Legenda: CHICK - vírus Chickungunya; p – valor de significância estatística; NS – valor sem significância estatística; COVID-19 – amostras de pacientes que encontravam-se em infecção pelo vírus SARS-CoV-2; Pós-COVID-19 – amostras de pacientes que apresentaram sequelas tardias apos o curso da infecção pelo vírus SARS-CoV-2; (A) Subpopulações de monócitos Clássicos (CD14++CD16-) nas diversas amostras analisadas; (B) Subpopulações de monócitos Intermediários (CD14+CD16+) nas diversas amostras analisadas; (C) Subpopulações de monócitos Não-Clássicos (CD14^{fraco}CD16++) nas diversas amostras analisadas .

6. PRODUTO TÉCNICO TÉCNOLÓGICO (CARTA AO EDITOR)

TITLE: Patterns of monocyte subpopulations during the course of acute SARS-CoV-2 virus infection and in late post-COVID-19 patients with sequelae in the Amazon, Pará, Brazil.

Short title: Monocytes in acute SARS-CoV-2 and post-COVID-19 virus infection.

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Conflict of interest: Nothing to declare

Letter to the Editor

The end of 2019 was marked by the emergence of a new strain of Coronavirus, the SARS-CoV-2 virus, with high transmission capacity between human beings and which soon spread across the world causing a pandemic of unimaginable proportions for the modern era[1].

New Coronavirus disease (COVID-19) has a wide spectrum of clinical manifestations, with systemic repercussions and severe respiratory complications[1,2]. And with monocytes and macrophages[2,3,4] as the main cells involved in the immunopathology and clinical evolution of a patient with COVID-19. So, for a better understanding of the activation dynamics of monocyte subpopulations during SARS-CoV-19 virus infection, in our studies we analyzed, through flow cytometry, samples from patients with acute infection, until the 8th day of infection, by that virus or that had sequelae after the late course of COVID-19. These results were compared with those of patients who had positive serology for Zika or Chickungunya viruses, diseases that also progress with monocyte activation during the infection.

In this sense, the analysis of the blood count of all these patients revealed that only two who were positive for the Zika virus showed an increase in the absolute quantity of monocytes >1,000/mm³. Suggesting that used in this study, and under the conditions that we established, there is no increase in the concentration of monocytes in the bloodstream. These data are corroborated by the studies by Peruzzi et al4 and Sanchez-Cerrillo et al5, who observed that absolute monocyte counts between patients with COVID-19 and healthy individuals did not show statistical difference.

Yun et al[3], however, comparing only the relative value of monocytes in patients with COVID-19 or negative for the SARS-CoV-2 virus, observed that the percentage of monocytes in patients with COVID-19 was higher than that found in patients of the control group. Meidaninikjeh et al2 and other authors[2,3,4] argue in their studies that there is still no agreement in the literature on variations in the number of monocytes and their subpopulations in the blood of patients during infection with the SARS-CoV-2 virus.

We also sought to understand which subpopulations of monocytes are present in the course of acute infection by the SARS-CoV-2 virus and in the late post-COVID-19 patient with sequelae, we performed the analysis, by flow cytometry, of these subpopulations based on the expression of cell receptors CD14 and CD16 that define cell activation. And further comparisons of these results with the profile of monocyte subpopulations in samples from patients infected with Zika and Chickungunya viruses (Figure 1).

Figure 1. Immunophenotypic characterization of peripheral blood monocyte subpopulations from IgG and/or IgM positive samples for Zika or Chickungunya viruses, or with detectable RT-PCR for SARS-CoV-2 virus, or from samples from carriers of Post sequelae -Late COVID-19, resulting from a spontaneous demand from the Clinical Pathology Laboratory Dr Paulo C Azevedo or from the Physiotherapy Clinic of the State University of Pará in the period from March 2019 to June 2021.
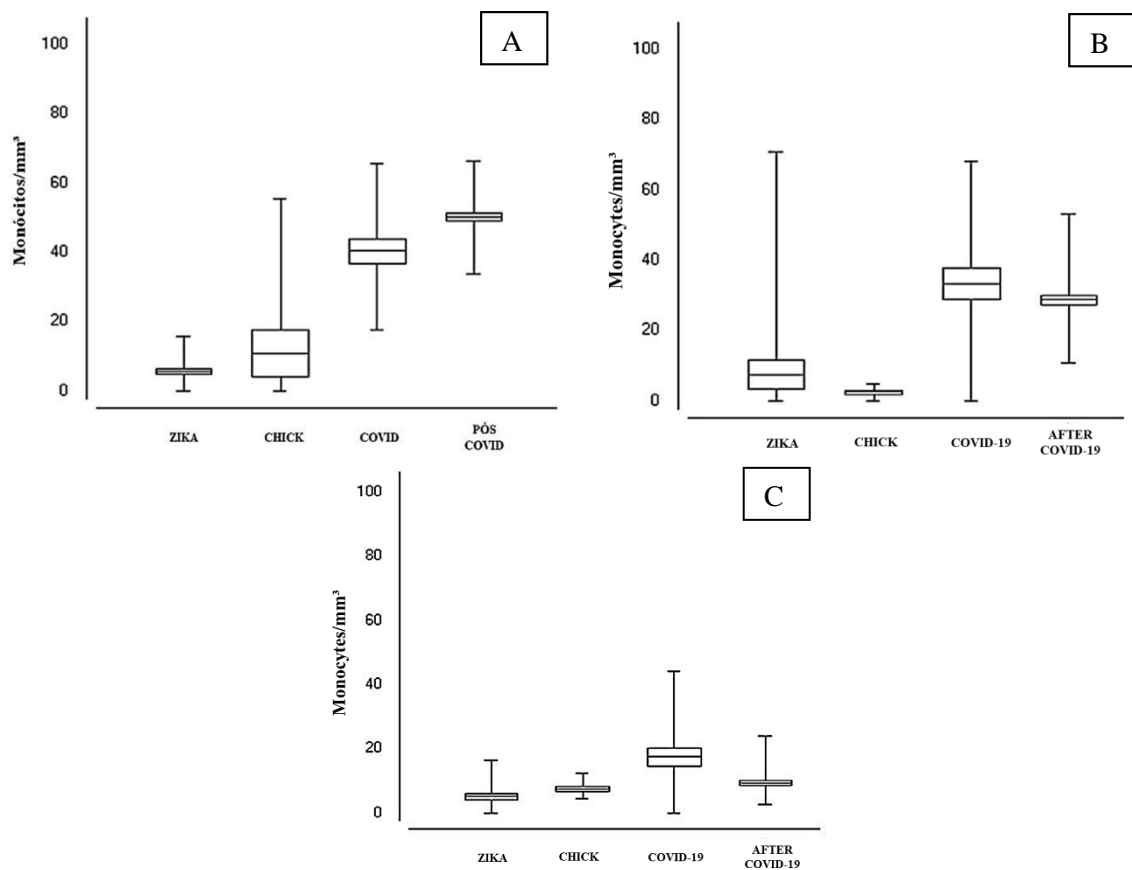
Legend: CHICK - Chickungunya virus; p – value of statistical significance; NS – value without statistical significance; COVID-19 – samples from patients who were infected by the SARS-CoV-2 virus; Post-COVID-19 – samples from patients who presented late sequelae after the course of SARS-CoV-2 virus infection; (A) Classic monocyte subpopulations (CD14^{++}CD16^{-}) in the different samples analyzed; (B) Intermediate monocyte subpopulations (CD14^{+}CD16^{+}) in the different samples analyzed; (C) Non-Classic monocyte subpopulations (CD14^{weak}CD16^{++}) in the various samples analyzed.

This is because some authors associate hyperinflammation in COVID-19 and its sequelae to deregulated activation of monocytes and macrophages[2]. Thus, a significant expansion of intermediate monocyte subpopulations (CD14^{+}CD16^{+}) has already been observed in the peripheral blood of patients with COVID-19 admitted to intensive care units (ICU) compared to patients who did not require hospitalization[5].

These findings, however, only partially converge with our results, probably because we have worked with patients in the acute phase of COVID-19, up to the 8th day of infection, or with late post-COVID-19 patients with sequelae. In our results, we observed an increase in subpopulations of classic monocytes (CD14^{++}CD16^{-}) and to a lesser extent the subpopulations of intermediate (CD14^{+}CD16^{+}) and non-classical (CD14^{weak}CD16^{++}) monocytes. Showing that there may possibly be differences in the number of monocytes and in the concentration of subpopulations of these cells throughout the course of COVID-19 and even post-COVID-19.

When the monocyte subpopulations were evaluated in samples with positive serology for Zika virus, it was observed that our results corroborate literature data describing the increase in intermediate monocytes (CD14^{+}CD16^{+}) in the peripheral blood of patients with infection by the African strain, the most common in Brazil. However, even so, this increase in intermediate monocytes was quantitatively smaller than those observed for the acute phase samples of COVID-19 or with late post-COVID-19 patients with sequelae.

The same was not observed in patients with positive serology for Chickungunya virus, where the subpopulation of classical monocytes (CD14^{++}CD16^{-}) was the most frequent. Different data from the findings by Michlmayr et al6 who described the predominance of intermediate monocytes in patients with Chickungunya virus infection.

It is noteworthy that non-classical monocytes (CD14^{weak}CD16^{++}) were the ones with the lowest concentration among all the groups analyzed by us. Still, these non-classical monocytes showed a significant increase in patients in the acute phase of COVID-19 when compared to samples associated with Zika and Chickungunya viruses, or among post-COVID-1 patients.

REFERÊNCIAS

1. Machhi J, Herskovitz J, Senan AM, Dutta D, Nath B, Oleynikov MD, Blomberg WR, Meigs DD, Hasan M, Patel M, Kline P, Chang RC, Chang L, Gendelman HE, Kevadiya BD. The Natural History, Pathobiology, and Clinical Manifestations of SARS-CoV-2 Infections. J Neuroimmune Pharmacol. 2020;15(3):359-386. doi: 10.1007/s11481-020-09944-5.

2. Meidaninikjeh S, Sabouni N, Marzouni HZ, Bengar S, Khalili A, Jafari R. Monocytes and macrophages in COVID-19: Friends and foes. Life Sci. 2021;269:119010. doi: 10.1016/j.lfs.2020.119010.

3. Yun H, Sun Z, Wu J, Tang A, Hu M, Xiang Z. Laboratory data analysis of novel coronavirus (COVID-19) screening in 2510 patients. Clin Chim Acta. 2020;507:94-97. doi: 10.1016/j.cca.2020.04.018.

4. Peruzzi B, Bencini S, Capone M, Mazzoni A, Maggi L, Salvati L, et al. Quantitative and qualitative alterations of circulating myeloid cells and plasmacytoid DC in SARS-CoV-2 Infection. Immunology. 2020;161(4):345-353. doi: 10.1111/imm.13254. .

5. Sanchez-Cerrillo I, Landete P, Aldave B, Sanchez-Alonso S, Sanchez-Azofra A, Marcos-Jimenez A, Avalos E, Alcaraz-Serna A, de Los Santos I, Mateu-Albero T, Esparcia L, Lopez-Sanz C, Martinez-Fleta P, Gabrie L, Del Campo Guerola L, Calzada MJ, Gonzalez-Alvaro I, Alfranca A, Sanchez-Madrid F, Munoz-Calleja C, Soriano JB, Ancochea J, Martin-Gayo E. Differential Redistribution of Activated Monocyte and Dendritic Cell Subsets to the Lung Associates with Severity of COVID-19. medRxiv [Preprint]. 2020 May 16:2020.05.13.20100925. doi: 10.1101/2020.05.13.20100925. PMID: 32511573; PMCID: PMC7274254.

6. Michlmayr D, Pak TR, Rahman AH, Amir ED, Kim EY, Kim-Schulze S, Suprun M, Stewart MG, Thomas GP, Balmaseda A, Wang L, Zhu J, Suaréz-Fariñas M, Wolinsky SM, Kasarskis A, Harris E. Comprehensive innate immune profiling of chikungunya virus infection in pediatric cases. Mol Syst Biol. 2018;14(8):e7862. doi: 10.15252/msb.20177862.

7. CONSIDERAÇÕES FINAIS

Diante dos resultados obtidos foi produzida carta ao editor da revista Journal of Leukocyte Biology com os dados obtidos até o momento com a nossa pesquisa que, por sua vez, é apenas um braço de um conjunto de dados que estão sendo compilados quanto a associação o efeitos das seqüelas do pós-COVID-19 tardio em cidadãos comuns da sociedade civil, onde se avalia a relação seqüela perfil da subpopulação de monócitos, e a presença de seqüelas do pós-COVID-19 tardio em árbitros de futebol que praticam atividade física de alta performance.

Nesse sentido então essa dissertação alem de ter gerado a carta ao editor à revista Journal of Leukocyte Biology, também gerou um artigo científico (Anexo II) que já foi enviado para a mesma revista científica.