Prevalence of asymptomatic *Leishmania* infection in HIV-positive people and progression to symptomatic visceral leishmaniasis in Bihar, India

*Raman Mahajan[1], Sophie Owen[2], Shiril Kumar[3], Shahwar Kazmi[4], Pradeep Das[3], Krishna Pandey[3], Neena Verma[3], Vikash Kumar[1], Amit Harshana[1], Estrella Lasry[5], Laura Moretó Planas[5], Emily Adams[2], **Sakib Burza**[1]

[1]Médecins Sans Frontières (MSF), New Delhi, India; [2]Liverpool School of Tropical Medicine, Liverpool, UK; [3]Rajendra Memorial Research Institute of Medical Sciences, Patna, India; [4]MSF, Patna, India; [5]MSF, Barcelona, Spain

*msfe-delhi-epidem@barcelona.msf.org

Introduction

People coinfected with visceral leishmaniasis and HIV (VL-HIV) typically present with advanced HIV disease and in poor clinical condition. The reasons for this are complex, but one major challenge relates to difficulties in ensuring early diagnosis of VL, a stage IV opportunistic infection, in the context of HIV. In VL-endemic areas, it is recognised that between 2 and 20% of the general population may harbour asymptomatic *Leishmania* infection (ALI), the vast majority of whom will not progress to symptomatic disease. However, similar data are absent for people living with HIV (PLHIV) in South Asia. Being able to diagnose ALI may provide a screen-and-treat opportunity to prevent progression to the fatal symptomatic form. We investigated the prevalence and determinants of ALI in PLHIV living in VL-endemic areas, and the risk of progression to symptomatic VL.

Methods

We conducted a cross-sectional survey, enrolling PLHIV aged ≥18 with no diagnosis of or history of leishmaniasis symptoms, at three antiretroviral therapy centres within VL-endemic regions of Bihar, India. ALI was defined as a positive rK39 enzyme-linked immunosorbent assay (ELISA), rK39 rapid diagnostic test (RDT), and/or quantitative polymerase chain reaction (qPCR) result on blood. In addition, we tested for the *Leishmania* antigen in urine using ELISA as a novel non-invasive alternative. Participants were followed up at three-monthly intervals over 18 months to assess status and progression to symptomatic infection.

Ethics

This study was approved by the ethics boards of the Rajendra Memorial Research Institute of Medical Sciences, Patna, India, and Liverpool School of Tropical Medicine, UK, and the MSF Ethics Review Board. Clinical Trial Registry-India number, CTRI/2017/03/008120.

Results

1,296 PLHIV were included in the analysis. The baseline prevalence of ALI was 7.4% (n=96). All were found positive using rK39 ELISA, while 0.5% (n=6) and 0.4% (n=5) were positive using qPCR and rK39 RDT, respectively. 2.2% (n=28) patients were positive using urinary *Leishmania* antigen ELISA testing. Independent risk factors ($p<0.05$) for ALI were CD4 count <100 cells/mm^3 (adjusted odds ratio, aOR, 3.1; 95%CI 1.2-7.6), and CD4 count between 100-199 cells/mm^3 (aOR=2.1; 95%CI 1.1-4.0), as compared to CD4 ≥300 cells/mm^3 and living in a household size ≥5 (aOR=1.8; 95%CI 1.1-3.2). Concordance between diagnostic tests was poor. A total of 109 asymptomatic patients were followed up prospectively, including 13 additional patients who were identified during pilot testing. Overall, 3.7% (n=4) patients converted from asymptomatic to symptomatic infection over the study period. Conversion rates of participants identified as positive using rK39 ELISA, rK39 RDT, qPCR, and urinary *Leishmania* antigen ELISA, were 3.7% (4/109), 40% (2/5), 57% (4/7), and 14% (4/29), respectively. Risk of all-cause mortality in those with ALI over 18 months' follow-up was 6.4% (n=7), compared with 2.5% (n=30) in those without (risk ratio, 2.6, 95%CI 1.2-5.7, p=0.018).

Conclusion

PLHIV living in highly VL-endemic areas have a relatively high prevalence of ALI. Although progression rates to symptomatic infection appear low, all-cause mortality rates are higher and may reflect the impact of sub-clinical infection on HIV outcomes. The results may justify further studies investigating early treatment of ALI in PLHIV.

Conflicts of interest

None declared.

Sakib Burza

Sakib is a practicing clinician who first started working with MSF in 2003. He completed a MSc in public health in developing countries at the London School of Hygiene and Tropical Medicine (LSHTM), and returned to work on diagnostic algorithms for neglected tropical diseases (NTD's). Sakib completed his PhD on the clinical management of visceral leishmaniasis at the Institute of Tropical Medicine, University of Antwerp under the late, great Prof Marleen Boelaert. Since February 2016 Sakib has been working as Medical Advisor, Asia for MSF Spain, and holds an honorary position at the LSHTM as an Associate Professor. He has long-standing interests in the clinical aspects of leishmaniasis, and also NTD's in general. He has also conducted research in severe acute malnutrition, dengue, and advanced HIV. More recently, Sakib has been working on prognostic biomarkers in sepsis and COVID-19. He is also interested in melioidosis too, and is perpetually trying to get MSF interested in it.