# Real-World Outcome of Acute Promyelocytic Leukemia Treatment in a Resource-Constrained Setting: An Experience from Nepal

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## Introduction

- Acute promyelocytic leukemia (APL), defined by the t(15;17) translocation, carries a high risk of early death from coagulopathy but is highly curable with ATRA and arsenic trioxide (ATO).
- While this combination has transformed outcomes in high-income countries (HIC), disparities in access to ATO and supportive care remain a major challenge in low- and middle-income countries (LMIC).
- In Nepal, oncology services are centralized in few urban centers and face challenges in workforce, treatment supplies, and finances, yet the Clinical Hematology Unit at Civil Service Hospital has been delivering leukemia care since 2011.

## Aim

- The aim of this study is to present real-world outcomes of patients with APL treated at the Clinical Hematology Unit in Civil Service Hospital between March 2015 and June 2024.

## Methods

- Study population: 90 consecutive patients of all ages diagnosed with APL.
- Diagnosis: Based on characteristic leukemic cell morphology in blood/marrow, confirmed by PML-RARA fusion/translocation via FISH, cytogenetics, or RT-PCR.
- Data collected: Age, sex, date of diagnosis, WBC, platelet count, treatment details (ATRA, ATO, chemotherapy), adverse events, follow-up duration, and survival status.
- MRD monitoring: RT-PCR every 3 months for first 2 years.
- Statistical analysis: OS estimation by KM, group comparison by log-rank test.

## Results

**Treatment strategies:**

- Early initiation: ATRA started within 1 hour of clinical suspicion based on abnormal promyelocytes in peripheral smear.
- Low-risk protocol (APL0406):

➢ ATO + ATRA daily until CR or max 60 days.

➢ Consolidation: ATO (5 days/week, 4 wks on/4 wks off x 4 courses) + ATRA (2 wks on/2 wks off x 7 courses).

- High-risk protocol (North American Leukemia Intergroup, no cytarabine):

➢ Cycle 1: ATRA + daunorubicin

➢ Then: 8 wks ATO + 2 cycles ATRA + daunorubicin

➢ Maintenance: 2 yrs ATRA

**Table 1 - Baseline characteristics of the cohort**

| | High risk (N = 34), N (%) | Low risk (N = 56), N (%) | p-value |
|---|---|---|---|
| **Age (in years)** | | | 0.09 |
| Mean +_ SD | 38.09 ± 15 | 32.8 ± 11.9 | |
| Median | 36.5 | 32 | |
| Range | 14-70 | 15-71 | |
| **Sex** | | | 0.74 |
| Male | 19 (55.9) | 28 (50) | |
| Female | 15 (44.1) | 28 (50) | |
| **WBC count (per µL)** | | | <0.001 |
| Median | 49000 | 3400 | |
| Range | 10400-173400 | 600-8200 | |
| **Platelet count (per µL)** | | | 0.39 |
| Median | 17000 | 23000 | 20000 |
| Range | 1000-85000 | 3000-92000 | 1000-92000 |
| **CNS disease** | 1 (2.9) | 0 | <0.001 |
| **Complete Remission** | 26 (76.5) | 55 (98.2) | 0.003 |
| **Mortality** | 8 (23.5) | 1 (1.8) | 0.004 |
| **Transplant** | 1 (2.9) | 2 (3.6) | 0.9 |
| **Follow-up duration** | | | 0.36 |
| Median | 2082.5 | 2268.5 | 2246.5 |
| Range | 4-3315 | 13-3268 | 4-3315 |

## Results

**KM curve of overall survival based on high-risk vs low-risk**

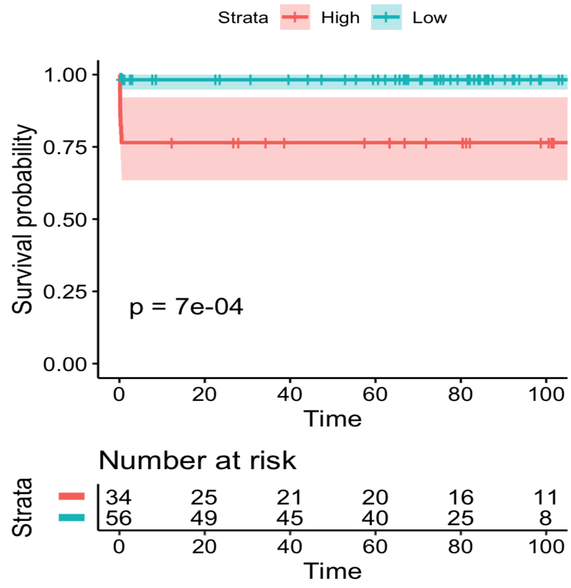



**Table 2 – Overall survival details**

| | High risk | Low risk | Overall |
|---|---|---|---|
| **1-year survival** | 76.5 (63.5 - 92.1) | 98.2 (94.8 - 100) | 90.0 (84 – 96.4) |
| **5-year survival** | 76.5 (63.5 - 92.1) | 98.2 (94.8 - 100) | 90.0 (84 – 96.4) |

**Table 3 – Adverse event profile**

| | High risk (N = 34), N (%) | Low risk (N = 56), N (%) | p-value |
|---|---|---|---|
| **Febrile neutropenia** | 29 (85.3) | 44 (78.6) | 0.60 |
| **Coagulopathy** | 26 (76.5) | 36 (64.3) | 0.33 |
| **Fungal infection** | 7 (20.6) | 17 (30.4) | 0.44 |
| **Differentiation syndrome** | 10 (29.4) | 15 (26.8) | 0.97 |
| **Gastric ulcer** | 1 (2.9) | 3 (5.4) | 0.99 |
| **Intracranial bleed** | 8 (23.5) | 1 (1.8) | 0.004 |
| **Fournier gangrene** | 0 | 3 (5.4) | 0.46 |
| **Dilated cardiomyopathy** | 2 (5.9) | 1 (1.8) | 0.67 |

## Discussion

- Publicly funded hospital and largest hematology center in Nepal with >150 acute leukemia/ year and BMT services.
- CR rate in our cohort was 90%, higher than reported in Pakistan (86.3%) and Latin America (85.4%).
- Induction mortality in the high-risk group was 24%, comparable to the North American Leukemia Intergroup Study (ATRA + chemotherapy).
- Hemorrhage was the sole cause of induction deaths, consistent with prior studies.
- 1-year OS (90%) better than that reported from other South Asian countries (India and Pakistan).
- OS comparable to high-income countries (HIC) — e.g., low-risk cohort 1-year OS of 98% vs. 97% in a European study.
- Availability of ATRA, generic ATO in LMIC.

## Limitations

- Selection bias possible due to diagnostic and access challenges.
- Socioeconomic factors (income, travel burden) not collected; prior work shows most acute leukemia patients in Nepal are from outside Kathmandu, often unemployed, and socioeconomically disadvantaged.
- Retrospective design
- Quality of life data not collected.