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Bacterial sepsis in patients with visceral leishmaniasis in Northwest Ethiopia

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Background: Sepsis isone of the major predictor of death in patients with visceral leishmaniasis(VL).However, there are currently no reliable data available on bacterial sepsis in VL patients in Ethiopia. This study aimed to assess the prevalence of bacterial sepsis, causative agents and their antimicrobial susceptibility patterns and focus of infection in patients with VL.

Methods & Materials: A prospective cross sectional study was conducted among parasitologically confirmed VL patients suspected of sepsis admitted to University of Gondar Hospital, Northwest Ethiopia from February 2012 to May 2012.Socio-demographic characteristics and clinical manifestations were documented after patient interview and physical examination. Samples (blood, urine and others as indicated) were collected and culturedusing standard methods.Isolates were tested for antimicrobial susceptibility using the disc diffusionmethod.Data were entered and analyzed using SPSS version 20.

Results: Most of the patients 81 (97.6%), 67 (80.7%), 75 (90.4%), 80 (96.4%) were febrile, tachycardic, tachypnic, and leukopenic, respectively. The prevalence of culture confirmed bacterial sepsis was 19.3% (16/83). The most frequently isolated organism was *Staphylococcus aureus*, accounting for 11/16 (68.8%) of cases. There was a concordance rate of 11/12 (91.6%) between bacterial isolates and their susceptibility pattern between focal infections and blood stream infections. The overall multiple resistance was 13/16 (81.3%). The highest rate of resistance was for ampicillin 11/11 (100%), and two were MRSA. Vancomycin, gentamicin and ceftriaxone were found to be effective against most isolates. Focal bacterial infection was showed significant association with bacterial sepsis (P = 0.00; Odds ratio = 11.65; 95% confidence interval 4.29-31.60). Factors such as sex, age, HIV status, < 200 CD4 count, anemia, leucopenia, malnutritionand > 72 hour hospital staywere not associatedwith bacterial sepsis.

Conclusion: The prevalence of culture confirmed bacterial sepsis was high, multiple drug resistant *Staphylococcus aureus* being the frequent isolate. Focal bacterial infections are potential sources for bacterial sepsis among VL patients. Therefore, clinicians should give emphasis to treat VL patients with focal bacterial infection before developing to sepsis. Rational use of antibiotics should be practiced in order to minimize the spread of drug resistant bacteria.

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RNA-Seq reveals strain-specific immune gene expression by epithelial cells infected with *Mycobacterium tuberculosis* strains of varying pathogenicity

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Background: An insight into host mechanisms, genes and pathways, at the molecular level, is essential for our understanding of the host immune response to infection, especially with different strains of *M. tuberculosis.* Therefore, this study was undertaken in order to gain a better understanding of differential and strain specific immune responses of epithelial cells during infection by *Mycobacterium tuberculosis* strains of varying pathogenicity.

Methods & Materials: Transcriptomics was used to investigate changes in gene expression of immune related genes by directly sequencing RNA transcripts from pulmonary epithelial cells infected with strains belonging to four different genotypes and a Unique strain of *M. tuberculosis* associated with drug resistance in KwaZulu-Natal. RNA was extracted from infected and uninfected epithelial cells at 48 hr after infection. The Illumina HiSeq 2000 platform was used to sequence 50 bp reads that were mapped to the human genome (hg19) using Tophat (2.0.10). Differential expression between the uninfected and infected cells, as well as among the different strains, was quantified using Cufflinks (2.1.0).

Results: Enrichment analysis revealed differential expression of a varying number of immune-related genes by the different strains: F15/LAM4/KZN (KZN) (450), Beijing (319), F11 (422), F28 (325), Unique (334) and H37Rv (383). All strains induced 178 immune related genes in common at different levels. These included surface receptors (TLRs), interleukins, cell differentiation markers and genes involved in signalling pathways for cytokine production and immune response pathways. Additionally, changes were induced in a number of immune related genes distinct for the different strains: KZN (49), Unique (34), H37Rv (16), F11 (14), F28 (3), Beijing (0).

Conclusion: The highly virulent Beijing strain failed to induce genes specific to its genotype in contrast to other strains. The KZN strain displayed the highest number of genotype-specific immune related genes compared to the others. Strain-specific gene expression signature patterns during infection by different strains of *M. tuberculosis* may reflect varying pathogenicity and represent potential biomarkers that can be exploited for vaccine development. However, this will need to be confirmed *in vivo*.

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