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Diagnosis and prognosis of blood Xpert Ultra and Myco/F blood culture for TB in advanced HIV disease

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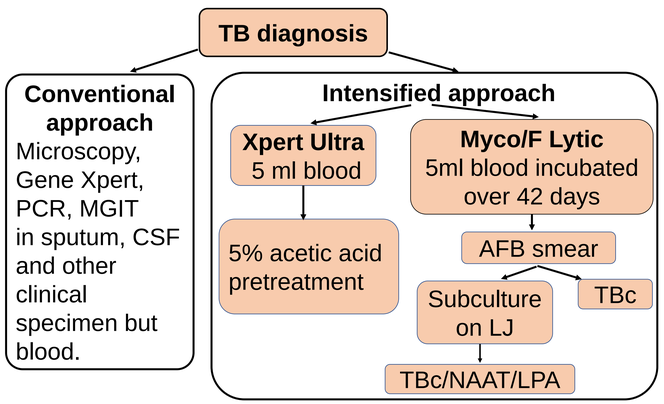
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BACKGROUND

- Current TB diagnostics are suboptimal to detect TB in patients with advanced HIV disease (AHD) who are at high risk for disseminated TB and mortality. Blood has been overlooked as a compartment for TB diagnostics in AHD.
- We determined (1) the diagnostic yield of routine screening for TB in blood using Xpert Ultra (UXpert) and Myco/F Lytic (MFL) culture, and (2) the utility of the positivity in blood and blood UXpert cycle threshold (Ct) in predicting mortality.

METHODS

- **Design:** Prospective observational study of hospitalized adult patients with AHD at 3 hospitals, followed monthly over 6 months
- **Inclusion criteria**: CD4 counts ≤ 100 cells/μL or WHO stage 3 or 4; not on ART or on ART for ≤ 3 months or >12 months with suspected ART failure.
- **Intervention:** TB was diagnosed by conventional and intensified approaches:



- **Analysis:** Cox proportional hazard models, adjusted for site, age, BMI, CD4 count and TB treatment, were used to assess the association between TB positivity in blood, and Uxpert Ct value of IS6110-1081 gene (Ct_{IS}) in blood versus mortality.

- Screening for TB in blood using Xpert Ultra and Myco/F lytic blood culture detected **26.5% additional TB cases** in hospitalized patients with advanced HIV disease; **over 70% additional diagnosed cases were by blood UXpert**, enabling rapid initiation of TB therapy.
- **Positive TB in blood** and having **UXpert Ct_{IS} value ≤ 21** in blood was associated with **higher mortality**, highlighting the important role of blood Xpert Ultra and Myco/F lytic blood culture in the early diagnosis and prognosis of disseminated TB.

RESULTS

- **901** patients were recruited between Feb 2021 and Jul 2023; 76 were excluded due to active TB therapy or missing Uxpert/MLF results.
- 83% were male. Median age: 36 years. Median CD4 cell count: 18 cells.
- **239/825 (28%)** had microbiologically confirmed TB (TB positive in smear, culture, and/or Uxpert of a clinically relevant specimen).
  - **33%** by the conventional method only;
  - **40.3%** by both conventional and intensified approaches;
  - **26.5%** were identified by the intensified approach only.
- **71.1%** of additionally diagnosed TB cases were from UXpert performed directly in blood.

ACKNOWLEDGEMENTS

All patients who participated in the study and collaborators

RESULTS

Figure 1: The Venn diagram of 223 TB patients diagnosed by conventional and intensified approach in blood sample.

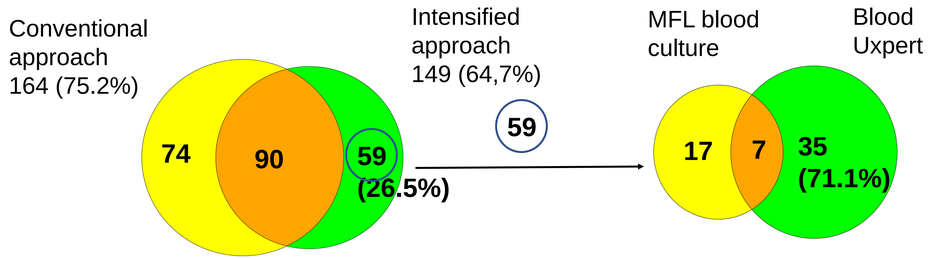


Figure 2: Survival probability of 223 TB patients over 24 weeks: A) Survival in patients with pos vs. neg TB in blood; B) Survival by Uxpert values in blood

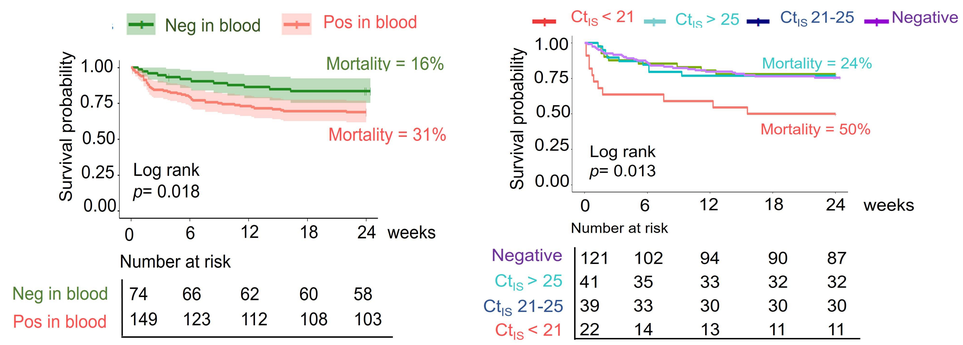
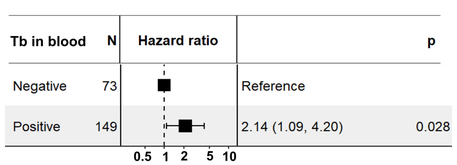
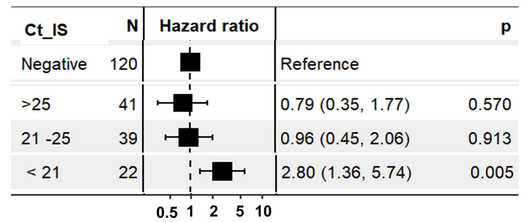


Figure 3 : The Cox proportional hazard models adjusted for site, age, BMI, CD4 count, TB treatment identified positive TB in blood and CT_{IS} predictors of 24-week mortality





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