

coleta de dados clínicos. A genotipagem foi feita por qPCR usando o sistema de sondas TaqMan e a análise estatística foi feita pelo software SPSS Statistics 19.0. **Resultados e discussão:** Com base na velocidade do fluxo sanguíneo cerebral medida pelo DTC, os pacientes foram agrupados em: DTC normal (155 pacientes; 64,8%), DTC condicionante (56 pacientes; 23,5%) e DTC alto risco (28 pacientes; 10,4%). A distribuição genotípica encontrada para o polimorfismo rs489347 foi como se segue: 65,5% para o genótipo CC (homozigoto selvagem), 25,9% para o genótipo heterozigoto CG e 8,5% para o genótipo homozigoto variante GG. A taxa de ocorrência de AVE no grupo analisado foi 6,6% (18 pacientes) com mediana de idade de 06 anos (01- 10 anos). Quando comparado com o DTC, o polimorfismo não mostrou associação significativa: $p=0,181$. Quanto à associação com AVE e DCV, também não foram encontradas associações estatísticas sendo $p=0,721$ para o AVE e $p=0,692$ para DCV de forma que os resultados apontam para discordâncias dos achados com o gene TEK em relação a literatura estudada. **Conclusões:** O polimorfismo rs489347 do gene TEK, apesar de já descrito como modulador genético das complicações da AF, não se mostrou associado com o desenvolvimento de DCV em pacientes pediátricos com AF na população estudada.

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ASSOCIATION BETWEEN INFLAMMATORY MOLECULES, OXIDE NITRIC METABOLITES AND LEG ULCERS IN INDIVIDUALS WITH SICKLE CELL ANEMIA



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Aim: Leg ulcers (LU) are relatively common in patients with sickle cell anemia (SCA). The role of inflammation and nitric oxide (NO) pathways in the pathophysiology of LU is not understood. The aim of this study was to verify the association between inflammatory molecules and nitric oxide metabolites (NOx) and the occurrence of LU in patients with SCA. **Methods:** It was a cross-sectional study carried out in adult participants with SCA followed at Fundação Hemominas, a public blood center in Brazil. Eligible participants were recruited and included in one of two groups: group 1 - cases with SCA (Hb SS) and at least one LU at the time of inclusion in the study; group 2 - controls with SCA without history of LU, matched by sex and age to cases. Participants were interviewed to collect sociodemographic data and blood samples were collected. Clinical and laboratory data were abstracted from medical

records. Nitric oxide metabolites (NOx) and inflammatory molecules were quantified using an immunoassay and Multiplex xMAP® technology, respectively. **Results:** Eighty-seven individuals were included, ranging in age from 17 to 61 years (mean 40 ± 10.7 years); 30 had LU and 57 were controls without LU. Participants with LU had significantly higher levels of interleukin (IL)-8, IL-10, IL-15, NOx, platelets and white blood cells (WBC) count when compared to those without LU. Additional analysis using the median value revealed 3.5 times (OR=3.51, 95%CI 1.27–9.69; $p=0.017$) greater odds of having LU in participants with IL-10 above the median. Similarly, participants with IL-8 above the median had 2.9 times (OR=2.86, 95%CI 1.06–7.78; $p=0.05$) greater odds of having LU. Participants with nitrite and nitrate above the median had 6.3 (OR: 6.3, 95%CI 2.16–18.20; $p=0.001$) and 7.4 (OR: 7.4, 95%CI 2.53–21.71; $p<0.001$) times greater odds of having LU, respectively. Participants with LU had significantly higher risk of history of osteomyelitis (OR=6.88; 95%CI 1.29–36.54; $p=0.018$) and higher use of antiseptic soap (OR=6.47; 95%CI 1.79–23.45; $p=0.004$) in bathing when compared to those without LU. **Discussion:** IL-15 is a proinflammatory cytokine that play a central role in defense mechanisms against pathogens, and in tissue-resident memory T cell homeostasis in the epidermis, which may explain the association with LU found in our study. In turn, IL-8 and IL-10 are important inflammatory molecule and their level has been reported to be increased in patients with SCA during VOE and albuminuria. Production of NO is increased in wounded tissue due to activation of endothelial nitric oxide synthase and increased production of inducible nitric oxide synthase. It is possible that the higher NOx levels observed in participants with LU are a consequence of a higher requirement for NO to neutralize inflammation, promote vasodilatation, inhibit platelet aggregation and endothelial activation. Our data showed that individuals with LU had about 7 times higher odds of history of osteomyelitis. From this data, it is reasonable to conclude that one bacterial source of contamination affecting bones of patients with SCD is the ulcerations, suggesting that patients with LU should be strictly monitored for the occurrence of osteomyelitis. **Conclusion:** In conclusion, our results showed that NOx, inflammatory molecules, and hematological features were associated with LU in Brazilian adults with SCA.

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