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COVID-19 in patients with primary and secondary immunodeficiency: The United Kingdom experience

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Background: As of November 2020, severe acute respiratory syndrome coronavirus 2 has resulted in 55 million infections worldwide and more than 1.3 million deaths from coronavirus disease 2019 (COVID-19). Outcomes following severe acute respiratory syndrome coronavirus 2 infection in individuals with primary immunodeficiency (PID) or symptomatic secondary immunodeficiency (SID) remain uncertain.
Objectives: We sought to document the outcomes of individuals with PID or symptomatic SID following COVID-19 in the United Kingdom.
Methods: At the start of the COVID-19 pandemic, the United Kingdom Primary Immunodeficiency Network established a registry of cases to collate the nationwide outcomes of COVID-19 in individuals with PID or symptomatic SID and determine risk factors associated with morbidity and mortality from COVID-19 in these patient groups.
Results: A total of 100 patients had been enrolled by July 1, 2020, 60 with PID, 7 with other inborn errors of immunity including autoinflammatory diseases and C1 inhibitor deficiency, and 33 with symptomatic SID. In individuals with PID, 53.3% (32 of 60) were hospitalized, the infection-fatality ratio was 20.0% (12 of 60), the case-fatality ratio was 31.6% (12 of 38), and the inpatient mortality was 37.5% (12 of 32). Individuals with SID had worse outcomes than those with PID; 75.8% (25 of 33) were hospitalized, the infection-fatality ratio was 33.3% (11 of 33), the case-fatality ratio was 39.2% (11 of 28), and inpatient mortality was 44.0% (11 of 25).
Conclusions: In comparison to the general population, adult patients with PID and symptomatic SID display greater morbidity and mortality from COVID-19. This increased risk must be reflected in public health guidelines to adequately protect vulnerable patients from exposure to the virus. (J Allergy Clin Immunol 2021;147:870-5.)

Key words: COVID-19, SARS-CoV-2, primary immunodeficiency, secondary immunodeficiency

INTRODUCTION

As of November 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in 55 million infections worldwide and more than 1.3 million deaths from coronavirus disease 2019 (COVID-19). Risk factors associated with severe disease and mortality from COVID-19 include advancing age and comorbidities associated with direct or indirect suppression of the immune system.[1] The consequences of SARS-CoV-2 infection in individuals with primary immunodeficiency (PID), or those with symptomatic secondary immunodeficiency (SID), remain uncertain. In the United Kingdom, individuals with immunodeficiencies were advised to follow government guidance and either shield or undertake strict social distancing because of their potentially increased risk of mortality from COVID-19.[2] In March 2020, The United Kingdom Primary Immunodeficiency Network began to systematically document the outcomes of COVID-19 in individuals with PID and SID. We report the findings of the first 100 individuals enrolled in this case series.

RESULTS AND DISCUSSION

One hundred individuals, 60 with PID, 3 with autoinflammatory diseases, 4 with C1 inhibitor deficiency, and 33 with symptomatic SID, had been enrolled in this case series by July 1, 2020 (Table I). Fifty-six percent (56 of 100) individuals were female, and 16.3% (15 of 92) were of Black, Asian, or Minority Ethnic backgrounds. Ethnicity data were unavailable for 8 individuals. Seventy percent (70 of 100) individuals had SARS-CoV-2 infection confirmed by PCR (69 of 100), or retrospectively inferred using serology (1 of 100; this individual was not receiving immunoglobulin therapy). The remaining individuals suffered illnesses consistent with COVID-19 that were not confirmed by PCR, due to limited availability of community testing. Fifty-nine percent (59 of 100) individuals were admitted to hospital, and 8% (8 of 100) were admitted to intensive care units.

In individuals with PID, the infection-fatality ratio (IFR) was 20.0% (12 of 60), the case-fatality ratio (CFR) was 31.6% (12 of 38), and the inpatient mortality was 37.5% (12 of 32) in a

population of median age 42.0 years. Univariate analysis demonstrated that increasing age, chronic lung disease, cardiovascular disease, and diabetes mellitus were associated with hospitalization with COVID-19 (Table II). Individuals taking prophylactic antibiotics were also at a higher risk of hospitalization, potentially reflecting chronic infection uncontrolled by immunoglobulin replacement or a more severe immune deficiency. Increasing age, lower baseline lymphocyte count, diabetes mellitus, and chronic renal disease were associated with mortality (Table II). Analysis including only those individuals in whom COVID-19 was proven by

PCR, confirmed increasing age (median age, 37.0 vs 64.0 years; $P = .01$), and lower baseline lymphocyte counts (median lymphocyte count, 1.60 vs 1.00 × 10^9 cells/L; $P = .03$) were associated with mortality. Multiple logistic regression, to consider whether mortality was independently influenced by the prevalence of comorbidities, was partially prohibited by multicollinearity between chronic renal impairment and other variables within this small cohort. A model incorporating all variables except chronic renal impairment found that increasing age was the only variable significantly associated with mortality in patients with PID (odds ratio for mortality, 1.10 per year; CI, 1.02-1.24; $P = .0491$).

Common variable immunodeficiency (CVID) was the most common PID in this cohort (n = 23); an IFR of 34.8% and a CFR of 50.0% were observed in this subgroup, and chronic lung disease was significantly associated with mortality (prevalence in survivors vs nonsurvivors, 46.7% vs 100.0%; $P = .02$). It has been postulated that immune dysregulation associated with CVID confers an increased risk of severe manifestations of COVID-19.[3] In this study, inpatient mortality was greater among individuals with CVID than among those with undefined primary

TABLE I. Description of cohort

Diagnosis	n	Age (y)	Sex, n (% female)	Ethnicity, n (% BAME)*	PCR- proven infection,† n (%)	Hospitalized, n (%)	Deaths (n)	Inpatient mortality (%)	CFR (%)	IFR (%)
Inborn errors of immunity (all)	67	42.0 (28.0-57.0)	38 (56.7)	10 (14.9)	42 (62.7)	34 (50.7)	12	35.3	28.5	17.9
PID (all)	60	42.0 (28.0-58.2)	34 (56.6)	7 (11.7)	38 (63.3)	32 (53.3)	12	37.5	31.6	20.0
SID (all)	33	64.5 (56.0-79.8)	18 (54.5)	5 (15.2)	28 (84.8)	25 (75.8)	11	44.0	39.2	33.3
PIDs										
CVID	23	54.0 (31.8-70.8)	14 (60.9)	2 (8.7)	16 (69.6)	13 (56.5)	8	61.5	50.0	34.8
Undefined primary antibody deficiency	12	43.5 (26.5-71.8)	10 (83.3)	0 (0.0)	6 (50.0)	6 (50.0)	1	16.7	16.7	8.3
Undefined combined immunodeficiency	4	43.0 (30.0-53.75)	2 (50.0)	1 (25.0)	1 (25.0)	1 (25.0)	1	100.0	100.0	25.0
XLA	4	30.5 (28.5-31.0)	0 (0.0)	1 (25.0)	2 (50.0)	3 (75.0)	0	0.0	0.0	0.0
Specific polysaccharide antibody deficiency	3	56.0 (50.0-69.0)	2 (66.7)	0 (0.0)	2 (66.7)	2 (66.7)	1	50.0	50.0	33.3
Chronic granulomatous disease (XL and AR)‡	3	23.0 (3.0-47.0)	2 (67.7)	1 (33.3)	3 (100.0)	1 (100.0)	0	0.0	0.0	0.0
NF-κB haploinsufficiency	2	30.5 (27.0-34.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)	0	0.0	0.0	0.0
CTLA-4 haploinsufficiency	1	Adult	0 (0.0)	1 (100.0)	1 (100.0)	1 (100.0)	1	100.0	100	100.0
ICOS deficiency	1	Adult	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	0	0.0	0.0	0.0
GATA2 deficiency	1	Adult	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	0	0.0	0.0	0.0
Kabuki's syndrome	1	Adult	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0	0.0	0.0	0.0
X-linked lymphoproliferative disease	1	Adult	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0	0.0	0.0	0.0
Wiskott-Aldrich syndrome	1	Adult	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	0	0.0	0.0	0.0
Autoimmune lymphoproliferative syndrome	1	Child	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	0	0.0	0.0	0.0
22q microdeletion syndrome	1	Adult	0 (0.0)	NA	1 (100.0)	1 (100.0)	0	0.0	0.0	0.0
MBL deficiency	1	Adult	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	0	0.0	0.0	0.0
Autoinflammatory diseases										
Hyper-IgD syndrome	1	Adult	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	0	0.0	0.0	0.0
Aicardi-Gouteres syndrome	1	Child	1 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)	0	0.0	0.0	0.0
A20 haploinsufficiency	1	Child	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	0	0.0	0.0	0.0
Other inborn errors of immunity										
C1 inhibitor deficiency	4	46.5 (33.3-53.8)	1 (25.0)	1 (25.0)	2 (50.0)	1 (25.0)	0	0.0	0.0	0.0

AR, Autosomal recessive; *BAME*, Black, Asian, Minority Ethnic; *CGD*, chronic granulomatous disease: *CTLA4*, cytotoxic T-lymphocyte associated protein 4; *GATA2*, GATA-binding factor 2; *ICOS*, inducible T-cell co-stimulator; *NA*, not available; *NF-kB*, nuclear factor kappa B; *XL*, X-linked; *XLA*, X-linked agammaglobulinemia.
Median age and interquartile ranges are provided.
*Ethnicity data not provided for 8 individuals.
†Includes 1 individual proven by serology.
‡Includes 1 X-linked CGD carrier under Immunology care.

TABLE II. Univariate analysis of risk of hospitalization and mortality from COVID-19 in 60 patients with PID

Variable	Not hospitalized	Hospitalized	OR for hospitalization (95% CI)	P value	Survived	Died	OR for mortality (95% CI)	P value
n	28	32			48	12	—	—
Age (y)	32.0 (27.0-46.0)	56.0 (31.0-71.0)	—	.005	34.5 (28.0-53.0)	64.0 (52.3-78.5)	—	.001
Baseline lymphocyte count ($\times 10^9$/L)	1.61 (1.18-2.59)	1.30 (0.92-1.81)	—	.10	1.58 (1.20-2.30)	1.00 (0.58-1.68)	—	.02
Body mass index (kg/m^2)	26.6 (24.4-26.8)	26.45 (24.2-31.9)	—	.82	26.0 (24.4-27.2)	28.0 (22.9-33.1)	—	.88
Sex (% female)	57.1	56.3	1.04 (0.40-2.73)	>.99	56.3	58.3	1.08 (0.30-3.65)	>.99
Ethnicity (%BAME)	7.7	17.2	2.50 (0.44-13.32)	.43	11.4	18.2	1.73 (0.30-11.3)	.62
IgRT (%)	60.7	78.1	2.31 (0.75-6.87)	.17	64.6	91.7	6.03 (0.84-68.49)	.09
Prophylactic antibiotics (%)	35.7	68.8	3.96 (1.28-10.86)	.02	50.0	66.7	2.00 (0.56-6.54)	.35
Current immunosuppression (%)	21.4	15.6	0.68 (0.22-2.61)	.56	18.8	16.7	0.87 (0.17-4.12)	>.99
Chronic lung disease (%)	21.4	62.5	6.11 (2.00-18.79)	.002	37.5	66.7	3.33 (0.92-10.87)	.10
Cardiovascular disease (%)	0.0	18.8	—	.03	8.33	16.7	2.20 (0.37-10.86)	.59
Chronic liver disease (%)	10.7	12.5	1.19 (0.30-5.07)	>.99	10.42	16.7	1.72 (0.30-10.74)	.62
Diabetes mellitus (%)	0.0	21.9	—	.01	6.25	33.3	7.50 (1.67-32.66)	.02
Chronic renal disease (%)	0.0	6.25	—	.49	0.0	16.7	NA	.04
Organ-specific autoimmunity (%)	28.6	25.0	0.83 (0.29-2.40)	.77	29.2	16.7	0.49 (0.10-2.36)	.49
Chronic gastrointestinal disease (%)	25.0	12.5	0.43 (0.13-1.69)	.21	18.8	16.7	0.87 (0.17-4.12)	>.99

BAME, Black, Asian and Minority Ethnic; *IgRT*, immunoglobulin replacement therapy; *OR*, odds ratio.

Median and interquartile ranges are provided for continuous variables. Differences between the distributions evaluated using 2-tailed Mann-Whitney *U* test. Differences between categorical variables, evaluated using 2-tailed Fisher exact test with ORs calculated using the Baptista-Pike method.

antibody deficiencies or X-linked agammaglobulinemia. However, individuals with CVID were, on average, older and a greater percentage were receiving immunoglobulin replacement (86.9% vs 50.0%), suggesting more severe immunodeficiency.[1]

Individuals with SID had worse outcomes than those with PID. The IFR was 33.3% (11 of 33), the CFR was 39.2% (11 of 28), and inpatient mortality was 44.0% (11 of 25) in a population of median age 64.5 years. The most common causes of SID in this cohort were chronic lymphocytic leukemia (8 of 33) and non-Hodgkin's lymphoma (8 of 33). The only significant risk factor associated with hospitalization in this group was age; however, age did not confer a significantly increased risk of mortality (Table III). Hematological malignancy is an independent risk factor for morbidity and mortality from COVID-19, even 5 years beyond the index diagnosis,[1] and our findings are consistent with other studies that describe an overall mortality of 40.0% to 54.4% in hemato-oncology patients.[4,5] Heterogeneity within the SID cohort should be more thoroughly investigated to determine whether biomarkers can prospectively stratify the risk of poor outcome from COVID-19.

A prospective case-control study is necessary to comprehensively understand the risk of morbidity and mortality from COVID-19 in individuals with PID and SID. Nevertheless, comparisons can be made between these data and existing estimates of IFR, CFR, and inpatient mortality for the UK general population (Table IV). In May 2020, the UK CFR in the general population was estimated to be 14.3%; a revised estimate of 1.5% was made on August 4, 2020.[6,7] In this cohort, the CFR of individuals with PID (31.6%) and SID (39.2%) exceed both the original and the revised estimate.

Estimates of the UK IFR have been modeled on data from other countries.[8,9] The overall IFR is estimated to be less than 1%. The highest estimated IFR in any subgroup of the UK general population is 7.8%, in those 80 years and older.[9] In comparison, the overall IFR in the PID cohort was 20.0% and that in the SID cohort was 33.3%, with consistently higher IFR in those 40 years and older (Table IV). Regular, longitudinal PCR sampling and symptom reporting in large PID and SID cohorts will be necessary to accurately determine the spectrum of disease and the IFR and the CFR within these populations.

Comparison of inpatient mortality between the immunodeficiency cohort and the general population provides further evidence that PID or SID is a risk factor for mortality from COVID-19: the International Severe Acute Respiratory and emerging Infections Consortium study documented the outcomes of 20,133 UK patients hospitalized with COVID-19. In this cohort, representative of the general population unwell enough to require hospital admission, inpatient mortality was 26% in a cohort of median age 73 years.[10] The inpatient mortality among individuals with PID (37.5%) or SID (44.0%) exceeded that in this reference population, in cohorts of lower median age (PID, 56.0 years; SID, 67.5 years). Furthermore, inpatient mortality in individuals with PID exceeded that of the general population in all groups older than 40 years (Table IV).

The contribution of comorbidities to this increased risk was considered; compared with the general hospitalized population, preexisting chronic lung disease (62.5% vs 16.7%; *P* <.0001) was more prevalent in the hospitalized PID cohort overall, and in the 18 to 49, 50 to 59, and 70 to 79 age groups (Fig 1). Chronic liver disease was also more prevalent compared with the general population (12.5% vs 3.1%; *P* = .02), but other chronic comorbidities demonstrated similar overall and age-associated prevalence (Fig 1). The prevalence of immunodeficiency-associated comorbidities was not reported by the International Severe Acute Respiratory and emerging Infections Consortium;

TABLE III. Univariate analysis of risk of hospitalization and mortality from COVID-19 in 33 patients with SID

Variable	Not hospitalized	Hospitalized	OR for hospitalization (95% CI)	P value	Survived	Died	OR for mortality (95% CI)	P value
n	8	25	—	—	22	11	—	—
Age (y)	57.5 (47.8-66.0)	67.5 (57.3-80.8)	—	.03	65.0 (56.5-76.5)	60.0 (50.0-81.0)	—	.97
Baseline lymphocyte count (×10^9/L)	1.47 (0.82-1.75)	1.15 (0.65-2.02)	—	.70	1.32 (0.70-1.97)	0.95 (0.60-3.01)	—	.94
Body mass index (kg/m^2)	28.6 (25.7-29.4)	25.2 (20.3-30.0)	—	.25	26.6 (22.8-28.6)	25.8 (20.4-37.3)	—	>.99
Sex (% female)	37.5	60.0	0.40 (0.09-2.24)	.42	55.6	44.4	0.31 (0.08-1.35)	.27
Ethnicity (%BAME)	12.5	16.8	0.71 (0.05-6.24)	.78	14.3	18.2	0.75 (0.13-4.86)	>.99
IgRT (%)	75.0	56.0	0.42 (0.08-2.45)	.43	61.5	54.6	0.69 (0.16-3.12)	.71
Prophylactic antibiotics (%)	62.5	80.0	2.40 (0.49-11.04)	.37	27.3	18.2	1.69 (0.28-9.44)	.69
Current immunosuppression (%)	25.0	40.0	2.00 (0.34-11.07)	.68	27.3	54.6	3.20 (0.74-13.2)	.15
Chronic lung disease (%)	25.0	48.0	2.78 (0.48-15.10)	.42	40.9	45.5	1.20 (0.27-4.91)	>.99
Cardiovascular disease (%)	25.0	32.0	1.41 (0.22-8.00)	>.99	27.3	36.4	1.52 (0.38-7.27)	.70
Chronic liver disease (%)	0.0	4.0	—	>.99	0.0	9.1	—	.33
Diabetes mellitus (%)	0.0	24.0	—	.30	13.6	27.3	2.38 (0.46-11.63)	.38
Chronic renal disease (%)	0.0	20.0	—	.30	13.6	18.2	1.41 (0.22-7.83)	>.99
Organ-specific autoimmunity (%)	0.0	4.0	—	>.99	0.0	9.1	—	.33
Chronic gastrointestinal disease (%)	12.5	4.0	0.29 (0.01-6.28)	.38	9.1	0.0	—	.54

BAME, Black, Asian and minority ethnic; *IgRT*, immunoglobulin replacement therapy; *OR*, odds ratio.
Median and interquartile ranges are provided for continuous variables. Differences between the distributions evaluated using 2-tailed Mann-Whitney *U* test. Differences between categorical variables, evaluated using 2-tailed Fisher exact test with ORs calculated using the Baptista-Pike method.

TABLE IV. Age-stratified risk of mortality from COVID-19 in patients with PID and SID in comparison to UK national data

									PID (n = 60)		
Age group (y)	n	%	PCR^+	Hospitalized	Deaths	%	IFR (%)	CFR (%)	Inpatient mortality (%)	UK IFR (general population)	UK inpatient mortality (general population)
0-9	2	3.3	2	1	0	0.0	0	0	0.0	0.001	0.7
10-19	1	1.7	0	0	0	0.0	0	0	NA	0.007	1.9
20-29	12	20.0	5	3	1	8.3	8.3	20.0	33.3	0.03	4.3
30-39	12	20.0	7	6	0	0.0	0.0	0.0	0.0	0.08	4.2
40-49	9	15.0	5	4	1	8.3	11.1	20.0	25.0	0.16	6.3
50-59	11	18.3	7	7	4	33.3	36.4	57.1	57.1	0.60	10.8
60-69	3	5.0	2	2	1	8.3	33.3	50.0	50.0	1.93	20.2
70-79	6	10.0	6	5	2	16.7	16.7	16.7	40.0	4.28	34.1
>80	4	6.7	4	4	3	25.0	75.0	75.0	75.0	7.8	41.7
									SID (n = 33)		
Age group (y)	n	%	PCR^+	Hospitalized	Deaths	%	IFR (%)	CFR (%)	Inpatient mortality (%)	UK IFR (general population)	UK inpatient mortality (general population)
0-9	0	0.0	NA	NA	NA	0.0	NA	NA	NA	0.001	0.7
10-19	0	0.0	NA	NA	NA	0.0	NA	NA	NA	0.007	1.9
20-29	1	3.0	1	0	0	0.0	0	0	0.0	0.03	4.3
30-39	0	0.0	NA	NA	NA	0.0	NA	NA	NA	0.08	4.2
40-49	3	9.1	3	2	2	16.7	66.6	66.6	100.0	0.16	6.3
50-59	8	24.2	6	6	2	16.7	25.0	33.3	33.3	0.60	10.8
60-69	9	27.3	6	5	2	16.7	22.2	33.3	40.0	1.93	20.2
70-79	4	12.1	4	4	1	8.3	25.0	25.0	25.0	4.28	34.1
>80	8	24.2	8	8	4	33.3	50.0	50.0	50.0	7.8	41.7

NA, Not available.
Estimates of age-stratified IFR in the UK general population are based on modeling studies,[9] and UK inpatient mortality data for the UK general population are based on data derived from the International Severe Acute Respiratory and emerging Infections Consortium study.[10]

however, bronchiectasis (12 of 33) and granulomatous lymphocytic interstitial lung disease (4 of 33) were common in the PID cohort.

The relationship between comorbidities, their severity, and outcomes from COVID-19 in patients with immunodeficiency appears complex. In keeping with the general population,[1]
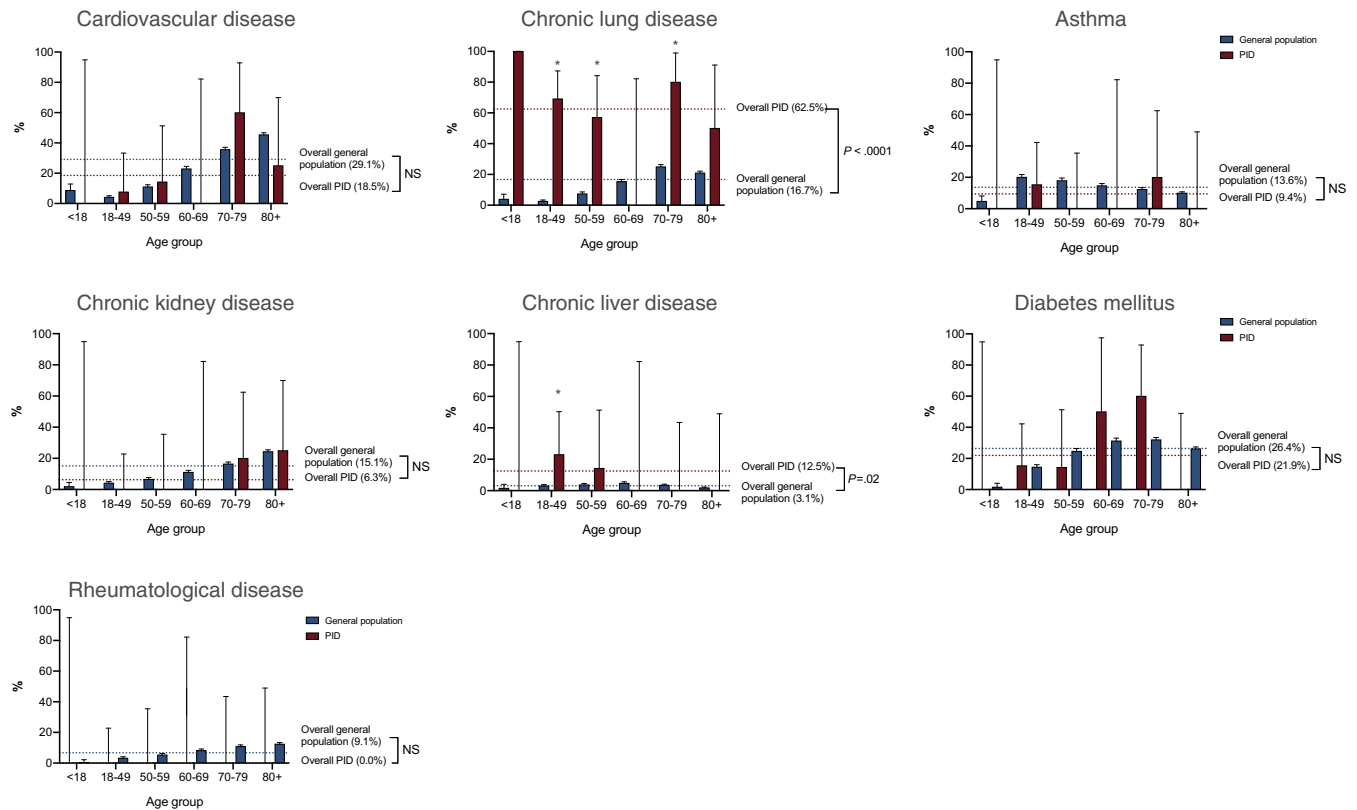
FIG 1. Prevalence of common comorbidities in patients with PID hospitalized with COVID-19 (red bars) compared with the general population (blue bars) based on data from the ISARIC study.[10] Data represent the percentage of individuals within each age bracket with comorbidity. Binomial CIs were calculated by Wilson's method. The overall prevalence of each comorbidity in the general population and in the PID cohort is presented as horizontal dotted lines. Proportions were compared using Fisher exact test. For the purposes of this analysis, the ISARIC categories of "Mild Liver Disease" and "Moderate to Severe Liver Disease" were combined into a single "Liver Disease" and "Diabetes without complications" was combined with "Diabetes with complications" into a single "Diabetes mellitus" category. *ISARIC*, International Severe Acute Respiratory and emerging Infections Consortium; *NS*, not significant. *$P < .05$, Fisher exact test.

increasing age was associated with mortality from COVID-19; however, immunodeficient patients succumb to COVID-19 at significantly younger ages. Advancing age may be associated with progressive worsening of comorbidities associated with PID, such as chronic lung disease, with consequent reductions in physiological reserve. Larger studies must explore the relationships between underlying immunologic defects and the severity of immunodeficiency-associated comorbidities with respect to COVID-19 outcomes. Heterogeneity in outcomes will exist between the different immunodeficiencies that have been collectively analyzed in this study (eg, CVID vs pure antibody deficiency). However, from a public health perspective, it is difficult to justify risk stratification until the immunologic mechanisms and risk factors associated with susceptibility to COVID-19 in immunodeficient patients are better understood.

As a clinician-reported registry, we are unable to guarantee that all SARS-CoV-2 infections in immunodeficient patients have been captured by this study. Children with immunodeficiencies are underrepresented: only 5% of recorded cases occurred in individuals younger than 18 years, all of whom survived. National data suggest very low mortality in healthy children and the underrepresentation of pediatric cases herein may represent

highly effective shielding or unrecognized mild or asymptomatic disease. The International Union of Immunological Societies' COVID-19 case series reported a lower overall COVID-19 mortality of 10.0% (10 of 100) in individuals with inborn errors of immunity[11]; that cohort contained 32.0% (32 of 100) children, providing further evidence that age is a significant risk factor for COVID-19 morbidity and mortality.

Because of national shortages in PCR testing, only 34.1% (14 of 41) of nonhospitalized cases of COVID-19 were molecularly confirmed in this study. It is possible that these individuals may have suffered a clinically indistinguishable, non–SARS-CoV-2 infection. However, the overall inpatient mortality of 39.0% (23 of 59), 94.9% of whom had PCR-proven disease, appears to be a valid reflection of the increased risk faced by adults with immunodeficiency compared with the general population.

The comparatively high morbidity and mortality in PID and SID should inform public health policy and be communicated to patients so they can take appropriate actions to reduce their exposure to the virus.

For detailed methods, please see the Methods section in this article's Online Repository at www.jacionline.org.

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Key messages

- Individuals with PID had an overall IFR of 20.0%, a CFR of 31.6%, and inpatient mortality of 37.5%.
- Individuals with symptomatic SID had an IFR of 33.3%, a CFR of 39.2%, and an inpatient mortality of 44.0%.
- The IFR, CFR, and inpatient mortality in patients with PID or SID are far greater than estimates for the general population.

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METHODS

In March 2020, the United Kingdom Primary Immunodeficiency Network, the professional body for clinical immunologists in the United Kingdom, established a fully anonymized case series to collate clinical information on outcomes following SARS-CoV-2 infection in patients with PID and SID across the United Kingdom. Data collection proformas were sent to all UK pediatric and adult immunologists by email. Data collected included age, sex, ethnicity, body mass index, pre–COVID-19 lymphocyte count, treatments patients were receiving before COVID-19 (eg, immunoglobulin replacement, immunosuppression, and antibiotic prophylaxis), existing chronic comorbidities, whether infection was suspected or proven by PCR or serology, whether individuals were hospitalized, and whether individuals survived or died. No patients have been previously reported.

These data were collated and analyzed by the authors using GraphPad Prism 8.4.2 (GraphPad Prism Software, San Diego, Calif). Differences between the distributions of continuous variables were evaluated using the 2-tailed Mann-Whitney U test. Differences between categorical variables were evaluated using the 2-tailed Fisher exact test. Odds ratios were calculated using the Baptista-Pike method. CFR is defined as the ratio between total deaths and total PCR-proven infections. IFR is defined as the ratio between total deaths and total suspected or proven SARS-CoV-2 infections. National data regarding COVID-19 epidemiology were sourced from UK government statistics, the International Severe Acute Respiratory and emerging Infections Consortium study,[E1] and previous modeling.[E2,E3] When analyzing the distribution of baseline lymphocyte counts in the SID cohort, patients with chronic lymphocytic leukemia were excluded.

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