Assessing Cytokine Profiles and COVID Serology in Patients on Immunosuppression to Guide Care Recommendations

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Objective/Purpose

- The severe acute respiratory syndrome (SARS) coronavirus (Cov-2) and resulting 2019 novel coronavirus (COVID-19) pandemic has led to an ongoing global public health crisis.
- The COVID-19 pandemic is especially terrifying for patients on immunosuppression for autoimmune disease.
- Cytokine storm is thought to contribute to death in COVID-19.
- The purpose of this project is to collect pilot data on testing strategies at the healthcare system level to address barriers and facilitators in the treatment of high-risk populations.

Methods

- Participants were consented prior to blood collection for routine toxicity monitoring (IRB #00131823).
- Patients verified their autoimmune diagnosis; current immunosuppression medication list; and whether they believe they currently have or had symptoms of COVID-19.
- They were asked if they had previous COVID PCR testing and those results.
- A cytokine panel developed by ARUP (Test #0051394) assessed the concentrations of interleukin (IL)-2 receptor (IL-2r), soluble, TH1 cytokines (interferon (IFN)-γ, IL-2, IL-12); TH2 (IL-4, IL-5, IL-10, IL13); Monokines (tumor necrosis factor (TNF)-α, IL1β, IL6, IL8) and IL-17.
- COVID-19 IgG serologic testing developed by ARUP for research purposes was performed.
- We summarized demographics and clinical outcomes of interest using median and range for distribute skew continuous variable; we reported counts for categorical variables.

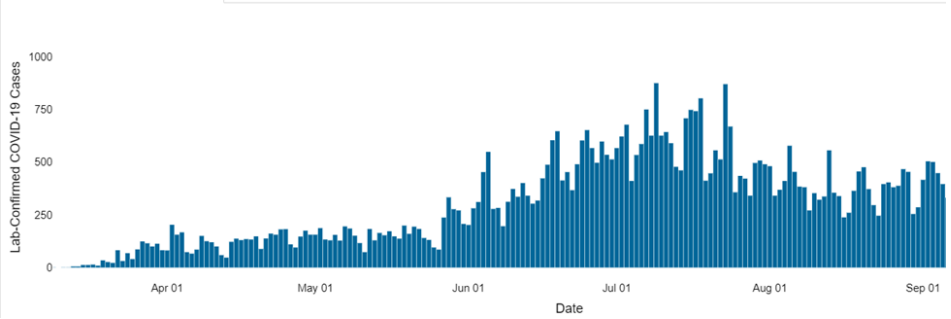

Figure 1**: Number of Confirmed COVID-19 cases in Utah during testing period 4/28 -8/12/2020

Results

- 150 patients with autoimmune disease on immunosuppressive or immunomodulatory therapy were enrolled between April 18 and August 12, 2020 and had blood collected. **Figure 1** shows the number of positive cases in UT.
- The clinical features of these autoimmune disease patients are shown in **Table 1**.
- Most of these patients were on hydroxychloroquine (n=90, 59%).
- In regard to COVID-19 PCR testing, 124 (82.1%) had been tested and were negative. Only one patient tested positive by COVID-19 PCR.
- This COVID-19 PCR patient was the only subject positive for COVID IgG, 5 weeks after acute infection. This subject had RA and was on Enbrel. She reported diarrhea and a low-grade fever for one day, a cough that was mild, and loss of taste and smell for 5 days.
- Ten patients (6.6%) believed that they had symptomatic COVID-19, but were not tested by PCR. Fifteen patients (9.9%) were symptomatic for COVID-19 and PCR tested negative.
- We did not identify any asymptomatic carriers of SARS-Cov-2 by PCR or IgG serology testing.
- The majority of the patients with IL-10 elevated (87.5%), reported concern for previous infection. The most common elevated cytokines were IL-10 in 24 (16%), IL-6 in 14 (9.3%), and TNFα in 10 (6.6%) patients (**Table 2**).

Table 2: Elevated Cytokine Profiles in Participants

CYTOKINE	NUMBER OF TEST (%)	MEDIAN (RANGE)
Interferon-gamma	0	0
Interleukin 12	1 (0.7)	9.3 (0-9.3)
Interleukin 2	1 (0.7)	7.5 (0-7.5)
Interleukin 4	0	0
Interleukin 5	0	0
Interleukin 10	24 (16)	3.8 (2.9-15.8)
Interleukin 13	3 (2)	14.1 (2.7-26.5)
Interleukin 1-beta	3 (2)	10.8 (10.2-32)
Interleukin 6	14 (9.3)	4.3 (2.4-99.2)
Interleukin 8	0	
TNF-alpha	10 (6.6)	12.7 (9-23.3)
Interleukin 2 receptor	8 (5.3)	1185.7 (866.5-2409.5)
Interleukin 17	2 (1.4)	35.2 (5.4-65)

Table 1: Clinical Features of Participants

PATIENT CHARACTERISTIC	# OF PATIENTS (%)
Male	21 (13.9)
Female	129 (86.1)
Age (median, range)	55.7 (24-85)
Ethnicity	
• Hispanic	12 (7.9)
• Not Hispanic	132 (87)
• Not reported	7 (4.6)
Diagnosis	
• CDIP	1 (0.7)
• SSc	73 (48.7)
• RA	28 (18.4)
• Inflammatory Arthritis	4 (2.6)
• UCTD	7 (4.6)
• SLE	17 (11.2)
• Sjogrens	7 (4.6)
• Psoriatic arthritis	3 (2)
• Inflammatory myositis	9 (6)
• Vasculitis	1 (0.7)
• Ankylosing spondylitis	2 (1.3)
• Spondyloarthritis	1 (0.7)
• JIA	2 (1.3)
• Sarcoid	2 (1.3)
• ILD	5 (3.3)
Medications	
• Methotrexate	31 (20.4)
• Hydroxychloroquine	90 (59.2)
• Mycophenolate	40 (26.3)
• TNF-inhibitor	11 (7.2)
• IVIG	2 (1.3)
• Prednisone	13 (8.6)
• Azathioprine	15 (10)
• Rituximab	4 (2.6)
• Anakinra	1 (0.7)
• Leflunomide	4 (2.6)
• Secukinumab	2 (1.3)
• Sulfasalazine	2 (1.3)
• Tofacitnib	2 (1.3)
• Ustekinumab	2 (1.3)
• Apremilast	1 (0.7)

Conclusions

- Our study supports the continued use of immunosuppression in autoimmune disease patients during the COVID-19 pandemic.
- Our study highlights the value of testing that includes PCR for acute viral symptoms, cytokine profiling for assessment of active inflammation, and COVID serology testing for assessment of past infection.

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