The cytokine storm, a form of systemic inflammatory response syndrome, is one of the most dreadful complications that can occur during COVID-19. In this work, we aimed at studying the occurrence of a cytokine storm in a cohort of COVID-19 patients (Cpts) from Córdoba (Argentina). During first wave, we collected sera from individuals with RT-PCR+ for SARS-CoV-2 hospitalized in Hospital Privado with moderate (MOD) and severe (SEV) disease (n=62, aged 21-80 years) as well as healthy controls (HC n=24, age matched), to determine the concentrations of IL-1β, IL-6, IL-8, IL-10, IL-12, IL-28A/B, IL-29, TNF, IFN-γ, IFN-κ, IFN-γ, GM-CSF by LEGENDplexTM. Males represented 74% of MOD and 67% of SEV Cpts. Hypertension (HT, 48%), obesity (31%), dyslipidemia (DL, 24%), and diabetes (24%) were the most frequent comorbidities. All cytokines, except IL-28A/B, were significantly increased in total Cpts in comparison with HC (p<0.01). Elevated levels of IL-6 and CRP (p<0.01) between 4-7 days after hospitalization were found in all Cpts who died, but the cytokine profiles were different in deceased SEV than in MOD Cpts. Mortality in SEV group was associated with high levels of IL-6 (p<0.001), GM-CSF (p<0.01), IL-8, CRP, leukocytosis and decreased platelets (p<0.001 for all), Comorbidities were linked to particular patterns of immune mediators on admission but not afterwards during infection, with HT Cpts exhibiting increased IP-10 levels but DL Cpts showing lower concentration of IL-1β, GM-CSF and IL-10 compared to no-HT and no-DL Cpts, respectively (p<0.05). The frequency of Cpts who required O2 support was higher in HT compared to HC (p<0.05). The cytokine storm was the immune response responsible for the severe manifestations of COVID-19.
were taken at the time of admission (d0) and five days after (d5) for routine laboratory tests and the characterization of BIC by flow cytomtery. Most of the patients were men (70%) aged between 60 and 78 years. The 70% of patients had DM while 50% had arterial hypertension. At d0, all the patients had increased neutrophils and inflammatory markers (C reactive protein and D-dimers) and reduced numbers of lymphocytes, HLA-DR+ monocytes, CD16+CD56+ NK cells, CD3+HLA-DR+CD25+ cells, CD4+ and CD8+ T cells in blood. Patients received a standard treatment for COVID-19 care (O2, corticosteroids and antibiotics). The treatment normalized the levels of BIC (d5) in 30% of patients who were those with no comorbidities. In patients with DM, BIC recovery was variable. In DM patients who required administration of plasma (30%), prolonged O2 therapy (40%) or referral to the intensive care unit (10%) significant reductions of CD16+CD56+, CD3+HLA-DR+CD25+, CD4+ and CD8+ cells were observed between d0 and d5. In line with previous studies, our results shows that absolute counts of major lymphocyte subsets in blood are significantly and substantially decreased during the course of severe COVID-19 disease in elderly patients. These BIC alterations may persist despite clinical care in elderly patients with DM. Further studies are needed to investigate the utility of early lymphocyte subset measurements as prognostic biomarkers of disease severity, mortality, and response to treatment in COVID-19 elderly patients with DM.

288. (543) MOLECULAR DETECTION OF CLOSTRIDIODES DIFFICILE BY DIRECT PCR: NEW TOOLS FOR THE DIAGNOSIS OF C. DIFFICILE INFECTION
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Clostridioides difficile infection (CDI) is the major cause of hospital-acquired diarrhea associated to antibiotics treatment in developed countries. CDI has become a health security threat and a considerable challenge to public health worldwide. The increased incidence and the severity of disease have been linked to the emergence and fast spread of hypervirulent epidemic strains. Moreover, a further increase in community-acquired infections and the zoonotic potential of C. difficile lead to a highly dynamic epidemiology of CDI. Enzyme immunoassay (EIA), a technique with high specificity but low sensitivity, is widely used as a diagnostic tool for C. difficile nowadays. To optimize the diagnosis and provide information for epidemiological surveillance strategies, the expression of glutamate dehydrogenase and toxin B (TcdB) of C. difficile was determined by EIA, direct PCR of stool samples and colony PCR of anaerobic culture. We also conducted comparative analysis to determine the performance of the direct PCR for C. difficile. Faecal samples from 81 hospitalized individuals with diarrhea were collected. Clinical and demographic data were analyzed. We found a frequency of 18.5% for toxigenic strains. Treatment with antibiotics or proton-pump inhibitors were the main risk factors for CDI present in our cohort. No differences were observed between CDI+ and CDI- individuals for the aforementioned risk factors, nor comorbidities or age distribution. However, we did detect an increase in leukocytes, lymphocytes and monocytes counts in CDI patients (<p<0.05).

To validate our direct PCR method we used the EIA as the reference test. Our results showed a sensitivity of 1.0 and a Negative Predictive Value of 0.85 compared to EIA. Although a larger number of samples is needed to validate the method and determine specificity, this technique could be a useful method for C. difficile infection screening.

289. (546) EFFECT OF TOFACITINIB ON THE ACTIVATION OF T LYMPHOCYTES IN PATIENTS WITH RHEUMATOID ARTHRITIS
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Tofacitinib (Tofa) is a Jak1/3 inhibitor that blocks the intracellular signaling of inflammatory cytokines and is used as 3rd line of treatment in Rheumatoid Arthritis (RA). Tofa is very effective to achieve disease remission but it is associated to higher incidence of herpes zoster reactivation likely due to alterations in cellular immunity. While several studies have evaluated on the effects of Tofa on the immune system in the context of RA, knowledge about its impact on the activation and differentiation of T lymphocytes (TL) is scarce. We aimed to study this aspect in vivo and in vitro by determining the functional status of TL in different groups of treated RA patients (Tx RA) and the effect of Tofa in the activation of T cells from healthy donors (HD), respectively. Thirty-one HD and 106 RA patients were recruited in the Rheumatology Service (HNC) to evaluate numerous biochemical and immunological parameters. Principal component analysis showed that 82 of these variables explain around 70% of the variance, with variables related to the activation and differentiation of TL as the main difference between HD and different groups of Tx RA. Compared to HD, Tofa Tx RA patients presented a significant increase in the % of populations with terminal differentiation characteristics including CD27-CD28- of CD4+ TL (p <0.01) and KLRG1+CD57+ CD4+ and CD8+ TL (p<0.05). In addition, in vitro studies showed that Tofa reduced the activation of purified CD4+ and CD8+ TL as evidenced by a decrease in the upregulation of CD25, T-bet and the frequency of Ki-67+ cells. These effect were a dose-dependent and observed in total, naïve and, mainly, memory TL. Interestingly, Tofa increased the expression of senescent marker p21 in memory CD8+ TL. Altogether, our findings suggest that Tofa-induced replicative immunosenescence could underlie the biological effects of this drug in RA and be also involved in side effects, restraining the activity of memory TL involved in viral control.

290. (558) CHEDDIK HIGASHI SYNDROME: CASE REPORT
Introduction: Chediak Higashi Syndrome (CHS) is a rare autosomal recessive disorder, characterized by partial oclocutaneous albinism, prolonged bleeding, immune and neurologic dysfunction, and risk for the development of hemophagocytic lymphohistiocytosis. The presence of giant granule secretaries in leukocytes is the classical diagnostic feature, which distinguishes CHS from closely related Griscelli and Hermansky Pudlak syndromes.

The accelerated phase or HLH, is the primary cause of mortality in CHS and can occur at any age

Objective: Present patient with late diagnosis without development of accelerated phase

Clinical case: 5 year old male referred by Hematology due to the presence of accelerated phase HLH, is the primary cause of mortality in CHS and can occur at any age

First child of healthy parents, not consanguineous. Recurrent obstructive bronchitis treated with budesonide with good response. No recurrent infections. Difficult management of epistaxis and mild neurocognitive delay. Physical examination only shows gray hair and nystagmus.

In laboratory, moderate neutropenia and mild anemia. Negative EBV and CMV serologies

Hair’s microscopic evaluation detects dispersal of pigment clumps throughout the hair shaft.

Normal abdominal ultrasound.