JOURNAL READING

Effect of Empiric Anti–Mycobacterium tuberculosis Therapy on Survival Among Human Immunodeficiency Virus–Infected Adults Admitted With Sepsis to a Regional Referral Hospital in Uganda

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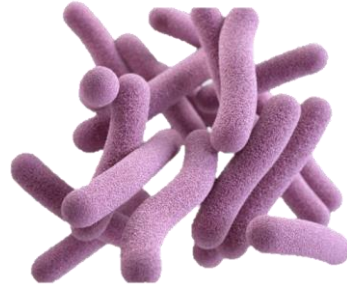
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INTRODUCTION

1. In sub-Saharan Africa, sepsis is a leading cause of disease and death. Approximately 65%–85% of all patients with sepsis are human immunodeficiency virus (HIV) infected, and *Mycobacterium tuberculosis* is the leading cause of bacteremia in this population.

2. Reduction of sepsis-associated mortality rates relies on early detection and prompt initiation of antimicrobial therapy

3. Culture is the reference standard for the microbiological detection of tuberculosis but is expensive, labor intensive, and has a long turnaround time, making it impractical for clinical decision making in patients with sepsis.

INTRODUCTION
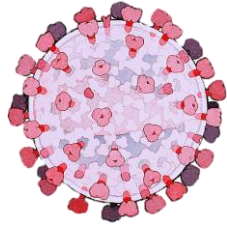
Given that tuberculosis is the leading cause of sepsis in areas with a high prevalence of HIV and tuberculosis, such as Uganda, and given the high mortality rates associated with tuberculosis sepsis and the lack of available rapid and reliable tuberculosis diagnostic tests, therefore this study aimed to determine the proportion of

1. HIV-infected patients admitted with sepsis who received antituberculosis therapy during their hospitalization

2. Identify predictors of receiving antituberculosis therapy

3. Determine the relationship between empiric antituberculosis therapy and 28-day survival rates.

METHODS

STUDY METHOD

This is retrospective cohort study at the Mbarara Regional Referral Hospital. .

National HIV prevalence is 6%, and the incidence of tuberculosis

infection is 201 per 100 000 population

SAMPLE

Obtained from **All cases** of patients admitted with infection to the medical ward between **January 2014 and December 2015** and

analyzed data from all **HIV-infected individuals** who were **admitted with sepsis**

STATISTICAL ANALYSIS

This study used the **χ2 test** to compare proportions and the **Mann Whitney U test** to compare continuous variables.

This study determined clinical associations with receipt of antituberculosis therapy using **multivariable logistic regression.**

A **significance level of < 0.05** to be statistically significant.

For all the included patient, it is obtained some following data: clinical history, vital signs, examination findings, diagnostic investigations, antituberculosis therapy, and the in-hospital outcomes of death or discharge.

Recorded vital sign obtained in the emergency or medical ward to impute any missing admission vital signs.

SAMPLE

INCLUSION

- Patients who had a valid discharge or death date
- Patient who had a valid date of antituberculosis therapy administration if it was given.
- Have more than 2 SIRS criteria

EXCLUSION

- Patients who had microbiologically proved tuberculosis or had received antituberculosis therapy before admission.

RESULT

340 records reviewed

→ 191 records excluded
  - 97 with invalid or missing discharge, death, or anti-TB therapy date
  - 46 missing ≥1 vital sign
  - 35 did not have ≥2 systemic inflammatory response syndrome criteria
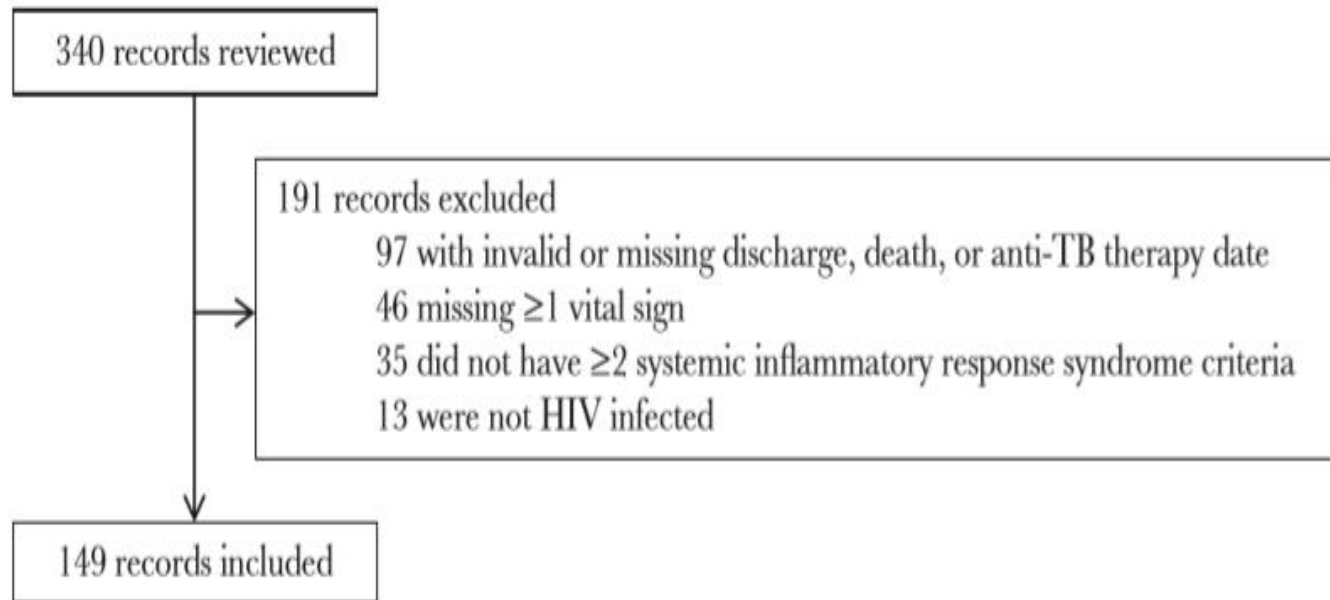 - 13 were not HIV infected

149 records included

Table 1. Clinical Characteristics of Human Immunodeficiency Virus–Infected Patients With Sepsis or Severe Sepsis Admitted to Mbarara Regional Referral Hospital (January 2014 to December 2015)

Variable	All Patients (n = 149)	Patients With Severe Sepsis (n = 74)
Age, median (IQR), y	33 (28–40)	35 (29–40)
Female sex, no. (%)	67 (45)	32 (58)
Vital signs, median (IQR)		
Temperature, °C	38.2 (36.8–38.7)	38.3 (36.7–38.8)
Respiratory rate, breaths/min	30 (24–36)	28 (24–36)
Heart rate, beats/min	118 (102–126)	118 (101–124)
Systolic blood pressure, mm Hg	98 (90–110)	90 (80–100)
Diastolic blood pressure, mm Hg	60 (60–70)	60 (50–70)
Glasgow coma scale (score), median (IQR)	15 (14–15)	14 (13–15)
Cough, no. (%)	102 (68)	48 (65)
Shortness of breath, no. (%)	51 (34)	19 (26)
Treatment, no. (%)		
Antituberculosis therapy	55 (37)	26 (35)
Antibiotics	129 (87)	63 (74)
Oxygen	44 (30)	27 (37)
Blood transfusion	42 (29)	18 (25)
Death, no. (%)	48 (32)	32 (43)

Abbreviation: IQR, interquartile range.

RESULT

Of the 55 patients (37%) who received antituberculosis therapy, 19 (35%) died compared with 29 of 94 (31%) who did not receive such therapy.

Among the 74 patients with severe sepsis, 9 of 26 (35%) who received antituberculosis therapy died, versus 23 of 48 (48%) who did not receive such therapy.
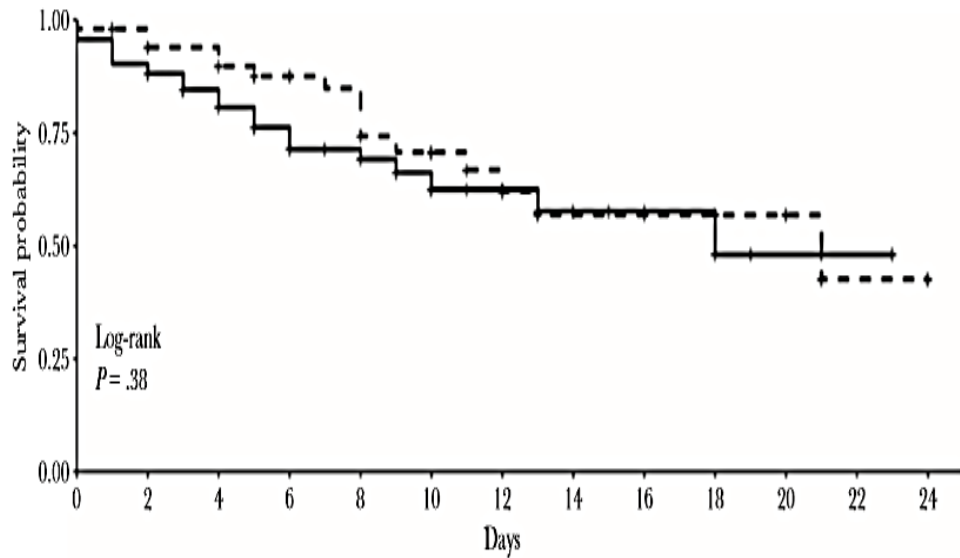
The 28-day survival rates did not differ significantly between these 2 groups.

In patients with severe sepsis, antituberculosis therapy was associated with an improved 28-day survival rate and with a reduced mortality rate

Table 3. Adjusted Hazard Ratios for Mortality Among Human Immunodeficiency Virus–Infected Patients With Sepsis or Severe Sepsis Admitted to Mbarara Regional Referral Hospital (January 2014 to December 2015)

Variable	Adjusted HR (95% CI)	P Value
Age (years)	1.01 (.97–1.04)	.74
Female sex	0.76 (.39–1.47)	.41
Temperature (°C)	0.82 (.66–1.02)	.08
Respiratory rate (breaths/min)	1.01 (.97–1.05)	.54
Heart rate (beats/min)	1.01 (.99–1.02)	.41
Systolic blood pressure (mm Hg)	0.98 (.96–1.00)	.85
Diastolic blood pressure (mm Hg)	1.01 (.98–1.03)	.63
Glasgow coma scale (score)	0.64 (.53–.78)	<.01
Receipt of oxygen	3.13 (1.63–5.99)	<.01
Receipt of blood transfusion	1.00 (.49–2.03)	>.99
Empiric antituberculosis therapy		
Patients with sepsis	1.24 (.53–2.90)	.63
Patients with severe sepsis	0.32 (.13–.80)	.03

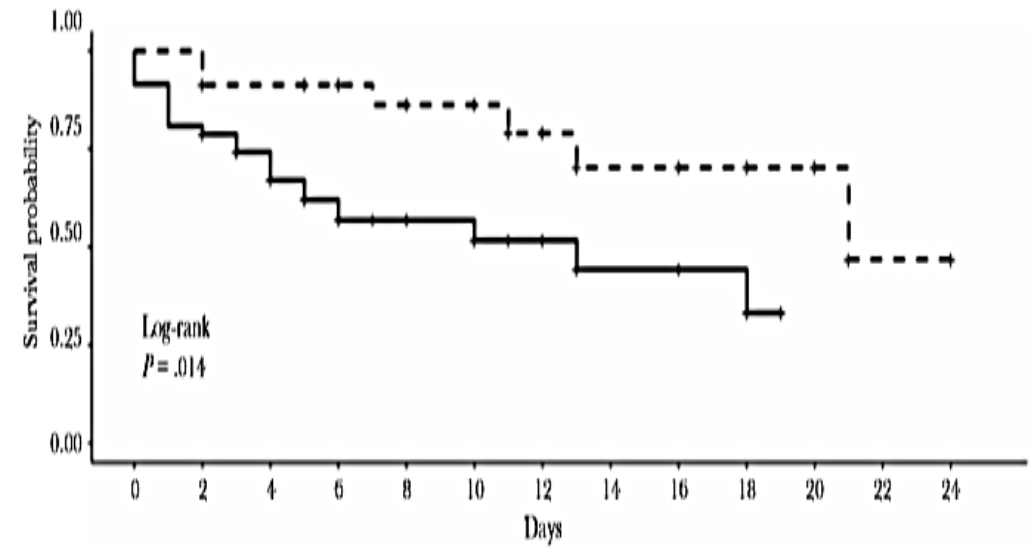Abbreviations: CI, confidence interval; HR, hazard ratio.

Figure 3. Survival curves over 28 days for human immunodeficiency virus–infected patients with severe sepsis admitted to Mbarara Regional Referral Hospital from January 2014 to December 2015, according to whether they received (*dashed line*) or did not receive (*solid line*) antituberculosis therapy. Patients were censored at death and at hospital discharge.

DISCUSSION

The WHO recommends that hospitalized patients with a history of cough for 2–3 weeks in settings with high HIV prevalence should initially be treated with parenteral antibiotics for bacterial infection, followed by antituberculosis therapy if there has been no clinical improvement after 3–5 days.

Study	Result
Jacob et al, 2018 **Katagira et al, 2013**	In an observational study of patients with tuberculosis bloodstream infection in Uganda, the 30-day **mortality rate was decreased in patients who received empiric antituberculosis therapy** at admission compared with those who did not (31% vs 53%). In another study from Uganda, patients with **suspected pulmonary tuberculosis** and clinical danger signs who received WHO algorithm–based antituberculosis **treatment had a 44% reduction in 8-week mortality**
Kethireddy et al,2013	In a study of patients with septic shock due to tuberculosis from North America and Saudi Arabia, **the mortality rate was 63% for patients who received early antituberculosis therapy compared with 93% for patients who did not, and all patients who did not receive any antituberculosis therapy died**
Gupta-Wrigh et al, 2018	In a 2018 randomized study, the use of urinary LAM testing to guide antituberculosis therapy in hospitalized HIV-infected patients in Zambia and South Africa **did not reduce the overall mortality rate** in all patients but **did reduce the mortality rate in a subgroup of high-risk patients**

1. This was a retrospective study with **data missing** for some patients, which could have affected our findings; however, its believed missing data occurred randomly and did not lead to bias regarding diagnosis, treatment, or outcome in the patients.

2. This study also **did not have stored samples** for subsequent molecular or other diagnostic testing. Therefore, it was **unable to microbiologically confirm the diagnosis of tuberculosis.**

3. Collected data from **patients admitted over a calendar year,** and the total cohort size may have been underpowered to determine a difference in outcomes between all patients who did or did not receive empiric antituberculosis therapy for sepsis.

LIMITATIONS

CONCLUSION

In conclusion, in HIV-infected patients admitted with sepsis to a regional referral hospital in Uganda, we found that 37% of patients received empiric antituberculosis therapy.

Although empiric antituberculosis therapy was not associated with improved 28-day survival for all patients, it was associated with improved survival for patients with severe sepsis

Immediate rather than delayed empiric antituberculosis therapy, as may be a good strategy for treating patients with sepsis in areas with high HIV and tuberculosis prevalence.