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

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What is the natural history of acute Covid in patients with immunodeficiencies?

Study Population

100 patients

60 PID

33 SID

3 Autoinflamm.

4 C1-INH deficiency

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

PID: Risks for hospitalization and death

Age

ALC

Abx

CLD

DM

ESRD

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

Secondary Immunodeficiency

Chronic lymphocytic leukemia (8 of 33)

Non-Hodgkin Lymphoma (8 of 33)

Note: hematological malignancy has already been established as an independent risk factor for mortality from acute Covid

SID: Risk factors for hospitalization and death

Age

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 ($\times 10^9$/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

Fatality Ratios

Infection fatality ratio (IFR):

$$\frac{\text{Total deaths}}{\text{Suspected or proven Covid}}$$

Case fatality ratio (CFR):

$$\frac{\text{Total deaths}}{\text{PCR-proven Covid}}$$

Fatality ratios: PID

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

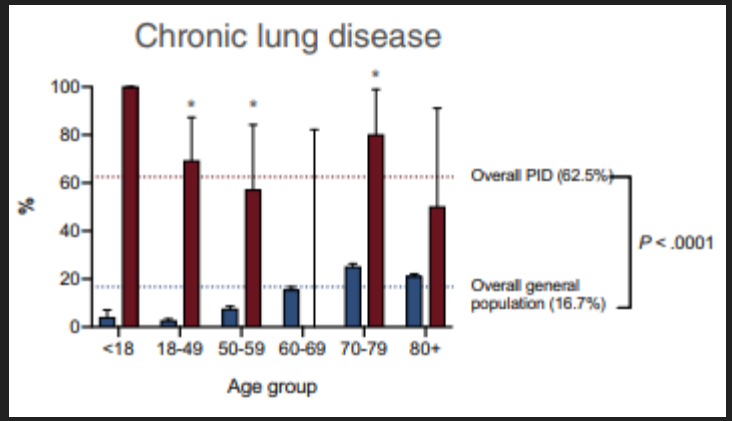
		PID (n = 60)									
Age group (y)	n	%	PCR+	Hospitalized	Deaths	%	IFR (%)	CFR (%)	Inpatient mortality (%)	UK IFR (general population)	UK inpatient mortality (general population)
0-9	2	3.3	2	1	0	0.0	0	0	0.0	0.001	0.7
10-19	1	1.7	0	0	0	0.0	0	0	NA	0.007	1.9
20-29	12	20.0	5	3	1	8.3	8.3	20.0	33.3	0.03	4.3
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

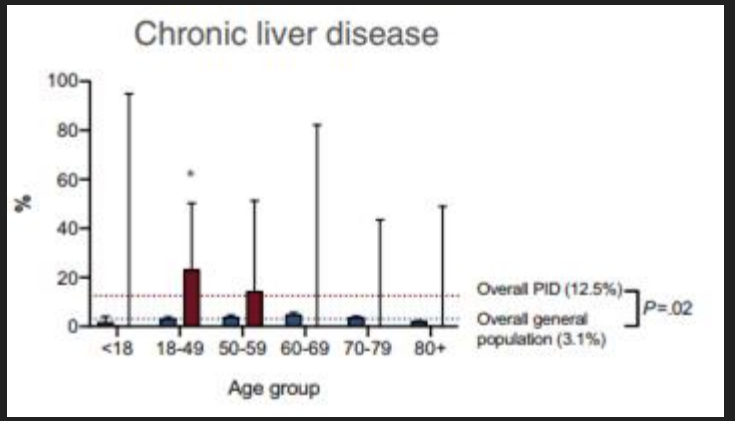
Fatality Ratios: SID

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

	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

Comorbidities in hospitalized Covid patients





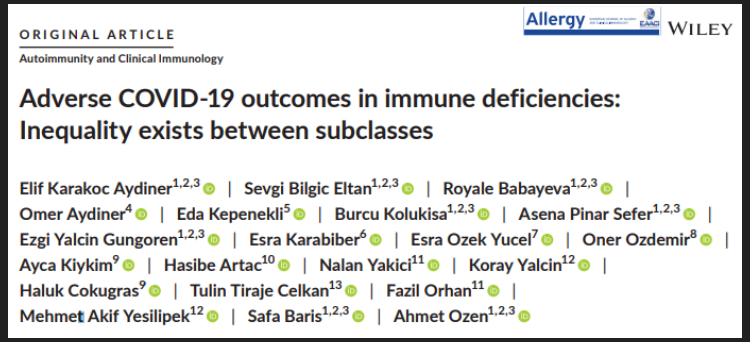
Conclusions

Individuals with PID were much more likely to die of acute Covid compared to the general population

Individuals with SID died at even higher rates than those with PID

Sequelae of PID (chronic lung disease) contributed to poor outcomes among older patients

Follow up studies



ORIGINAL ARTICLE

Autoimmunity and Clinical Immunology

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Adverse COVID-19 outcomes in immune deficiencies: Inequality exists between subclasses

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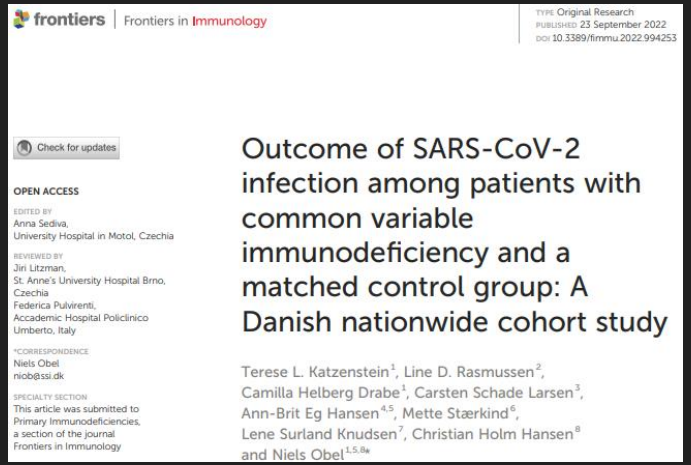

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Outcome of SARS-CoV-2 infection among patients with common variable immunodeficiency and a matched control group: A Danish nationwide cohort study

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Questions