Title

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Journal

JAIDS Journal of Acquired Immune Deficiency Syndromes, 79(5)

ISSN

1525-4135

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Publication Date

2018-12-15

DOI

10.1097/qai.0000000000001855

Peer reviewed

HHS Public Access

Author manuscript

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2019 December 15.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2018 December 15; 79(5): 624–630. doi:10.1097/QAI.0000000000001855.

Predictors of Mortality among Hospitalized Patients with Lower Respiratory Tract Infections in a High HIV Burden Setting

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Abstract

Introduction—Lower respiratory tract infections (LRTIs) are a leading cause of mortality in sub-Saharan Africa. Triaging identifies patients at high-risk of death but laboratory tests proposed for use in severity-of-illness scores are not readily available, limiting their clinical use. Our objective was to determine whether baseline characteristics in hospitalized participants with LRTI predicted increased risk of death.

Methods—This was a secondary analysis from the MIND-IHOP cohort of adults hospitalized with LRTI who underwent standardized investigations and treatment. The primary outcome was all-cause mortality at two months. Predictors of mortality were determined using multiple logistic regression.

Results—Of 1887 hospitalized participants with LRTI, 372 (19.7%) died. The median participant age was 34.3 years (Interquartile Range, IQR, 28.0–43.3 years), 978 (51.8%) were men, and 1192 (63.2%) were HIV-positive with median CD4 counts of 81 cells/μL (IQR 21–226 cells/μL). Seven hundred eleven (37.7%) participants had a microbiologically confirmed diagnosis. Temperature <35.5ºC (aOR=1.77, 95% CI=1.20–2.60; p=0.004), heart rate >120/minute (aOR=1.82, 95% CI=1.37–2.43; p<0.0001), oxygen saturation <90% (aOR=2.74, 95% CI=1.97–3.81; p<0.0001), being bed-bound (aOR=1.88, 95% CI=1.47–2.41; p<0.0001) and being HIV-positive (aOR=1.49, 95%CI=1.14–1.94; p=0.003) were independently associated with mortality at two months.

Conclusions—Having temperature <35.5°C, heart rate >120/minute, hypoxia; being HIV positive and bed-bound independently predicts mortality in participants hospitalized with LRTI. These readily-available characteristics could be used to triage patients with LRTI in low-income settings. Providing adequate oxygen, adequate intravenous fluids; and early antiretroviral therapy (in people living with HIV/AIDS) may be life-saving in hospitalized patients with LRTI.

Keywords

Predictors; Mortality; Pneumonia; HIV; sub-Saharan Africa

Introduction

Despite current advances in diagnostic techniques, improved treatment algorithms, and improved intensive care[1,2], lower respiratory tract infections (LRTIs) remain a major cause of mortality globally[3]. Establishing the severity of disease and identifying specific pathogens causing infection is critical in guiding treatment of hospitalized patients with suspected LRTI. Severity of LRTI may be assessed using validated severity-of-illness scores[4–6], while specific pathogens causing LRTI can be identified using conventional microbiological tests (sputum gram stain and bacterial cultures), serological tests or novel molecular tests[7]. Despite the wide array of tests available, pathogens are identified in only 14–40% patients with LRTI[7,8]. For this reason, empiric antibiotic treatment for LRTI is justifiable pending results of bacteriological studies.

Most studies predicting outcomes of patients with LRTI and using severity-of-illness scores have been done in HIV-negative participants[9,10]. The prognosis of HIV-positive patients with LRTI may be poor due to the HIV-related immunosuppression that leads to increased susceptibility to recurrent and multiple coinfections but there are only a few studies addressing this. In one study by Cordero and colleagues, shock, a CD4 count <100 cells/μL, pleural effusions, cavitary disease, and multilobar infiltrates were identified as poor prognostic markers in participants with HIV infection and bacterial pneumonia[11].

In sub-Saharan Africa, which has a high burden of HIV and LRTI[3], tests for diagnosing LRTI and for triaging patients with LRTI using severity-of-illness scores are rare. Vital signs and simple laboratory tests may therefore be more practical for initial patient assessment in urgent care. We have previously studied predictors of mortality in HIV-positive participants with pneumonia, and attributed the increased mortality to delays in TB diagnosis[12] and severe disease[13,14]. At the time of the current study, there was a noticeable shortening in the turn-around time for TB diagnosis due to the routine use of Xpert MTB/RIF testing.

In this study of HIV-positive and HIV-negative participants, we determined whether baseline patient characteristics and vital signs identified adults with pneumonia at increased risk of death within two-months of hospitalization. We also compared mortality and clinical predictors of mortality in HIV-positive and HIV-negative participants. Baseline characteristics associated with increased risk of mortality would identify a population of patients that could benefit from early and targeted interventions to improve clinical outcomes in LRTI.

Methods

Population and study design

We present a secondary analysis of a prospective cohort study, the Mulago Inpatient Non-invasive Diagnosis-International HIV-associated Opportunistic Pneumonias (MIND-IHOP) Study. Adult patients (≥18 years) with LRTI and cough of any duration who consented for the study underwent a standardized evaluation for pneumonia as described previously[12,13]. This included an administered questionnaire on history, measured vital signs, physical examination related to respiratory disease, and assessment of their functional status (i.e.,

whether they were ambulatory > or ≤50% of the day and what activities they were capable of performing). Additional investigations included HIV serology, CD4 cell counts (for HIV-positive patients), chest radiography, and sputum examination by microscopy (two sputa for acid-fast bacilli (AFB)), sputum mycobacterial cultures ((Lowenstein-Jensen (LJ) and liquid culture (Mycobacterial Growth Indicator Tube (MGIT)), and a single Xpert MTB/RIF. Patients who were HIV-positive, AFB sputum smear-negative (SS-) and Xpert negative (Xpert-) underwent bronchoscopy if clinically indicated. During bronchoscopy, a diagnosis of pulmonary Kaposi's sarcoma (pKS) was made on visualization of typical Kaposi's sarcoma lesions in the endobronchial tree. We performed bronchoalveolar lavage (BAL) and sent samples to be analyzed for *P. jirovecii* using a modified Giemsa staining method as well as for acid-fast bacilli and mycobacterial cultures (LJ and MGIT).

All participants with presumed pneumonia received empiric treatment with antibiotics for 7–10 days unless an alternative diagnosis was made. Additional therapy with intravenous fluids and supplemental oxygen were administered as was clinically indicated.

Participants who improved on the above treatment were discharged and given an appointment for review by the study team two months after the date of their enrollment into the study. The two-month follow-up was done in person or by telephone (if the study participant was unable to come to the clinic). The purpose of the two-month appointment was three-fold: 1) to assess vital status; 2) to assess clinical response to treatment; and 3) to provide results of pending diagnostic tests (*e.g.* mycobacterial culture results) and appropriate treatment for those who were unable to be contacted earlier.

Study Outcomes

Study outcomes included participant vital status at hospital discharge and at two months from the date of enrollment into the study (alive or dead). Participants who failed to return for follow-up and were unreachable by phone after sixteen attempts over an eight-week period were deemed lost to follow-up.

Statistical analysis

We summarized baseline characteristics and vital sign measurements using medians with interquartile range (IQR) for continuous variables or percentages with 95% confidence intervals (CI) for categorical variables. Continuous variables were categorized using clinically relevant cut-offs. The primary outcome was all-cause mortality at two months of follow up and the primary predictors were age (in years), gender, smoking status, HIV serostatus, functional status[15] and danger signs (axillary temperatures, heart rate (HR), respiratory rate (RR) and oxygen saturation). Secondary predictors included CD4 counts and the use of antiretroviral therapy (ART) for the HIV-positive participants. We assessed strength of associations between clinical characteristics and mortality at two months using chi-square tests for categorical variables, t-tests or rank sum tests for continuous variables (whether or not they were normally distributed, respectively), odds ratios and 95% CI. We stratified mortality analyses by TB status, HIV serostatus, and CD4 count strata (if HIV-positive), and history of empiric TB treatment. Variables that had a p-value of <0.2 at

bivariate analysis were included in a multivariable model using multiple logistic regression to identify variables that independently predicted mortality.

Ethical Approval

Ethical approval was obtained from the Makerere University School of Medicine Research and Ethics Committee, the University of California San Francisco Committee on Human Research, and the Uganda National Council for Science and Technology. All participants provided written informed consent.

Results

Patient characteristics

Of 2297 participants enrolled between April 11, 2011, and September 2, 2015, 1887 (82.2%) had two-month follow-up information. Of these 1887 participants, 372 (19.7%) had died by two months of follow-up; 138 (37.1%) had died during hospitalization and the median duration of hospitalization was short, 3 days (Interquartile Range, IQR, 1–5 days). The median age of study participants was 34.3 years (IQR, 28.0–43.3 years) and 978 (51.8%) were men. The majority 1192 (63.2%) were HIV-positive with a median CD4 count of 81 cells/μL (IQR 21–226 cells/μL). One-third (388/1192) of the HIV-positive participants were taking ART at admission. The median duration of cough was 4 weeks (IQR 2–10 weeks) and 1376 (72.9%) had received antibiotics prior to hospitalization. The participants with complete data had similar baseline characteristics to those who had missing data except that the former were younger, had a higher temperature and had a larger proportion of people who were bed-ridden (Supplementary Table 1).

Patient outcomes

Two hundred (10.6%) participants had severe hypoxemia with an oxygen saturation <90% while breathing room air, and 1287 (68.2%) had one or more danger signs (pulse >120/min, respiratory rate >30/min and temperature >39^{O}C) present. A total of 711 (37.7%) participants had a microbiologically confirmed diagnosis; 670 (35.5%) had TB, 26 (1.4%) had pKS, and 15 (0.8%) had *Pneumocystis* pneumonia (PcP). Of 288 patients who underwent bronchoscopy, 55 (19.1%) died during follow up. At two months of follow-up, only 388/920 (42.2%) of the HIV-positive participants were on ART. There was a significant difference among participants who died and who were alive at two months in respect to HIV serostatus, pKS and PcP diagnosis; and presence of danger signs (Table 1).

Mortality by HIV status

The HIV-positive participants differed from the HIV-negative participants. In addition to being younger, a greater proportion of HIV-seropositive participants hospitalized with LRTI were female, did not smoke, had a diagnosis of TB, had danger signs or were bed-bound compared to those who were HIV-negative (Table 2). In addition, there was a significantly higher mortality among the HIV-positive participants than the HIV-negative participants both during hospitalization (99 (8.3%) in HIV-positive versus 32 (4.6%) in HIV-negative, $p<0.0001$) and at two months of follow-up (272 (22.8%) HIV-positive versus 100 (14.4%) in HIV-negative, $p<0.0001$).

Predictors of mortality

Several baseline patient characteristics and vital signs were associated with increased two-month mortality. In the univariate analysis (Table 3), temperature <35.5ºC, temperature 37.2ºC-39^{O}C, heart rate >120/min, and respiratory rate >30/min were associated with increased mortality. In addition, oxygen saturation <90%, being bed-bound and being HIV-positive were also associated with increased mortality. In the multivariable analysis, temperature <35.5ºC (aOR=1.77, 95% CI=1.20–2.60; p=0.004), heart rate >120/min (aOR=1.82, 95% CI=1.37–2.43; p<0.0001), oxygen saturation <90% (aOR=2.74, 95% CI=1.97–3.81; p<0.0001), being bed-bound (aOR=1.88, 95% CI=1.47–2.41; p<0.0001) and being HIV-positive (aOR=1.49, 95%CI=1.14–1.94; p=0.003) were independently associated with increased mortality at two months.

Predictors of mortality by HIV status

When stratified by HIV status, participants who were HIV-seropositive had a higher odds of dying if they had a heart rate >120/min (aOR=1.54, 95% CI=1.10–2.15; p=0.01) compared to those with a heart rate ≤120/minute. Having an oxygen saturation <90% on room air was associated with twice the odds of death (aOR=2.56, 95% CI=1.71–3.84; p<0.0001) compared to oxygen saturation >90%. Participants who were bed-bound had a higher odds of death (aOR=1.48, 95% CI=1.09–2.00; p=0.01) than those who were not. Lastly, participants with CD4 counts 50–100 cells/μL had twice the odds of death (aOR=2.03, 95% CI=1.24–3.35; p=0.005) and participants with <50 cells/μL had thrice the odds of death (aOR=3.42, 95% CI=2.29–5.11; p<0.0001) than those with CD4 counts >200 cells/μL (Table 4).

For participants who were HIV-seronegative, the following variables were independently predictive of mortality: age >40 years (aOR=2.04, 95% CI=1.18–3.53; p=0.01), body temperature <35.5ºC (aOR=2.17, 95% CI=1.08–4.37; p=0.03), heart rate >120/min (aOR=2.13, 95% CI=1.16–3.92; p=0.02), oxygen saturation <90% (aOR=2.75, 95% CI=1.48–5.10; p=0.001) and being bed-bound (aOR=2.37, 95% CI=1.49–3.75; p<0.0001) (Table 5).

Mortality during and after hospitalization

The independent predictors of in-hospital mortality were heart rate >120/min (aOR=1.61, 95% CI=1.06–2.46; p=0.03), oxygen saturation <90% (aOR=3.25, 95% CI=2.12–5.00; p<0.0001) and being bed-bound (aOR=4.36, 95% CI=2.70–7.04; p<0.0001) (Supplementary Table 2). After discharge and during the post-hospitalization study period, the following predictors were independently associated with mortality: temperature >39ºC was associated with a 58% odds of reduction in mortality (aOR=0.42, 95% CI=0.19–0.92; p=0.03). Heart rate >120/minute (aOR=1.88, 95% CI=1.33–2.65; p<0.0001), oxygen saturation <90% (aOR=2.09, 95% (aOR=1.34, 95% CI=1.34–3.75; p<0.001) and being HIV-seropositive (aOR=1.49, 95%CI=1.08–2.05; p=0.015) were all independent risk factors for mortality (Supplementary Table 3).

Effect of empiric TB treatment on mortality

Of all the study participants, 1170 (62.0%) were both sputum smear negative and Xpert negative (SS- & Xpert-) for TB and 148 (12.6%) of these had positive sputum cultures for TB. Sixty-two participants (5.2%) who were SS- and Xpert- were empirically treated for TB; of these only 17 (27.4%) had culture confirmed TB at follow up. The majority of the participants (45, 73%) who were empirically treated had danger signs. At multivariable analysis, after adjusting for age, temperature, heart rate, respiratory rate, oxygen saturation, functional status, HIV serostatus, and functional status, empiric TB treatment was associated with a non-significant trend toward a reduction in mortality among participants with presumed pneumonia (aOR=1.02 95%CI=0.54–1.93; p=0.95). Of participants who were SS- and Xpert- and later had culture confirmed TB, 17/148 (11.2%) were empirically treated for TB during hospitalization. There was no difference in the two-month mortality between participants who were empirically treated during hospitalization or not (Fischer's exact, p=0.54).

Discussion

In this study of HIV-positive and HIV-negative adult patients with LRTI who underwent standardized evaluation for pneumonia and were followed for two months, we determined whether baseline patient characteristics and vital signs identified adults with pneumonia at increased risk of death within two-months of hospitalization. Despite detailed investigations to identify and appropriately treat respiratory pathogens in hospitalized patients with LRTI, mortality at two months remains high, at nearly 20%. We show that baseline patient characteristics and vital signs identified adults with LRTI at increased risk of death. Specifically, vital signs (temperature <35.5ºC, heart rate >120/min, oxygen saturation <90% on room air) and baseline characteristics (being bed-bound and HIV-positive) independently predict increased mortality within two months of hospitalization among patients with LRTI. These variables may be used to triage patients with LRTI at increased risk of death. Routinely measuring vital signs that are predictive of mortality may be useful for identifying hospitalized individuals with lower respiratory infection who are at risk of sepsis. Recently, newer scores have been derived to improve prediction of mortality in the emergency care unit and duration of ICU stay. These include the Sequential Organ Failure Assessment (SOFA) and the quick Sequential Organ Failure Assessment (qSOFA).[17] They have been principally validated in high income settings. The qSOFA uses simple clinical criteria (altered mentation, systolic blood pressure of 100 mmHg or lower or respiratory rate of at least 22 breaths per minute) and has a higher predictive value for mortality outside the ICU. Until these scores are widely validated in diverse populations in both high-income and low-income settings, early diagnosis of sepsis using easily measurable clinical parameters is important.

Second, mortality is related to hypoxemia and this has been observed in local[13,14] and regional studies[18,19]. This may be due to Acute Hypoxemic Respiratory Failure (AHRF) complicating pneumonia. AHRF has been associated with increased mortality, especially where facilities for mechanical ventilation and oxygenation are limited[19]. Similar to our study, hypoxemia was reported to be an independent predictor of the clinical severity of

pneumonia and is associated with an increased risk of death from severe sepsis[20]. When combined with validated severity-of-illness scores, hypoxemia leads to an improvement in their predictive value[21,22]. Oxygen is essential for management of patients who have severe pneumonia and are in respiratory failure. In usual care, oxygen is delivered by nasal prongs or by face mask but this may be inadequate and further management in an Intensive Care Unit (ICU) may be needed. There are very few hospitals in low income settings that have capacity to set up and efficiently run an ICU. Innovative ways of oxygen delivery to pneumonia patients outside the ICU like using Non Invasive Ventilation[23] and High Flow Nasal Cannulas[24] need to be urgently explored.

Third, advanced HIV-related immunosuppression remains an important predictor of mortality in settings with a high HIV burden. This finding is not entirely surprising because advanced HIV-related immunosuppression is associated with opportunistic diseases such as PcP and pKS which contribute to the increase in mortality due to LRTI[25,26]. Notably, only one-third of the HIV-positive participants in our study were on ART at hospitalization, a proportion that did not substantially change at two months. This shows the presence of important barriers to ART access. Most ART is provided in ambulatory settings where these patients are referred on discharge from hospital. A deliberate action to initiate these patients on ART during hospitalization or to follow up and ensure they are initiated on ART in sites to which they are referred for care is crucial.

Finally, failure to determine the cause of LRTI in the majority of study participants may contribute to the persisting high mortality due to pneumonia since many participants did not receive targeted therapy for LRTI. In addition, antimicrobial resistance (AMR) to commonly used antibiotics were not determined. There have been few studies on AMR for causative organisms for pneumonia in this setting but a recent report on AMR of isolates from blood cultures in this setting revealed high-level resistance to commonly used antibiotics[27]. This may be an additional cause of poor treatment outcomes. These should be considered in prospective studies of LRTI. Despite exhaustive testing for causes LRTI a minority of study participants have confirmed diagnoses even in settings with better resources[8,28]. Molecular testing has shown capacity to detect pathogens and resistance mutations in spite of prior antibiotic use, but these methods need to be further validated to establish proper standards for LRTI testing[28,29].

Our study had several limitations. We had a loss to follow-up of 21%, which is not unusual in a mobile urban population where patients seeking treatment at a tertiary urban centre return to their rural homes after clinical improvement or worsening. A proportion of these missing participants could have died. This could have led to an underestimate of the mortality and the predictive role of age category, a high temperature and being bed-ridden on mortality. Second, the findings of this study in a tertiary care centre can only be generalized to similar settings as these participants may represent a severely ill population not frequently found at lower levels of health care. Third, our findings are based only on parameters measured at the time of hospitalization. Kolditz, et. al. demonstrated that participants who do not have an immediate need for mechanical ventilation or vasopressor support at admission but deteriorated during hospitalization are associated with higher mortality than those who have abnormalities of vital signs at admission[30]. Additional measurement of vital

signs during hospitalization may better define the response of participants to antibiotic treatment, and better define their prognosis. Fourth, we did not measure the systolic blood pressure in all participants and were not able to assess the predictive role of this on outcomes of study participants as has been noted in the newer predictor scores[17]. Fifth, despite a better than standard work up for LRTI in a low-income setting, only 38% participants had a confirmed diagnosis for a respiratory pathogen. It was not possible to confirm presence of bacterial, viral or other pathogens using this approach. Finally, hypoxia was a major risk factor for mortality but the study was not able to provide data on the usage or availability of oxygen through out the study.

In conclusion, vital signs and some patient baseline characteristics identify hospitalized patients with LRTI at high risk of death who need urgent medical care and close monitoring. Quality improvement initiatives that promote routine collection and use of vital signs for clinical decision making and innovative techniques for oxygen delivery should be optimized for management of patients with pneumonia. Providing adequate oxygen, judicious intravenous fluids; and early antiretroviral therapy (in people living with HIV/AIDS) can be life-saving in hospitalized patients with LRTI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank the study participants for their involvement in this study. We also thank the Infectious Disease Research Collaboration, Kampala; Mulago Hospital and the Huang Lab – Serena Fong, Stephen Stone, Alisa Malki, Elizabeth Auld, Maggie McGing, Marlena Hartman-Filson, and Mathew Sommers - for their support to the study activities.

Funding Sources

NIH K24 HL087713 (LH), NIH R01 HL090335 (LH), NIH R01 HL128156 (LH)

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TABLE 1.

Population characteristics according to 2-month mortality status

Variable	Dead (n = 372)*	Alive (n = 1515)*	*p*-value
Male gender	185 (49.7)	793 (52.3)	0.37
Age	34.7 (28.5 – 44.0)	34.2 (27.7 – 43.2)	0.20
HIV category			<0.0001
no HIV	100 (26.9)	595 (39.3)	
HIV, ARV	78 (21.0)	310 (20.5)	
HIV, no ARV	194 (52.2)	610 (40.3)	
Ever smoke	95 (25.5)	388 (25.6)	0.98
Prior antibiotic use	276 (74.2)	1100 (72.6)	0.54
TB-positive (n = 1393)	123 (49.2)	547 (47.9)	0.70
Empiric TB (n = 1170)	15 (6.5)	47 (5.0)	0.38
PcP (n = 302)	6 (11.1)	9 (3.6)	0.02
pKS (n = 302)	13 (24.1)	13 (5.2)	<0.0001
Danger signs present	313 (84.1)	974 (64.3)	<0.0001
Body temperature			<0.0001
Normal (35.5^{O}C - 37.2^{O}C)	161 (43.3)	853 (56.3)	
Low (<35.5^{O}C)	44 (11.8)	141 (9.3)	
High (37.2^{O}C - 39^{O}C)	147 (39.5)	454 (30.0)	
Very High (>39^{O}C)	20 (5.4)	67 (4.4)	
High heart rate (>120)	140 (37.6)	301 (19.9)	<0.0001
High respiratory rate (>30)	185 (49.7)	515 (34.0)	<0.0001
Hypoxemia (O_2 sat < 90%)	86 (23.1)	114 (7.5)	<0.0001
Bed bound	252 (67.7)	697 (46.0)	<0.0001
CD4 category (n = 1881)			<0.0001
HIV negative	100 (27.0)	595 (39.4)	
CD4 >= 200	34 (9.2)	298 (19.7)	
CD4 < 200	236 (63.8)	618 (40.9)	

* Presented as either n (%) or Median (P25 - P75)

Abbreviations: HIV, Human Immunodeficiency Virus; ARV, Antiretroviral Therapy; TB, Tuberculosis; PcP, Pneumocystis Pneumonia; pKS, Pulmonary Kaposi's Sarcoma; O_2, Oxygen Saturation; CD4, cluster of differentiation 4. Danger signs refer to at least one of the following: respiratory rate>30/minute, heart rate >120/minute, fever>39°C or inability to walk unaided.

TABLE 2.

Population characteristics according to HIV status

Variable	HIV (n = 1192)*	no HIV (n = 695)*	*p*-value
Male gender	530 (44.5)	448 (64.5)	<0.0001
Age	34 (28.6 – 40.8)	35.2 (26.0 – 50.3)	0.02
Ever smoke	274 (23.0)	209 (30.1)	<0.0001
TB-positive (n = 1393)	449 (50.6)	221 (43.8)	0.01
Empiric TB (n = 1170)	46 (6.5)	16 (3.4)	0.02
Danger signs present	885 (74.2)	402 (57.8)	<0.0001
Body temperature			<0.0001
Normal (35.5^{o}C - 37.2^{o}C)	590 (49.5)	424 (61)	
Low (<35.5^{o}C)	121 (10.2)	64 (9.2)	
High (37.2^{o}C - 39^{o}C)	405 (34.0)	196 (28.2)	
Very High (>39^{o}C)	76 (6.4)	11 (1.6)	
High heart rate (>120/min)	337 (28.3)	104 (15.0)	<0.0001
High respiratory rate (>30/min)	494 (41.4)	206 (29.6)	<0.0001
Hypoxemia (O_2 sat < 90%)	136 (11.4)	64 (9.2)	0.13
Bed bound	661 (55.5)	288 (41.4)	<0.0001
Death at discharge	99 (8.3)	32 (4.6)	<0.0001
Death in 2 months	272 (22.8)	100 (14.4)	<0.0001
HIV-only variables			
On ARV	388 (32.6)		
CD4 count (n = 1186)	80.5 (21.0 – 225.8)		
PcP (n = 302)	15 (5.0)		
pKS (n = 302)	26 (8.6)		

*Presented as either n (%) or Median (P25 - P75)

Abbreviations: HIV, Human Immunodeficiency Virus; ARV, Antiretroviral Therapy; TB, Tuberculosis; PcP, Pneumocystis Pneumonia; pKS, Pulmonary Kaposi's Sarcoma; O_2 sat, Oxygen Saturation; CD4, cluster of differentiation 4. Danger signs refer to at least one of the following: respiratory rate>30/minute, heart rate >120/minute, fever>39°C or inability to walk unaided.

TABLE 3.

Multivariate analysis for 2-month mortality status

Variable	Unadjusted OR	95% CI	*p*-value	Adjusted OR	95% CI	*p*-value
Age (vs. 18–29 years)						
30–39	1.17	(0.89, 1.54)	0.26	1.09	(0.81,1.45)	0.58
>40	1.11	(0.84, 1.46)	0.48	1.24	(0.92, 1.68)	0.16
Body temperature (vs. Normal)						
Low (<35.5^{o}C)	1.70	(1.17, 2.47)	0.005	**1.77**	**(1.20, 2.60)**	**0.004**
High (37.2^{o}C - 39^{o}C)	1.77	(1.38, 2.27)	<0.0001	1.25	(0.95, 1.64)	0.10
Very High (>39^{o}C)	1.64	(0.97, 2.75)	0.062	0.81	(0.46, 1.42)	0.46
High heart rate (>120)	2.38	(1.86, 3.03)	<0.0001	**1.82**	**(1.37, 2.43)**	**<0.0001**
High respiratory rate (>30)	1.81	(1.44, 2.27)	<0.0001	1.16	(0.90, 1.50)	0.24
Hypoxemia (O_2 sat < 90%)	3.66	(2.70, 5.97)	<0.0001	**2.74**	**(1.97, 3.81)**	**<0.0001**
Bed bound	2.40	(1.89, 3.03)	<0.0001	**1.88**	**(1.47, 2.41)**	**<0.0001**
HIV seropositive (vs. HIV-)	1.76	(1.37, 2.26)	<0.0001	**1.49**	**(1.14, 1.94)**	**0.003**

Abbreviations: OR, Odds Ratio; HIV, Human Immunodeficiency Virus; O_2, Oxygen Saturation

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TABLE 4.

Multivariate analysis for 2-month mortality status for patients who were HIV seropositive

Variable	Unadjusted OR	95% CI	*p*-value	Adjusted OR	95% CI	*p*-value
Age (vs. 18–29 years)						
30–39	0.97	(0.71, 1.33)	0.84	1.00	(0.71,1.40)	0.99
>40	0.91	(0.64, 1.29)	0.59	1.06	(0.72, 1.55)	0.77
Body temperature (vs. Normal)						
Low (<35.5^{o}C)	1.44	(0.92, 2.28)	0.11	1.32	(0.82, 2.13)	0.25
High (37.2^{o}C - 39^{o}C)	1.57	(1.17, 2.11)	<0.003	1.10	(0.80, 1.53)	0.55
Very High (>39^{o}C)	1.24	(0.70, 2.19)	0.45	0.62	(0.33, 1.17)	0.14
High heart rate (>120)	2.00	(1.51, 2.66)	<0.0001	**1.54**	**(1.10, 2.15)**	**0.01**
High respiratory rate (>30)	1.58	(1.21, 2.06)	0.001	1.11	(0.82, 1.52)	0.47
Hypoxemia (O_2 sat < 90%)	3.18	(2.20, 4.60)	<0.0001	**2.56**	**(1.71, 3.84)**	**<0.0001**
Bed bound	2.01	(1.51, 2.66)	<0.0001	**1.48**	**(1.09, 2.00)**	**0.01**
CD4 count (vs. >200 cells/μL)						
100–200	1.67	(1.02, 2.73)	0.04	1.51	(0.91, 2.50)	0.11
50–100	2.62	(1.52, 4.24)	<0.0001	**2.03**	**(1.24, 3.35)**	**0.005**
<50	4.18	(2.84, 6.15)	<0.0001	**3.42**	**(2.29, 5.11)**	**<0.0001**

Abbreviations: OR, Odds Ratio; O_2, Oxygen Saturation; HIV, Human Immunodeficiency Virus; CD4, cluster of differentiation 4.

TABLE 5.

Multivariate analysis for 2-month mortality status for patients who were HIV negative

Variable	Unadjusted OR	95% CI	*p*-value	Adjusted OR	95% CI	*p*-value
Age (vs. 18–29 years)						
30–39	1.37	(0.76, 2.46)	0.289	1.41	(0.75,2.65)	0.28
>40	1.77	(1.08, 2.90)	0.02	**2.04**	**(1.18, 3.53)**	**0.01**
Body temperature (vs. Normal)						
Low (<35.5^{o}C)	2.25	(1.15, 4.37)	0.02	**2.17**	**(1.08, 4.37)**	**0.03**
High (37.2^{o}C - 39^{o}C)	2.06	(1.30, 3.26)	0.002	1.48	(0.89, 2.49)	0.13
Very High (>39^{o}C)	3.00	(0.77, 11.73)	0.11	1.66	(0.37, 7.52)	0.51
High heart rate (>120)	3.01	(1.85, 4.90)	<0.0001	**2.13**	**(1.16, 3.92)**	**0.02**
High respiratory rate (>30)	2.14	(1.39, 3.28)	<0.0001	1.31	(0.80, 2.13)	0.28
Hypoxemia (O_2 sat < 90%)	4.85	(2.79, 8.43)	<0.0001	**2.75**	**(1.48, 5.10)**	**0.001**
Bed bound	3.03	(1.96, 4.68)	<0.0001	**2.37**	**(1.49, 3.75)**	**<0.0001**

Abbreviations: OR, Odds Ratio; HIV, Human Immunodeficiency Virus; O_2, Oxygen Saturation

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