Challenges in the Diagnosis of Visceral Leishmaniasis in Sudan

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Editorial

Diagnosis of visceral leishmaniasis (VL) constitutes a major health problem in poor communities in developing countries with limited resources such as Sudan. An important challenge of the control of the disease is the absence of accurate diagnostic tests suitable for the field. Despite the development of new diagnostic tests for detection of VL that proved to be extremely useful, the existing tests reveal discrepant diagnostic outcome. The variable performance of these tests in various endemic regions has prompted research to focus on the genetic and geographic differences between *Leishmania* parasites that might influence the success of the conventional diagnostic tests. In this editorial we focused on challenges for laboratory diagnosis of VL in Sudan regarding availability of accurate diagnostic tests for field application.

Sudan is one of the six VL-endemic countries that contribute to about 90% of global VL cases.[1] In these countries, the disease affects poor communities in remote rural areas where many patients have no access to diagnosis and standard treatment services and can remain unrecognised by health authorities. The armed conflicts, over last decades, have caused serious environmental changes such as widespread destruction of houses and health infrastructures that resulted in less accessibility to health care facilities. This problem may have also been contributed to the re-emerge of the disease in areas after being absent for decades. Since 2006, cases of VL have been reported in White Nile State, Central Sudan, close to Khartoum.[2]

Highly sensitive tools are therefore badly needed in order to replace the low sensitive currently used for VL diagnosis. In 2013, we published a novel recombinant protein (rKLO8) of L. donovani from Sudan of diagnostic importance for VL.[3] The coding sequence of rKLO8 contains a conserved tandem repeat, which are targets of immune responses. Since immunodominant epitopes of *Leishmania* antigens from different regions are markedly variable,[3] it can be expected that antigenic variation will influence antibody reactivity in different regions. This explains why rK39 is less reliable in diagnosis of the disease in countries like Sudan. Antigenic variation due to diversity of L. donovani sub-species has been proposed by others to be the cause for the low sensitivity in VL diagnosis based on rK39.[4,5] Although several tests have been developed and evaluated in the Sudan, determining of which assay that most complies with the desired criteria remained unresolved. Since 1999, our laboratory at Ahfad University for Women in Omdurman has started production of a liquid DAT version used for diagnosing VL in referred cases. Several improvements have been introduced thereafter to this locally produced DAT version in order to maintain its stability under rural conditions and to overcome problems related to lack of or inaccessibility to reference diagnostics such the freeze-dried DAT or the rK39 rapid test. These two last

mentioned reference tests have however been experienced as being either expensive to import or vulnerable to cope with the ambient temperatures.[6]

Among other challenges for VL diagnosis in Sudan is that in some patients, weak antibody response may occur in the case of co-infection with diseases other than VL or in malnutrition.[4] Such patients usually have reduced immune responses and may therefore reveal false negative results. Prevalence of malaria and other diseases is common in areas that are also known to be endemic for VL. Therefore in addition to having high sensitivity, tests for VL diagnosis need to be discriminative to pathogens causing clinical symptoms assimilating VL. Based on our previous studies[3,7,8] sera of malaria don't crosses react with serological tests of *Leishmania*, a finding that has been previously shown[9,10] and thought to be due to the homology of *Leishmania* proteins and proteins of other prokaryote. Nevertheless, results with low antibody outcome should always be interpreted with caution and decisions for re-testing of individuals with initial positive result should remain as an option.

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