LEISHMANIA RNA VIRUS 1 AFFECTS PARASITE PROLIFERATION AND GENE EXPRESSION IN TEGUMENTARY LEISHMANIASIS PATIENTS

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Leishmania RNA Virus (LRV) has been associated with unfavorable clinical outcomes in infections with different *Leishmania* species. LRV1 is present in some species of the subgenus *Leishmania* (*Viannia*) and promotes an ineffective immune response in the infected host. Consequently, it leads to parasite persistence and is associated with the risk of developing mucosal leishmaniasis and cases of therapeutic failure when conventional treatment. We investigated the impact of LRV1 in samples from patients with tegumentary leishmaniasis (TL), its influence on the parasite load, and the expression of human genes of the immune response and *Leishmania* genes involved in the virulence of the parasite. We employed conventional PCR and qPCR to detect and quantify *Leishmania* and LRV1 loads, respectively, and used a large-scale qPCR assay (Fluidigm®) to analyze human and *Leishmania* gene expression in 96 clinical samples. Our main results highlight an association between LRV1 presence and samples with high parasite load ($p = 0.0016$). Gene expression analysis revealed that some human genes (IL21, IL12, NLRP3, and CASP1) and *Leishmania* genes (PRX and MAPK) were more expressed in samples from patients with low parasite load. The higher frequency of LRV1+ samples with a high parasite load suggests that the viral endosymbiont may promote increased parasite replication. When comparing LRV1+ and LRV1- samples, we identified distinct patterns of *Leishmania* gene expression: HSP60 and THIOL were more expressed in the LRV1+ group, while TRYR, GSH, PRX, and MAPK were overexpressed in the LRV1- group. Notably, the most expressed human genes are involved in critical signaling pathway of the immune response against infection, where the *Leishmania* genes appear to be linked to the mechanisms of resistance to host cell oxidative stress, potentially aiding the parasite in evading the immune defenses.

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