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COVID-19 infection in 10 common variable immunodeficiency patients in New York City

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Clinical Implications

- Of 135 patients identified with common variable immunodeficiency at Montefiore Medical Center in New York City during the peak of the spring 2020 COVID-19 pandemic, 10 patients had COVID-19 infection. One patient was hospitalized, there were no deaths, and all recovered.

Common variable immunodeficiency (CVID), the most prevalent humoral immunodeficiency, is characterized by hypogammaglobulinemia, impaired vaccine responses, and recurrent sinopulmonary infections.[1] Although known risk factors for more severe COVID-19 infection include older age, hypertension (HTN), obesity, and cardiovascular disease,[2] the association of immunocompromised patients and severity of COVID-19 infection is not well established. Studying specific immunocompromised cohorts may clarify risk of morbidity and mortality to these patients from COVID-19 infection. A case series by Quinti et al[3] described 4 patients with CVID and 2 with agammaglobulinemia, all of whom recovered except one, suggesting perhaps a similar mortality to the general population. Here, we assess the severity of infection, need for hospitalization, and mortality in a cohort of patients with CVID at our center.

This retrospective study was conducted at Montefiore Medical Center and approved by the institutional review board at the Albert Einstein College of Medicine in Bronx, NY. Clinical Looking Glass (CLG), a program that retrieves data from the electronic medical record, was used to identify patients with hypogammaglobulinemia or CVID International Classification of Diseases code. A manual chart review was performed, and patients were included in the cohort if they met International Consensus Document 2016 diagnostic criteria for CVID.[1] Patients with other primary or secondary immunodeficiency were excluded.

Demographics, clinical and laboratory characteristics, and history of COVID-19 infection were collected either by phone survey or chart review. COVID-19 infection was confirmed by documented or reported positive nucleic acid amplification test (NAAT), or convincing symptomatology with a positive COVID-19 IgG.

Of 560 patients identified by CLG, 229 met diagnostic criteria for CVID, of whom 125 were reached by phone and 10 were completed on chart review alone. Ten patients were deceased from non-COVID causes, and 84 declined inclusion or were unable to be reached and lacked chart data (Figure E1, available in this article's Online Repository at www.jaci-inpractice.org). COVID-19 infection was confirmed in 10 patients (Table I). Seven of these 10 patients were on immunoglobulin (IG) replacement therapy (RT). One patient declined IGRT due to noncompliance and the others due to a relatively low infection burden and instead opted for observation. The overall utilization rate of IGRT in our cohort was 75% (102 of 135), similar to the COVID-19-positive patients (7 of 10). Three patients had well-identified comorbidities for severe COVID-19 disease including HTN, diabetes mellitus (DM), and age. Eight of 10 patients had baseline lymphopenia with total counts less than 1500 cells/mm^3 (Table II). COVID-19 IgG was positive in 4 of 6 patients, of whom 2 were on biologicals.

Nine of 10 CVID patients with COVID-19 remained at home with mild-to-moderate symptoms. None of the patients were diagnosed with COVID-19-related pneumonia or required mechanical ventilation. Two patients were on biological therapies and had a mild course. Patient 7, an older patient with HTN, required hospitalization for dehydration and electrolyte abnormalities but did not require respiratory support. On admission, laboratory data were notable for a decreased total lymphocyte count to 200 cells/mm^3, absolute neutrophil count of 5200 cells/mm^3, C-reactive protein of 4.6 mg/dL, lactate dehydrogenase of 331 U/L, and partial thromboplastin time of 51.7 seconds. During a 16-day admission, the patient was treated with lopinavir/ritonavir, hydroxychloroquine, and 2 doses of intravenous IG (500 mg/kg/dose every 14 days).

Most notably, and reassuringly, all the patients with CVID infected with COVID-19 recovered. The patient requiring hospitalization had multiple known risk factors for severe COVID-19, explaining the need for hospitalization. Consistent with prior case series in patients with CVID and agammaglobulinemia,[3,4] our cohort had high rates of recovery and did not appear to have a higher mortality compared with the general population. This cohort likely had a milder course than seen in Quinti et al,[3] as the majority of patients reviewed here were younger in age. Despite lymphopenia, seen in 8 of 10 patients, all of the patients recovered and overall had mild courses. This is in agreement with reports of patients with HIV, in whom T-cell counts did not predict disease severity.[5] A recent analysis of patients with immune-mediated inflammatory disease showed that known risk factors of age, HTN, and DM were more likely to predict severe disease; notably, the hospitalization rate was lower among those receiving biologics or Janus kinase inhibitors, suggesting that biologics are not associated with severe COVID-19 infection.[6] This is in line with our cohort, in which both patients on biologic therapy did not require hospitalization.

IGRT was used in 7 of 10 patients, similar to our general cohort. Although the authors feel that IGRT may have contributed to the patients' recoveries, 3 patients who were not on IGRT also recovered, complicating this conclusion. In addition, there were insufficient data to draw a correlation between the ability to mount an antibody response and the patients' immunophenotypes.

TABLE I. Clinical characteristics of 10 CVID patients with COVID-19 infection

Patient	Age	Sex	BMI	COVID-19 symptoms (length of illness in days)	Other medical conditions	Medications (immunosuppressants, Abx, Ig)	Treatment specifically for COVID-19	COVID-19 IgG
1	28	M	22.8	Fever, cough, SOB, abdominal pain, fatigue, anosmia, ageusia, sore throat, and rash (28 d)	None	Abatacept IG replacement	Levofloxacin, azithromycin	Positive
2	33	F	20.5	Fever, sore throat, fatigue, and cough (14 d)	None	Rituximab (2005) IG replacement	Azithromycin	Negative
3	25	M	25.1	Fevers, fatigue, cough, anosmia, and ageusia (11 d)	None	None	Azithromycin	Not done
4	41	M	63 kg*	Fever and cough (7 d)	ID, seizures	Dapsone IG replacement	None	Not done
5	24	M	25.8	Fatigue, diarrhea, and anorexia (7 d)	Cystic acne, autism, osteoporosis	Adalimumab IG replacement	None	Positive
6	68	F	18.6	Fever, cough, SOB, and fatigue (42 d)	MS, HTN	None	None	Not done
7	66	F	27.4	Fever, fatigue, diarrhea, dehydration, decreased appetite, cough, and SOB (16 d)	Severe asthma, HTN, ARC, atrial fibrillation	Penicillin VK IG replacement	IVIG, lopinavir/ritonavir, hydroxychloroquine	Positive
8	45	F	23.8	Fever, cough, sore throat, and fatigue (7 d)	Colonic polyposis	IG replacement	Azithromycin	Negative
9	44	M	25	Rhinorrhea, cough, and SOB (7 d)	Mild asthma, DMII, bipolar disorder, schizoaffective disorder	None	Clindamycin	Not done
10	20	M	18.1	Sore throat, cough, and anosmia (5 d)	None	IG replacement	None	Positive

ARC, Allergic rhinoconjunctivitis; *BMI*, body mass index; *CVID*, common variable immunodeficiency; *DM*, diabetes mellitus; *HTN*, hypertension; *ID*, intellectual disability; *IVIG*, intravenous immunoglobulin; *MS*, multiple sclerosis; *SOB*, shortness of breath.
*Unable to obtain height.

Collectively, impaired B- and T-cell function, lymphopenia, and biologic therapy do not appear to increase COVID-19 disease severity. Rather, the dysregulation of the myeloid compartment, including resident lung macrophages, may in fact be the driver of inflammation and distinguish severe COVID-19 from mild cases.[7] Interestingly, ibrutinib, targeting Bruton's tyrosine kinase (expressed on B cell and myeloid-derived cells), is theorized to protect against macrophage-induced lung injury in a small case series.[8]

Limitations of this study include the likely underreported incidence of COVID-19 infection due to incomplete medical records, the inability to reach patients, false-negative NAAT, lack of testing, or asymptomatic patients who were never tested. In addition, several COVID-19-positive patients were no longer followed at our center, and therefore recent laboratory data and IGRT dosing were unavailable. Other limitations include small sample size, subjectivity to recall bias by using a survey, and its retrospective nature.

In conclusion, in our cohort of 135 patients with CVID, there was no mortality and low morbidity of COVID-19 infection, suggesting that the severity of infection in this cohort was typically mild, and that these patients are at standard risk for severe disease. These results are reassuring to providers caring for patients with CVID. Further research is needed to elucidate the mechanism of severe COVID-19 disease and how it impacts patients with primary and secondary immunodeficiency.

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TABLE II. Summary of phenotypic and immunologic data in 10 patients with CVID collected before the COVID-19 pandemic

Patient	Current age (age at diagnosis)	CVID comorbidities	TLC (mm^3)	T lymphocyte subset count (mm^3)	Recent serum IgG (mg/dL)	IG RT (mg/kg) q3-4 weeks	CD19 count ($mm^{3)}$ with B-cell panel	Specific antibody responses*
1	28 (19)	IBD, RA	1000		630	600		
2	33 (12)	Hypothyroidism, vasculitis, and encephalopathy	1300	CD3 958 CD4 561 CD8 361	2180	700	CD19 215	Post-Pneumovax 0/23 protective
3	25 (11)	Colitis and nodular hyperplasia of colon	1900	CD3 1093 CD4 757 CD8 282	568†	N/A	CD19 477	Post-Prevnar 1/14 protective Measles, mumps, rubella NI Varicella NI
4	41 (29)	TCL	500	CD3 226 CD4 136 CD8 72	591	400	CD19 104	Measles, mumps NI HAV I, HBV I Rubella, varicella I
5	24 (11)	Hidradenitis	1400	CD3 1047 CD4 765 CD8 261	1490	700	CD19 68↓ Normal class switched memory B cell, ↓plasmablasts	Post-Pneumovax 6/23 protective 6 months later: 0/23 protective
6	68 (52)	Celiac disease and AI thyroid disease	1300		660†	N/A		Post-Pneumovax 0/23 protective Diphtheria 0.7, tetanus 0.86
7	66 (62)	Bronchiectasis and TCL	1100	CD3 664 CD4 502 CD8 140	1080	600	CD19 35↓ ↓Class switched memory B cells	Post-Pneumovax 4/23 protective Tetanus < 0.10
8	45 (40)	AI thyroid disease	1400	CD3 1,192 CD4 582 CD8 518	1370	600	CD19 134	Post-Prevnar 0/14 protective Tetanus 0.2, MMR I HAV, HBV, VZV NI (p/v)
9	44 (40)	Anemia and thrombocytopenia	1050	CD3 678 CD4 501 CD8 148	418	N/A	CD19 212 ↓total memory B cells (1.5%) reflected in nonswitched and switched memory B cells	Post-Pneumovax 1/23 protective MMR I Tetanus 1.71, diphtheria 0.64
10	20 (11)	AI thyroid disease	1800	CD3 1242 CD4 666 CD8 486 CD19 378	686	500	CD19 378	Post-Prevnar 1/14 protective MMRV I, Hib I

AI, Autoimmune; *CVID*, common variable immunodeficiency; *HAV*, hepatitis A virus; *HBV*, hepatitis B virus; *I*, immune; *IBD*, inflammatory bowel disease; *MMR*, measles, mumps, rubella; *NI*, nonimmune; *N/A*, not applicable; *p/v*, postvaccination; *RA*, rheumatoid arthritis; *RT*, replacement therapy; *TCL*, T-cell lymphopenia; *TLC*, total lymphocyte count; *VZV*, varicella zoster virus.

↓Low/decreased.

*Protective titers post-Pneumovax are >1.3 mcg/dL and post-Prevnar >0.5 mcg/dL.

†IgG borderline low, with IgA and IgM 2 standard deviation below normal and impaired vaccine responses, being managed with clinical observation and antibiotics as needed.

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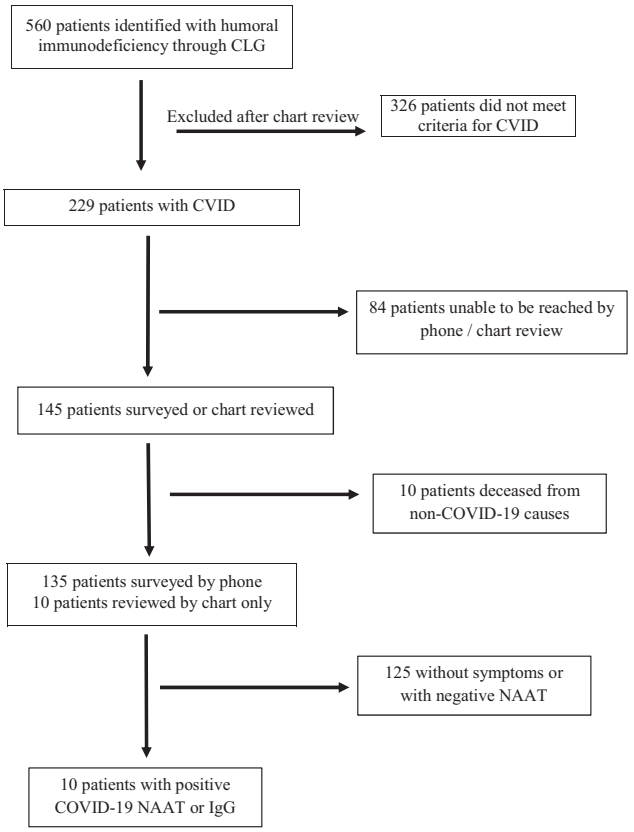

FIGURE E1. Inclusion of patient cohort. *CLG*, Clinical Looking Glass; *CVID*, common variable immunodeficiency; *NAAT*, nucleic acid amplification test.