Abstract

Leishmaniasis, a protozoan infection caused by *Leishmania* parasites is a neglected disease affecting millions across the world. It is exhibited by diverse clinical presentations that broadly classified as visceral (VL) and cutaneous (CL) leishmaniasis. Both CL and VL are endemic to Ethiopia, which the later is generally considered as fatal, if left untreated. *Leishmania donovani* is the sole agent of Ethiopian human VL. In Africa, the worst VL affected regions are found in Sudan and Ethiopia. VL is considered as an endemic and at the same time emerging disease in north, northwest, south and southwest with sporadic cases in Eastern Ethiopia. The epidemiology is more or less associated with seasonal migration to endemic areas and HIV/AIDS. The transmission of CL in Ethiopia is known to involve zoonotic cycle while VL transmission isn't clearly understood despite traditional generalization of anthroponosis in East African platform.

The aim of this dissertation is to determine VL transmission cycle and study variability *L. donovani* and *P. orientalis* in Ethiopia. Studies on human and non-human hosts were conducted to determine the transmission dynamics. To assess the role of symptomatic and asymptomatic *L. donovani* infected persons in the epidemiology of VL, a community based cohort was conducted. As the study is ongoing, in-depth analysis of more data will accrue and in this thesis, result from protocol validation study is presented. Of 4,757 dried-blood samples tested by qRT-PCR, 680 samples (14.3%) had *Leishmania* kDNA and ITS1 sequences revealed 19 *L. donovani* and two *L. major* infections. To assess the involvement of non-human hosts, studies on domestic animals, rodents and bats were conducted. A total of 546 domestic animals (cow, dog, sheep, goat, donkey and camels) were tested for natural infection and 32 animals were positive on *L. donovani* DNA. Moreover, 19 % and 23% of the animals were seropositive for anti-*L. donovani* IgG and anti-*P. orientalis* saliva IgG respectively. A total of 586 rodents were tested by PCR. Fifty *Leishmania* kDNA positives were found and further ITS1 sequence revealed five *L. donovani* and five *L. tropica* infected animals. To investigate sylvatic involvement, 163 bat's DNA was tested and revealed eight kDNA positive; of which two were *L. tropica* and *L. major* positive through ITS1 sequences. Variability study on *L. donovani* isolates were performed using ITS1, cpb and k26 locus. The k26 target divide isolates in to two clusters: southern and northern Ethiopia based on the amplicon size. To identify the variability, if any, between *P. orientalis* colonies originating from different geographical locations, their biology, susceptibility to *Leishmania* infection and genetic profile were assessed. Despite variability on a few biological cues no significant genetic and susceptibility pattern difference was observed.

Generally this dissertation provides a new insight on the role of non-human host in VL epidemiology and existence of variability in the parasite between geography despite no difference in its respective vector was seen. Further studies in determining the level of infection through parasite isolation and xenodiagnosis is recommended for a better understanding of the animal's role in the *Leishmania* transmission. Moreover, the existence of polymorphism on the parasite population is evident and further action on the role of this tropism on transmission cycle and other phenotypic profiles needs to be investigated.