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HEMATOLOGY: BRIEF REPORT

# Coronavirus disease 2019 and vaccination in patients with Shwachman-Diamond syndrome

Thomas J. Galletta[1] | Sara K. Loveless[2] | Maggie M. Malsch[3] | Akiko Shimamura[4,5] | Kasiani C. Myers[2,6]

[1]Cancer and Blood Diseases Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

[2]Division of Bone Marrow Transplantation and Immune Deficiency, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

[3]Institutional Centers for Clinical and Translational Research, Boston Children's Hospital, Boston, Massachusetts

[4]Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts

[5]Department of Pediatrics, Harvard Medical School, Boston, Massachusetts

[6]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio

**Correspondence**
Thomas Galletta, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue MLC 7018, Cincinnati, OH 45229.
Email: Thomas.Galletta@cchmc.org

## Abstract

Because they can experience neutropenia due to bone marrow failure, patients with Shwachman-Diamond syndrome (SDS) carry increased risk for serious infections compared with the general population; however, there has been a paucity of data on the incidence and severity of coronavirus disease 2019 (COVID-19) in patients with SDS. We compiled results from a survey distributed to participants in the SDS Registry in May-June 2021. In this report, we describe the characteristics and outcomes of patients with SDS who had COVID-19. Patients reported a short clinical course without significant complications or cytopenias. Additionally, COVID-19 vaccines were well tolerated with minor side effects.

**KEYWORDS**
Bone marrow failure, COVID-19, general hematology, infections in immunocompromised hosts, infectious disease, vaccines, viral infection

## 1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has had significant implications for patients with chronic medical conditions, particularly those who are immunocompromised due to malignancy or bone marrow failure (BMF). Shwachman-Diamond syndrome (SDS) is an inherited BMF disorder characterized by cytopenias, particularly neutropenia, exocrine pancreatic dysfunction, and predisposition to myeloid malignancies. Its manifestations are variable and can affect many body systems, including the skeletal, cardiac, endocrine, nervous, hepatic, and immune systems. In most cases, SDS is due to recessive mutations in the Shwachman-Bodian-Diamond syndrome (*SBDS*) gene located on chromosome 7q11. Because patients with SDS can experience neutropenia due to BMF, they carry a higher risk for serious infections compared with the general population; however, the incidence and severity of COVID-19 in the population of patients with SDS have not been described.

**Abbreviations:** BMF, bone marrow failure; CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; G-CSF, granulocyte colony-stimulating factor; IVIG, intravenous immune globulin; MIS-A, multisystem inflammatory syndrome in adults; MIS-C, multisystem inflammatory syndrome in children; PT, specific patient; *SBDS*, Shwachman-Bodian-Diamond syndrome gene; SDS, Shwachman-Diamond syndrome.

## 2 | METHODS

A survey was distributed to patients participating in the SDS Registry, and responses were anonymous. Results were compiled in May and June 2021. In this cohort study, we report the baseline characteristics and clinical outcomes of these 10 patients with SDS who had a COVID-19.

## 3 | RESULTS

Of the 73 survey respondents, 10 patients experienced COVID-19 (13.7%; Table 1). Seven of these 10 patients (70%) reported germline

  

**TABLE 1** Characteristics and outcomes of the SDS Registry patients with and COVID-19

| | Patient | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Variable:** | **PT-1** | **PT-2** | **PT-3** | **PT-4** | **PT-5** | **PT-6** | **PT-7** | **PT-8** | **PT-9** | **PT-10** |
| Genetically confirmed | – | – | – | + | + | + | + | + | + | + |
| Genetic mutation | Unknown | Unknown | Unknown | *SBDS* | *SBDS* | *SBDS* | *SBDS* | NR | *SBDS* | NR |
| Preexisting condition | – | – | – | – | – | – | – | – | – | – |
| SDS treatments | Pancreatic enzymes | – | – | HSCT, pancreatic enzymes | – | Pancreatic enzymes | Pancreatic enzymes | G-CSF, pancreatic enzymes | G-CSF | Pancreatic enzymes |
| Use of tobacco/vape | – | – | – | – | – | – | – | – | – | – |
| Regularly taking G-CSF prior to infection | – | – | – | – | – | – | – | + | + | – |
| Number of vaccine administrations | 2 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 |
| Vaccine adverse effects | – | N/A | N/A | – | Arm pain, fatigue | N/A | N/A | N/A | N/A | N/A |
| Received vaccine prior to infection | – | N/A | N/A | – | – | N/A | N/A | N/A | N/A | N/A |
| Time after infection to receiving vaccine | 6 months | N/A | N/A | 5 months | 2 months | N/A | N/A | N/A | N/A | N/A |
| At COVID-19 diagnosis: | | | | | | | | | | |
| Age (years) | 19 | 16 | 22 | 17 | 37 | 1 | 2 | 5 | 12 | 20 |
| Duration of symptoms (days) | 2 | 5 | 7 | 2 | 100 | 14 | 7 | 4 | 2 | 2 |
| Fever | – | + | + | + | – | + | + | – | + | – |
| Duration of fever (days) | N/A | 4 | 3 | 2 | N/A | 1 | 5 | N/A | 2 | N/A |
| Chills | – | + | + | + | – | – | – | – | – | – |
| Muscle aches | – | – | – | + | – | – | – | – | + | – |
| Dyspnea | – | + | – | – | – | – | – | – | + | – |
| Loss of taste/smell | – | + | + | – | – | – | – | – | – | – |
| Respiratory symptoms | Cough, congestion | Cough, congestion | Congestion | Cough | – | Congestion | Cough, congestion | Cough, congestion | Cough | Congestion |
| Other symptoms | – | – | – | – | "COVID toes" | – | – | – | – | Headache |
| Required hospitalization | – | – | – | – | – | + | – | – | – | – |

(Continues)

**TABLE 1** (Continued)

| | Patient | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Variable:** | **PT-1** | **PT-2** | **PT-3** | **PT-4** | **PT-5** | **PT-6** | **PT-7** | **PT-8** | **PT-9** | **PT-10** |
| Required supplemental oxygen support | – | – | – | – | – | – | – | – | – | – |
| Required blood product transfusion | – | – | – | – | – | – | – | – | – | – |
| Required new use of G-CSF | – | – | – | – | – | – | – | N/A | N/A | – |
| VTE | – | – | – | – | – | – | – | – | – | – |
| MIS-A or MIS-C | – | – | – | – | – | – | – | – | – | – |
| Treatment | – | – | – | Systemic corticosteroid | ASA, topical corticosteroid | – | – | – | – | Remdesivir |
| New medical problem following infection | – | – | – | – | Neutropenia | – | – | – | – | – |

Abbreviations: ASA, aspirin; G-CSF, granulocyte colony-stimulating factor; HSCT, hematopoietic stem cell transplant; MIS-A, multisystem inflammatory syndrome in adults; MIS-C, multisystem inflammatory syndrome in children; NR, no response; *SBDS*, Shwachman-Bodian-Diamond syndrome gene; VTE, venous thromboembolism.

*SBDS* mutations. The median age of the COVID-19–positive patients at the time of diagnosis was 16.5 years (range, 1-37 years). Of the three patients who both developed COVID-19and received a COVID-19 vaccine, all of them received the vaccine following COVID-19, two to six months following infection (median, 5 months). None of them experienced serious vaccine-related adverse events. All vaccinated patients received two mRNA vaccine doses. All patients in the SDS Registry who developed COVID-19 were symptomatic of infection, with the most common symptoms being respiratory, such as congestion or cough (70%), and fever (60%). The median duration of symptoms was 4.5 days (range, 2-100 days; excluding an outlier of 100 days, range, 4-14 days). Only one of 10 patients required hospitalization, and this patient was one year old (PT-6). She was hospitalized two days after symptom onset and was hospitalized for four days. She did not require supplemental oxygen, noninvasive positive-pressure ventilation, or intubation and mechanical ventilation. She did not require admission to the intensive care unit.

Of the survey respondents who developed COVID-19, none of them reported having a preexisting condition other than SDS. Preexisting conditions listed in the survey included hypertension, diabetes mellitus, asthma, and routine need for immune globulin (IVIG). Respondents were able to report other conditions that were not listed. No patients who developed COVID-19 reported a history of tobacco use or vaping. Six of them (60%) reported regularly taking pancreatic enzymes, and two of them (20%) reported regularly administering granulocyte colony-stimulating factor (G-CSF) prior to COVID-19 onset (PT-8 and PT-9). One patient reported a history of a hematopoietic stem cell transplant over 15 years ago (PT-4).

Survey respondents were asked if they received any of the following COVID-19 treatments: remdesivir, hydroxychloroquine/chloroquine, azithromycin, anakinra, tocilizumab, corticosteroids, immune globulin, or the investigational COVID-19 monoclonal antibody bamlanivimab. One patient (PT-10) received remdesivir, and one patient (PT-4) received systemic corticosteroids. One patient (PT-5) developed "COVID toes"—swelling, discoloration, and/or pain of the toes associated with COVID-19—and was treated with aspirin and topical corticosteroids. She also reported the longest duration of symptoms out of all respondents, 100 days. No patients required packed red blood cell or platelet transfusion during COVID-19, or new administration of G-CSF. No patients developed a venous thromboembolism, multisystem inflammatory syndrome in adults (MIS-A), or children (MIS-C).

In the cohort of SDS Registry patients described, most reported having a short duration of symptoms that did not require hospitalization or result in serious virus-related complications. Although the Centers for Disease Control and Prevention (CDC) recommends receiving the COVID-19 vaccine even after developing COVID-19, only 30% of patients with SDS and COVID-19 subsequently received the vaccine. Three of the respondents with COVID-19 were ineligible to receive the vaccine at the time of survey due to age less than 12. Of the 37 survey respondents who had not developed COVID-19 and were eligible by age to receive the vaccine at the time of survey distribution, 18 (48.6%) of them received at least one dose of the COVID-19 vaccine; 15 of whom (40.5%) received two doses. Of the 18 respondents who received at least one COVID-19 vaccine dose, arm pain was the most common side effect (66.7%),

followed by fatigue (50%), fever and/or chills (38.9%), and muscle aches (33.3%). Other side effects listed in the survey were rash and anaphylaxis; no respondents reported experiencing these symptoms. Five of the 18 recipients (27.8%) reported experiencing no side effects. Thirteen (72.2%) of the 18 vaccinated respondents received the Pfizer vaccine, whereas the remainder received the Moderna vaccine. A complete list of the questions included in the SDS Registry survey can be found in Supporting Information S1.

## 4 | DISCUSSION

In this report, we describe the largest cohort to date of patients with SDS and COVID-19. Most patients reported a short clinical course with few requiring COVID-19–directed therapy, and only one requiring hospitalization; none experienced significant complications or severe cytopenias. However, these results cannot be generalized to patients with more severe comorbidities, and the relatively small number of patients described limits our ability to comment on risk of developing serious COVID-19 compared with the general population. Because survey responses were anonymous, we were unable to follow up with respondents for further information, such as that related to possible vaccine hesitancy. However, for those respondents who did receive a COVID-19 vaccine, vaccines were well tolerated with only minor expected side effects, suggesting that vaccination should be encouraged according to CDC guidelines during this ongoing global pandemic.

## ACKNOWLEDGMENTS

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## CONFLICTS OF INTEREST

The authors would like to highlight a potential conflict of interest as Drs. Akiko Shimamura and Kasiani Myers work closely with Dr. Peter Newburger on the Severe Congenital Neutropenia International Registry.

## ORCID

*Thomas J. Galletta* https://orcid.org/0000-0001-6174-4319
*Akiko Shimamura* https://orcid.org/0000-0002-4683-9958
*Kasiani C. Myers* https://orcid.org/0000-0002-5528-4405

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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