S.K.: literature review, methodology, data interpretation, writing – original draft, review and edit; M.K.: literature review, methodology, data interpretation, writing – original draft, review and edit. All the authors approved the final version of the manuscript.

## Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

## Research registration unique identifying number (UIN)

1. Name of the registry: research registry.
2. Unique identifying number or registration ID: research-registry8853.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): researchregistry.

## Guarantor

Dr Prem Shankar Chaurasiya.

## Data availability statement

The datasets generated during and/or analyzed during the current study are publicly available.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

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