Fighting adult mortality through etiology of fever studies: Description of high mortality in an adult inpatient population in Mozambique





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During the study period, a total of 792 teenage (>15 yo) and adult patients were

recruited (445 (56,1%) outpatients, 347 (43,8%) inpatients). 92 died within the

Age (years)

first 28 days of recruitment, yielding a case fatality rate of 11.6%.

438 (98%)

7 (1.6%)

186 (42%)

252 (57%)

3 (0.7%)

4 (0.9%)

Background

Fever is a common symptom leading to health care seeking and hospital admission in Africa. Mortality rates in febrile adult inpatients in Mozambique are high and are associated with high underlying prevalence of co-morbidities like HIV and cardiovascular diseases, and delays in care-seeking. Better characterization of febrile teenage and adult patients in terms of clinical presentation, diagnostic laboratory findings, and outcomes may be important for a more evidence-based evaluation of current clinical management algorithms, with the aim of decreasing preventable mortality.

Methods

The observational study "FIEBRE: Febrile illness evaluation in a broad range of endemicities" recruited febrile patients in Mozambique, Zimbabwe, Malawi and Lao PDR to identify infectious causes of fever and antimicrobial susceptibility of bacterial pathogens. Comprehensive clinical and laboratory testing was conducted, including local and centralised analyses in reference laboratories.

We hereby present mortality data from adult Mozambican outpatients and inpatients (Jan 2019-Feb 2021) at Manhiça District Hospital, Mozambique.

- Patients presenting with fever were enrolled and provided clinical data, pharyngeal swabs and a venous blood sample; selected participants also provided a urine sample (those who had urinary symptoms and all HIV positive).
- Laboratory assessments target infections that are treatable and/or preventable.
- Selected point-of-care tests (POCT) [urine dipstick, malaria and HIV testing, serum cryptococcal antigen (CrAg) and urine lipoarabinomannan (uLAM), as well as blood and urine cultures and antimicrobial susceptibility testing, were performed on site.
- On day 28, patients provided a second venous blood sample for serology and information on clinical outcomes.

Further diagnostic assays were performed at international reference Laboratories including:

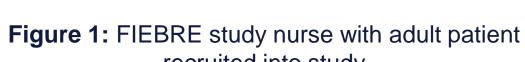
 blood parasites; bacterial, mycobacterial and fungal bloodstream infections; typhus group and spotted fever group Rickettsia spp; Orientia tsutsugamushi; Coxiella burnetii; Leptospira spp; Brucella spp; Borrelia spp that cause relapsing fever; Leishmania spp; and arboviruses (1)

(1)- Hopkins H, Bassat Q, Chandler CIR, et al. Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE):

protocol for a multisite prospective observational study of the causes of fever in Africa and Asia. BMJ Open

Results

Table 1: Adult Study Population, by site Variable N = 347N = 445Age (years) 38.0 (29.0, 52.0) 31.0 (24.0, 41.0) 16.0-90.0 17.0-76.0 Age group, n (%) 15 - <25 53 (15%) 123 (28%) 25 - <35 84 (24%) 135 (30%) 35 - <40 90 (26%) 99 (22%) 45 (13%) 45 - <55 46 (10%) 55 - <65 47 (14%) 28 (6.3%) 65+ 28 (8.1%) 14 (3.1%) Gender, n (%) 192 (55%) 335 (75%) Female 155 (45%) 110 (25%) Temperature (°C) Median (IQR) 38.2 (37.8, 38.9) 38.0 (37.7, 38.4) Range 37.5, 41.0 37.5, 40.5 Day 28 outcome



262 (76%)

85 (24%)

187 (54%)

153 (44%)

4 (1.2%)

3 (0.9%)

Dead

HIV status, n (%)

Positive

Negative

Unknown

Indeterminate



Median (IQR) 41.0 (33.0, 34.0 (25.0, 35.0 (26.0, 20.0, 86.0 16.0, 90.0 16.0, 90.0 Age group, n (%) 15 - <25 6 (3.4%) 176 (100%) 25 - <35 197 (90%) 22 (10%) 219 (100%) 35 - <40 162 (86%) 27 (14%) 189 (100%) 45 - <55 10 (11%) 91 (100%) 75 (100%) 55 - <65 17 (23%) 58 (77%) 65+ 32 (76%) 10 (24%) 42 (100%) Gender, n (%) 527 (100%) Female 481 (91%) Male 265 (100%) 219 (83%) 46 (17%) Patient group, n (%) 347 (100%) 262 (76%) 85 (24%) Outpatient 445 (100%) 438 (98%) 7 (1.6%) Temperature (°C) Median (IQR) 38.0 (37.7, 38.0 (37.7 38.2 (37.9, 37.5, 41.0 37.5, 41.0 Range 37.5, 40.6 HIV status, n (%) 57 (15%) 373 (100%) 316 (85%) Positive 373 (92%) 32 (7.9%) 405 (100%) 7 (100%) 2 (29%) Unknown 5 (71%) 1 (14%) 7 (100%) Indeterminate 6 (86%) HIV result POCT, n (%) 6 (86%) 1 (14%) 7 (100%) 370 (100%) 28 (7.6%) 342 (92%) 113 (100%) 89 (79%) 24 (21%) 263 (Missing) 302 Malaria POCT, n (%) 5 (100%) 2 (40%) 3 (60%) 724 (100%) 637 (88% 63 (100%) 2 (3.2%) 61 (97%) CrAg POCT, n (%) 53 (100%) 43 (81%) 10 (19%) 466 (100%) 75 (16%) 391 (84%) 5 (83%) 6 (100%) 1 (17%) (Missing) 261 uLAM POCT, n (%) 2 (100%) 2 (100%) indeterminate 249 (100%) 27 (11%) 222 (89%) negative 20 (87%) 3 (13%) 23 (100%) positive (Missing) Diabetes, n (%) 383 (87%) 59 (13%) 442 (100%) Unknown 28 (8.5%) 328 (100%) 300 (91%) 17 (77%) 5 (23%) 22 (100%) Sickle cell, n (%) 686 (100%) 71 (10%) 615 (90%) 21 (100%) **Unknowr** 18 (21%) 67 (79%) 85 (100%) Blood culture results, n

Table 2: Demographic and clinical characteristics of patients by day

28 outcome

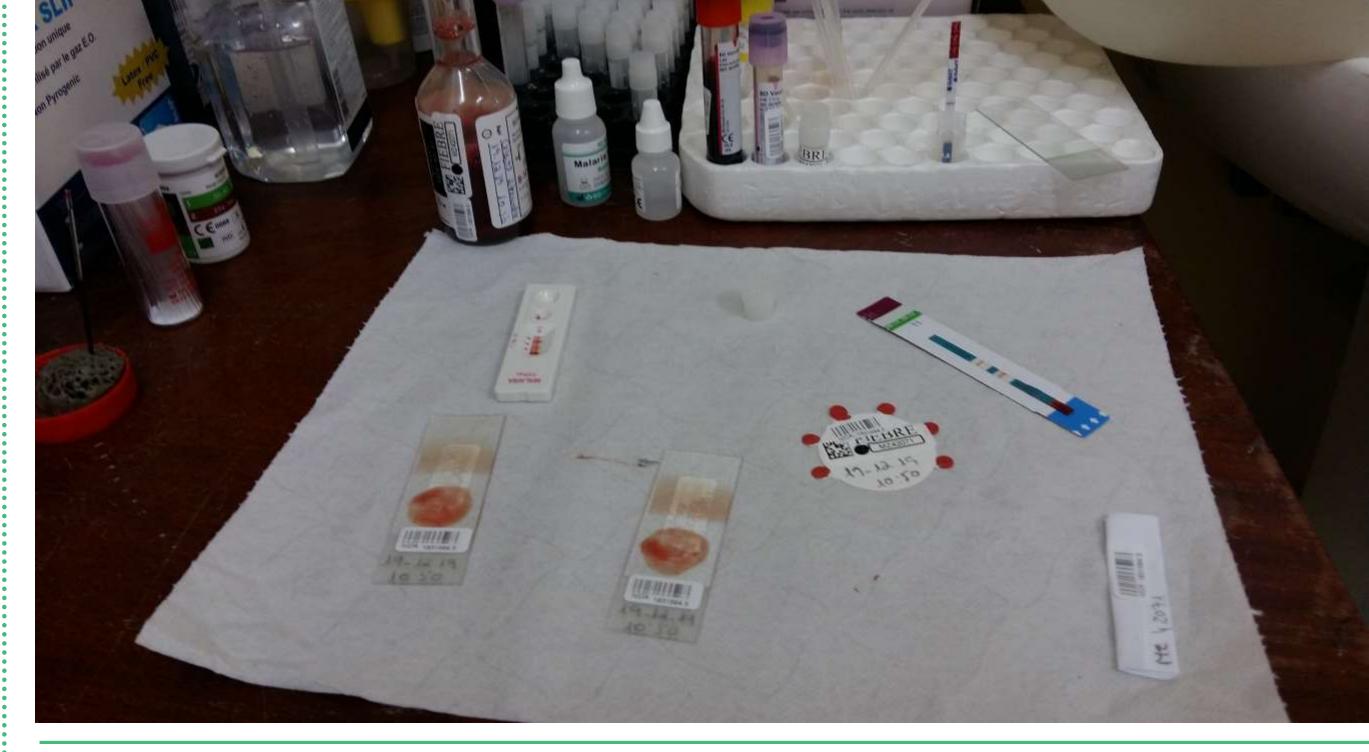
N = 92

N= 700

Overall

N = 792





Discussion and conclusions

- The FIEBRE multi-site study will provide an invaluable set of data on febrile illness across Africa and Asia
- Mortality among adult Mozambican inpatients with febrile illness remains unacceptably high
- Malaria plays an important role in febrile illness, but a minor role in terms of teenager and adult mortality
- Tuberculosis remains highly prevalent as a cause of febrile illness in this population, but with low short-term associated mortality
- Cryptococcal invasive diseases affected ~1% of patients in this population with very high prevalence of HIV (47%)
- Invasive bacterial infections were detected in 6.6% of patients, with a high associated mortality. However, the low yield of a single blood culture may have led to an important underestimate of the real burden
- HIV infection significantly increased the risk of dying among our febrile patients (p<0.001)
- Most deaths were related to preventable and treatable opportunistic infections in the context of underlying HIV infection
- Comprehensive strategies to address HIV infection at all stages (prevention, diagnosis and treatment) are needed to decrease mortality.
- While awaiting final centralized diagnostic results from reference laboratories, local laboratory results already reveal a number of causes of preventable deaths
- The detailed analysis of all patient's results will provide a roadmap upon which to base policy change to improve the management of fever in teenagers and adults, and ultimately increase their survival

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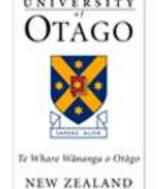






contaminated

(Missing)



10 (67%)

594 (92%)

43 (83%)



15 (100%)

646 (100%)

52 (100%)

5 (33%)

52 (8.0%)

9 (17%)

