

Cutaneous leishmaniasis (CL) cases have drastically increased due to civil unrest in the Middle East. CL outbreaks among refugee populations stress the need for effective disease diagnosis in conflict settings. Current molecular diagnostics do not have applicability within resource-stretched areas. We sought to identify CL-specific biomarkers to create more sensitive screening tools. *Leishmania major* and *L. tropica* are the two etiologic agents of CL in the Middle East. *L. major* has a plasma membrane containing glycoconjugates that contain alpha-galactosyl residues, which are highly immunogenic to humans. The role of the anti-alpha-Gal Abs in *L. major* infection remains elusive. We found that patients from Saudi Arabia with active CL infections can mount an IgG response to alpha-Gal-containing epitopes. However, the precise nature of these epitopes remains unknown. Using a panel of novel neoglycoproteins that contain alpha-galactosyl epitopes, we screened three patient groups: patients infected with *L. major* or *L. tropica*, patients that are cured, and patients that had other skin disorders mimicking CL. We show that patients with active CL have significantly higher IgG titres to specific alpha-Gal-containing NGPs compared to the cured and heterologous control patients. These results demonstrate that several alpha-Gal NGPs can act as CL biomarkers and be used for disease screening.