SOHO ANNUAL MEETING 2024

# Central Nervous System Hemorrhage in Acute Promyelocytic Leukemia – A tertiary centre experience

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## INTRODUCTION

Acute Promyelocytic Leukemia(APL) when identified in 1940s was a disease with almost 100% mortality. Now with therapeutic advancement and targeted therapies we are in the era of CRs approaching 100% and 2 year EFS approaching 90-95%. Still early death (within 30 days) in APL is a major concern with rates approaching 10-20%. Coagulopathy and its related complications especially Intracranial Bleed (IC Bleed) is a major contributor to this mortality.

## AIM

- To determine the incidence of IC bleed in newly diagnosed APL patients and its effect on induction outcome
- To identify risk factors and predictors of IC bleed .

## METHOD

- Observational Study at a tertiary care Centre in India from March 2021 to December 2022.
- Included all treatment naive patients with APL.
- Diagnosis was confirmed by PML RARA RT- PCR or break apart FISH.
- Non contrast computed tomography (NCCT) head was done at baseline for all.
- The outcome was assessed at 30 days or at discharge whichever is later in terms of survival and disease status.

## RESULTS

- 61 APL patients (median age: 26 yrs.) were included in the study.
- Male: Female= 1.2:1, 51% in high risk and 49% in low risk..
- High-risk patients received APML 4-based induction (Idarubicin replaced with Daunorubicin), while low-risk patients received ATRA + ATO-based induction.
- 27 patients experienced IC bleed, with 22 presenting initially and 5 developing it later. During induction
- Baseline TLC > 7500/µL, Promyelocyte count > 7500/µL, INR > 1.4, LDH > 320 IU/µL, and high-risk APL were associated with IC bleed in univariate analysis, but only INR > 1.4 remained significant in multivariate analysis.
- Low serum albumin and coexisting GI bleed were linked to higher mortality in IC bleed patients, but only low serum albumin was statistically significant in multivariate analysis.
- All patients who survived achieved morphological remission.

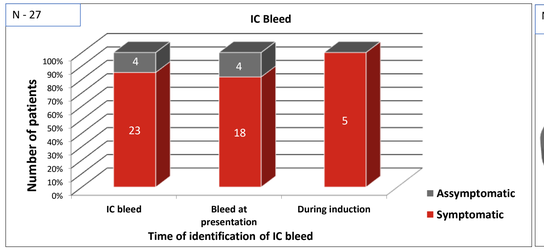



*Fig:1 IC Bleed in study subjects*

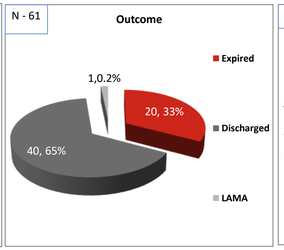



*Fig:2 Outcome of patients*

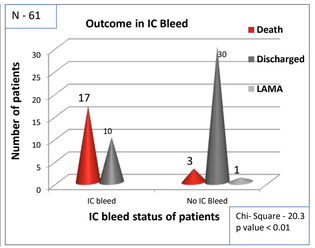



*Fig:3 Outcome in IC Bleed*

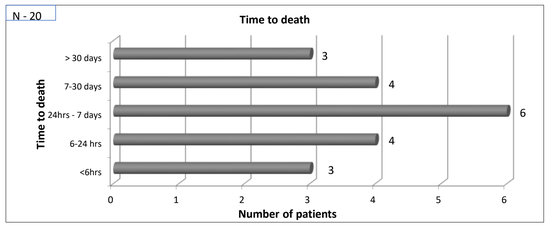



*Fig:4 Graph showing time to death in patients who expired*

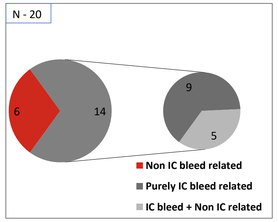



*Fig:5 Cause of death*

| Cause of death | No. ( %) N= 20 |
|---|---|
| DAH + respiratory failure | 2(10%) |
| IC Bleed | 9(45%) |
| DS + IC Bleed + MODS | 1(5%) |
| Pneumonia + Sepsis + ARDS | 1(5%) |
| Sepsis + Septic Shock | 2(10%) |
| IC bleed + Sepsis + Septic shock | 2(10%) |
| Pneumonia+ perianal abscess+ Sepsis | 1(5%) |
| Pneumonia + Sepsis + IC Bleed | 2(10%) |

*Table: 1 Causes of death*

## CONCLUSIONS

•In spite of having high CR rates coagulopathy and related bleeding continues to take a high toll on patients with APL

•Our cohort had a high incidence of IC bleed ( 44.3%) and associated mortality (32.8%)

•More awareness regarding the disease and early referral from periphery should be facilitated

•Identification of risk factors for IC bleed like High TLC, promyelocyte count, LDH and INR > 1.4 at presentation and more stringent correction of coagulopathy might help.

•Studies exploring strategies for prevention and management of coagulopathy and bleeding in APL is the need of the hour which can improve outcomes

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## ACKNOWLEDGEMENTS

We sincerely thank each and every staff of AIIMS, New Delhi for their constant support throughout the study.

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