COVID-19 Infection With Humoral Immunodeficiency in Midwestern United States

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Abstract

Background: The coronavirus 2019 disease (COVID-19) has infected many individuals worldwide and continues to pose a significant threat to those with weakened immune systems. A paucity of data exists evaluating the clinical outcomes of patients with humoral immunodeficiencies that contract COVID-19.

Objective: To describe the clinical outcomes of COVID-19 infections in patients with primary humoral immunodeficiency.

Methods: We conducted a retrospective cohort review on 15 patients with a humoral immunodeficiency including Common Variable Immunodeficiency, Specific Antibody Deficiency, or unspecified hypogammaglobulinemia, who contracted COVID-19. Severity scores were determined to evaluate the clinical outcomes of these patients.

Results: Of our 15-patient cohort, 33% of individuals with a humoral immunodeficiency infected with COVID-19 had a more severe disease, requiring hospitalization or resulting in death. COVID-19 mortality rate was found to be 7%. All 5 of our patients with more severe infection had at least 1 comorbidity.

Conclusion: Within our cohort of humoral immunodeficient patients infected with COVID-19 we found a higher rate of severe infections and worse clinical outcomes.

Introduction:

The Coronavirus Disease 2019 (COVID-19) pandemic which began in March of 2020 has irreversibly changed our society. This virus has been responsible for millions of deaths across the world and continues to infect our population and challenge our healthcare infrastructure. Infections vary from asymptomatic to life threatening acute respiratory distress syndrome (ARDS) and organ failure. Several risk factors have been identified which predispose individuals to worse outcomes including advanced age, male gender, preexisting heart conditions, hypertension, chronic kidney disease, increased body mass index (BMI), chronic pulmonary obstructive disease (COPD), and diabetes [1]. While COVID-19 research has been exponentially increasing, it is not clear whether an association exists between having an immunodeficiency and severe COVID-19 infection.

Immunocompromised patients are more susceptible to viral, bacterial, and fungal infections. A virus responsible for a pandemic would in theory severely impact this population, however, only a handful of cases have been published describing outcomes of COVID-19 infections in patients with primary immunodeficiencies (PID). Some authors suggest that most patients with PID infected with COVID-19 may have similar outcomes when compared to the general population [2]. Another recent literature review highlights a more severe infection risk in immunodeficient patients [3]. Humoral immunodeficiency encompasses Common Variable Immunodeficiency (CVID), Specific Antibody Deficiency (SAD), and unspecified hypogammaglobulinemia. We aim to present a descriptive clinical analysis of COVID-19

infection outcomes in patients with known primary humoral immunodeficiency in the Midwestern United States.

Methods:

A retrospective case review was conducted at the Allergy and Immunology Fellowship Program, University Hospitals, Cleveland Medical Center. The study was approved by the institutional review board at University Hospital, Cleveland Medical Center (STUDY20201805). Patients were identified for our study if they had a recent positive COVID-19 test and were either receiving intravenous IgG replacement therapy (IVIG), or had an International Statistical Classification of Diseases (ICD-10) code for Common Variable Immune Deficiency (CVID). Patients were selected if they had a true primary humoral deficiency including CVID, SAD, or unspecified hypogammaglobulinemia. Chart reviews were conducted to ensure patients met the International Union of Immunological Societies (IUIS) definition of CVID and SAD [4]. Fifteen patients met these qualifications. Once the patients were selected, charts were reviewed for demographic information, past medical history, current maintenance therapies, and clinical COVID-19 disease course: including symptoms and management. A severity score was developed to classify COVID-19 infection outcomes in our patients defined as the following: 1 = outpatient management only, 2 = hospital admission, 3 = ICU and /or intubation, and 4 = death (Table S1).

Results:

Fifteen patients with known humoral deficiency diagnosed with COVID-19 were included in our study (Table S2). Eight (53%) patients had the diagnosis of CVID, and 6 (40%) had the diagnosis of SAD. Six or 40% of patients in this group were over the age of 60. Ten (67%) were female and 5 (33%) were male. Five (33%) patients were classified as obese with a BMI of > 30 and 1 (7%) was morbidly obese with BMI > 40 . Fourteen (93%) patients were receiving regularly scheduled IVIG at the time that they contracted COVID-19. Severity score percentages were as follows: 10 (67%) scored 1, 4 (27%) scored 2, and 1 (7%) scored 4. Out of the 15 patients, 8 (53%) had at least one comorbidity for severe COVID-19 including hypertension ($n = 3$), diabetes mellitus ($n = 1$), COPD ($n = 2$) and obesity ($n = 5$). Ten (67%) of our patients were able to remain at home and receive outpatient management. All 5 patients with severe outcomes of COVID-19 infection had at least one comorbidity. Conversely, out of the 10 patients with mild disease, only 3 or 30% had a comorbidity. One patient in the cohort passed away from COVID-19 after being treated in the intensive care unit (ICU) and requiring intubation. She had 2 comorbidities including HTN and COPD, and a risk factor of advanced age > 60 years.

Discussion:

COVID-19 has had a profound impact on the world since it was first discovered in Wuhan, China. As COVID-19 research continues, questions including how this virus impacts certain populations remain unanswered. Due to the nature of the disease, immunodeficient patients would seemingly be at a greater risk for higher infection rates and worse outcomes than the general population. A recent review article

compiled data from 14 publications describing COVID-19 infections in patients with CVID. [3] Of the 68 total cases of COVID-19 in CVID patients reviewed, 39 patients (57%) had a mild infection, defined as not hospitalized and/or no oxygen supplementation. 20 patients (29%) were categorized as having moderate to severe infection defined as hospitalization required with oxygen supplementation, but no intubation. Seven (10%) patients had critical infection requiring hospitalization and intubation. Lastly, nine (13%) patients died. Cohen et al. described a cohort of ten CVID patients infected with COVID-19 in New York City [2]. Seven of the patients were on IVIG at the time of COVID-19 diagnosis and three patients had comorbidities for severe COVID-19. Nine of the patients had mild-to-moderate symptoms and were managed outpatient. The only patient hospitalized had multiple known risk factors for severe COVID-19. None of these patients were diagnosed with pneumonia or required mechanical ventilation, and all patients recovered. This cohort of CVID patients in NYC showed a low risk of severe COVID-19 disease. Results from our cohort of patients with primary humoral immunodeficiency diagnosed with COVID-19 show that 33% had a more severe infection, and 7% had fatal outcome. Comparing our results with the approximate general population mortality rate of 1.4%, we suggest that our cohort of humoral immunodeficient patients had a higher risk of severe disease [5].

Several reasons can be postulated to explain the increased severity of infections in our patients. First, consistent with literature, patients with comorbidities and risk factors, which include: advanced age, male gender, preexisting heart condition, HTN, chronic kidney disease, increased BMI, COPD, and diabetes are at a higher risk for worse outcomes [1]. In our cohort, 100% of the 5 patients with severe COVID-19 infection had at least 1 comorbidity. Comparatively, of the 10 patients with milder COVID-19 infection only 30% had at least 1 comorbidity. The only patient with a fatal outcome in our cohort had 2 comorbidities including HTN and COPD. Severe COVID-19 infections have also been associated with autoantibodies against type 1 interferon (IFN). [6] Although genetic testing was not analyzed, searching for inborn errors of type 1 IFN in our cohort could lead to another explanation for the severe COVID-19 infections seen.

Factors intrinsic to the virus itself can also contribute to the increased severity in our cohort. Over the course of the pandemic, there have been waves of increased infections and reports of virus mutations. The majority of our cohort of patients presented during end of 2020. Variations seen in the severity of infections could possibly be due to the time the individual was infected, whether it was during the initial wave of infections in Spring of 2020 or a later wave. Variability of viral load in patients can also account for the difference in severity of COVID-19 infections.

COVID-19 is a serious disease that continues to have global ramifications. Those living with primary immunodeficiencies are at an increased risk of contracting infections and may be more susceptible to COVID-19. Prior studies on patients with CVID have shown varied outcomes among those that have contracted COVID-19. Our study indicates a higher rate (33%) of severe COVID-19 infections in those with primary humoral immunodeficiency with a mortality rate of 7%. These results may differ from previous reports showing milder COVID-19 infections due to the existence of comorbidities, variability in viral load,

and presentation during different infection waves. Future studies with larger cohorts are necessary to further assess COVID-19 outcomes in immunocompromised patients.

Declarations

Funding: No funding was received for conducting this study.

Conflicts of interest/Competing interests: none

Availability of data and material: Not applicable

Code availability: Not applicable

Author contributions:

Maaz Jalil DO: Conception and design of the study, data generation, analysis and interpretation of the data, and preparation and clinical revision of the manuscript.

Julianne Pietras OMS-III: Data analysis, literature search, preparation and clinical revision of the manuscript.

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Phuong Daniels OMS-II: Literature search, preparation and clinical revision of the manuscript.

Robert Hostoffer DO: Conception and design of the study, analysis and interpretation of the data, and clinical revision of the manuscript.

Ethics approval: This study was approved by the institutional review board at University Hospital, Cleveland Medical Center (STUDY20201805).

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Supplementary Files

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