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Coronavirus (COVID-19) infection in children at a specialist centre: initial experience and outcome

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Key words: COVID-19, coronavirus, paediatric, childhood, infection

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The 2019 novel coronavirus SARS-CoV-2 causes potentially severe respiratory and gastrointestinal symptoms in humans (coronavirus disease; COVID-19).[1] As of late May 2020, there had been around 5 million confirmed cases of COVID-19, and >300,000 associated deaths.[1] COVID-19 can affect children but appears to be associated with fewer symptoms and less severe disease compared with adults, with correspondingly lower case-fatality rates.[2] In the United Kingdom, Public Health England (PHE) have outlined a shielding strategy designed to protect those deemed to be extremely vulnerable to COVID-19 infection,[3,4] such as individuals that are immunocompromised. We examined a cohort of paediatric patients presenting to a specialist children's hospital with suspected COVID-19 to document their clinical behaviour and outcomes with regard to presence of underlying medical conditions associated with vulnerability.

We retrospectively used routinely collected, deidentified hospital data within a secure digital research environment (REC approval 17/LO/0008) from children presenting to a specialist children's hospital in London, UK, with suspected COVID-19 between 1st March and 15th May 2020. COVID-19 positive cases (CoVPos) were those with clinical features of COVID-19 and a positive PCR-test for Sars-CoV-2 (either directly or positive familial Sars-Cov-2 testing). Patients were classified regarding vulnerability group using NHS Digital methodology.[4]

Sixty five CoVPos patients (median age 9 years (range 1 week – 17.2 years) presented during the study period (Table 1, Appendix), of which 31 (47.7%) were classed as vulnerable. The most common provisional diagnosis codes for the group were sepsis, fever and pneumonia. Only one patient died, with an underlying medical condition, which was not directly due SARS-CoV-2 infection.

Of the 65 CoVPos patients, 29 (44.6%) required admission to intensive care (ITU). Of these, 14 (48.3%) were classed as vulnerable ($p = 1$). The length of stay on ITU for all patients was 4 [2.4 – 10.6] days. Those patients classed as vulnerable had a significantly longer stay of 11[3.7 – 15.1] days ($p < 0.001$). Of the 29 patients admitted to ITU, 18 (62%) required mechanical ventilation, of which 10 (55.6%) were classed as vulnerable ($p = 0.53$). Overall hospital stay was also significantly shorter in the non-vulnerable group (3.9 [2.5 – 15.7] days vs 16.2 [3.8 – 20.8] days, $p < 0.001$). As of the end date, nine patients (13.8%) remained in hospital, three of whom (33%) were classed as vulnerable ($p = 0.35$). During the study period, with a daily average of 326 inpatients, on average 10 were CoVPos at any time, representing around 3% of the hospital inpatient population, much lower than the estimated 25% COVID-19+ inpatient proportion reported across adult London trusts during this period.[5]

These data demonstrate the characteristics and outcomes of children presenting to a specialist children's hospital with clinical features of COVID-19 disease and positive testing, and confirm that children may be infected with SARS-CoV-2, which may lead to severe disease with requirement for intensive care admission. It should be emphasised that the current cohort of patients are highly preselected, both for children with severe disease and those with underlying medical conditions, and therefore the findings are not applicable to the general paediatric population. Previous data from general centres suggests <1% of COVID-19 admissions represent children <18 years and data from multiple North American hospitals reported few COVID19 positive patients per intensive care unit.[6,7] As such, the present cohort disproportionately represents those with complex underlying medical conditions, consistent with the fact that around three quarters of inpatients registered with the hospital in the previous year would be considered as vulnerable according to COVID-19 guidance.[4] This is not unexpected, since the hospital represents a centre for paediatric transplantation, genetic diseases such as congenital immunodeficiency and paediatric malignancy.

Furthermore, in those with confirmed COVID-19, the proportion of patients with underlying vulnerable conditions requiring intensive care admission for mechanical ventilation were not significantly different to those classed as non-vulnerable. Whilst the possible effects of lockdown and shielding remain undetermined, given that the series includes cases pre and post-lockdown, these data raise the possibility that underlying medical conditions which place children at increased risk of COVID-19 disease or complications may differ from adults. This is consistent with a recent study reporting no mortality in a multicenter cohort of patients with cystic fibrosis affected by COVID-19,[8] and another using a renal registry, suggesting that children receiving immunosuppressive treatment appear to have a mild COVID-19 clinical course.[9] Susceptibility for COVID-19 among vulnerable groups may therefore be both disease-specific and related to patient age.

In addition to the typical features of COVID-19 disease described in adults, whilst most children who are infected appear to have mild disease,[2] some may represent an unusual associated systemic inflammatory condition, (paediatric inflammatory multisystem syndrome temporally related to Sars-Cov-2 infection; PIMS-TS).[10] The criteria for the definitive diagnosis of PIMS-TS are evolving, and it remains uncertain whether any of the current COVID+ patients could represent such cases, and further studies are underway examining the PIMS-TS phenomenon.

Limitations of these data include the retrospective nature using routine data, lack of a matched 'normal' control group and the highly preselected population, from a specialist children's hospital, which is not representative of the paediatric population as a whole; although these data do provide information regarding this potentially high risk group. It should also be noted that since vulnerable children may be shielded, the pattern of presentation reported may not be representative of a non-shielded situation, and further epidemiological studies are required.

Declaration of interests

The authors declare no conflicts of interests.

Funding

RI is funded by a British Heart Foundation Research Fellowship Grant. HH is funded by NIHR UCLH BRC and HDRUK, NJS is funded by GOSHCC and HDRUK.

Role of the funding source

The study sponsor / funders had no role or influence in study design, in the collection, analysis, and interpretation of data, in the writing of the report or in the decision to submit the paper for publication

Role of the authors

The corresponding author (RI) and NJS, JB confirm that they had full access to all the data in the study and had final responsibility for the decision to submit for publication. NJS, RI and AT conceived the study. JB, RI, MC, and WB performed the analyses. All authors contributed to the critical appraisal and writing of the manuscript and approved the final submission.

References

1. Coronavirus disease 2019 [Internet]. [cited 2020 May 3]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Feb 28;
3. Guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19 - GOV.UK [Internet]. [cited 2020 May 3]. Available from: https://www.gov.uk/government/publications/guidance-on-shielding-andprotectingextremely-vulnerable-persons-from-covid-19/guidance-on-shielding-andprotectingextremely-vulnerable-persons-from-covid-19
4. COVID-19 – high risk shielded patient list identification methodology - NHS Digital [Internet]. [cited 2020 May 3]. Available from: https://digital.nhs.uk/coronavirus/shielded-patient-list/methodology
5. Covid-19 hospital admissions 'flattening' | News | Health Service Journal [Internet]. [cited 2020 May 3]. Available from: https://www.hsj.co.uk/coronavirus/covid-19hospitaladmissions-flattening/7027364.article
6. Parri N, Lenge M, Buonsenso D. Children with Covid-19 in Pediatric Emergency Departments in Italy. *N Engl J Med*. 2020 May 1 [cited 2020 May 3];NEJMc2007617. Available from: http://www.nejm.org/doi/10.1056/NEJMc2007617
7. Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. *JAMA Pediatr* 2020 May 11 [cited 2020 May 12]; Available from: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2766037
8. Cosgriff R, Ahern S, Bell SC, Brownlee K, Burgel P-R, Byrnes C, et al. A Multinational report to characterise SARS-CoV-2 infection in people with cystic fibrosis. *J Cyst Fibros*. 2020 Apr [cited 2020 May 3]; Available from: https://linkinghub.elsevier.com/retrieve/pii/S1569199320301259
9. Marlais M, Wlodkowski T, Vivarelli M, Pape L, Tönshoff B, Schaefer F, Tullus K.The Severity of COVID-19 in Children on Immunosuppressive Medication. *Lancet Child Adolesc Health* 2020 May 13. doi: 10.1016/S2352-4642(20)30145-0. Online ahead of print.

10. Guidance - Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 | RCPCH [Internet]. [cited 2020 May 3]. Available from: https://www.rcpch.ac.uk/resources/guidance-paediatric-multisysteminflammatorysyndrome-temporally-associated-covid-19

Table. Patient demographic data, proportion in vulnerable groups, outcome and laboratory features of 65 CoVPos patients presenting to a specialist children's hospital with COVID-19 disease. (Median [interquartile range] and N (%))

	COVID–19 Positive
Number of Patients	65 (38.7)
Male	38 (58.5)
Female	27 (41.5)
Age (Years)	9 [0.9 - 14]
Vulnerable*	31 (47.7)
1 (National) Transplant	1 (3.2)
1d (National) Transplant Medication	1 (3.2)
2a (National) Cancer undergoing active chemo/radiotherapy	7 (22.6)
2b (National) Haematological Cancers	2 (6.4)
3 (National) Respiratory	1 (3.2)
4 (National) Rare genetic, metabolic and autoimmune diseases	5 (16.2)
C (Local) People with severe respiratory conditions	5 (16.2)
D (Local) People with rare diseases	1 (3.2)
E (Local) People on immunosuppression therapies	1 (3.2)
O (Local) Other potential factors	7 (22.6)
Mortality	1 (1.5)**
Mortality in Vulnerable	1 (1.5)
Mortality in Non-Vulnerable	0

Ethnicity	
Asian	12 (18.5)
Black African	6 (9.2)
Other	3 (4.6)
Unrecorded/Refused	31 (47.7)
White	13 (20)
Alanine Transaminase (U/L)	41.5 [29 – 74]
Albumin (g/L)	32 [27 – 36]
AntiDNAase B (U/mL)	310 [80.8 – 402]
AntiStreptolysin O (IU/mL)	285 [134 – 384]
Aspartate Transaminase (U/L)	70 [43 – 100]
C-Reactive Protein (mg/L)	28 [10 – 74]
Creatine Kinase (U/L)	63.5 [35 – 214]
Creatinine (µmol/L)	23 [14 – 46]
D-Dimers (µg/L)	1876 [1043 – 3618]
Ferritin (µg/L)	788 [445 – 1863]
Fibrinogen (g/L)	3.65 [2.4 – 4.8]
Interleukin-6 (pg/mL)	50 [50 – 152]
Interleukin-10 (pg/mL)	50 [50 – 50]
Lactate Dehydrogenase (U/L)	848 [654 – 1136]
Lymphocytes (x10*9/L)	1.44 [0.64 – 2.49]
Neutrophils (x10*9/L)	3.90 [1.46 – 8.60]
NT-pro-Brain Natriuretic Peptide (pg/mL)	3550 [626 – 6992]

Prothrombin time (seconds)	12 [11.3 – 13]
Total bilirubin (µmol/L)	6 [3 – 10]
Triglycerides (mmol/L)	2.48 [1.65 – 3.56]
Troponin I (ng/L)	54 [13 – 157]
Urine Total Protein (g/L)	0.12 [0.12 – 0.62]
White Blood Cells (x10*9/L)	8 [3.38 – 13.2]

*Based on UK guidance for vulnerable groups[4]
**The death in this group occurred in a child with proven SARS-CoV-2 infection but was related to pre-existing underlying conditions and associated coinfection.

Figure (Top). Presentations to a specialist children's hospital of children with COVID-19 infection by vulnerability status.

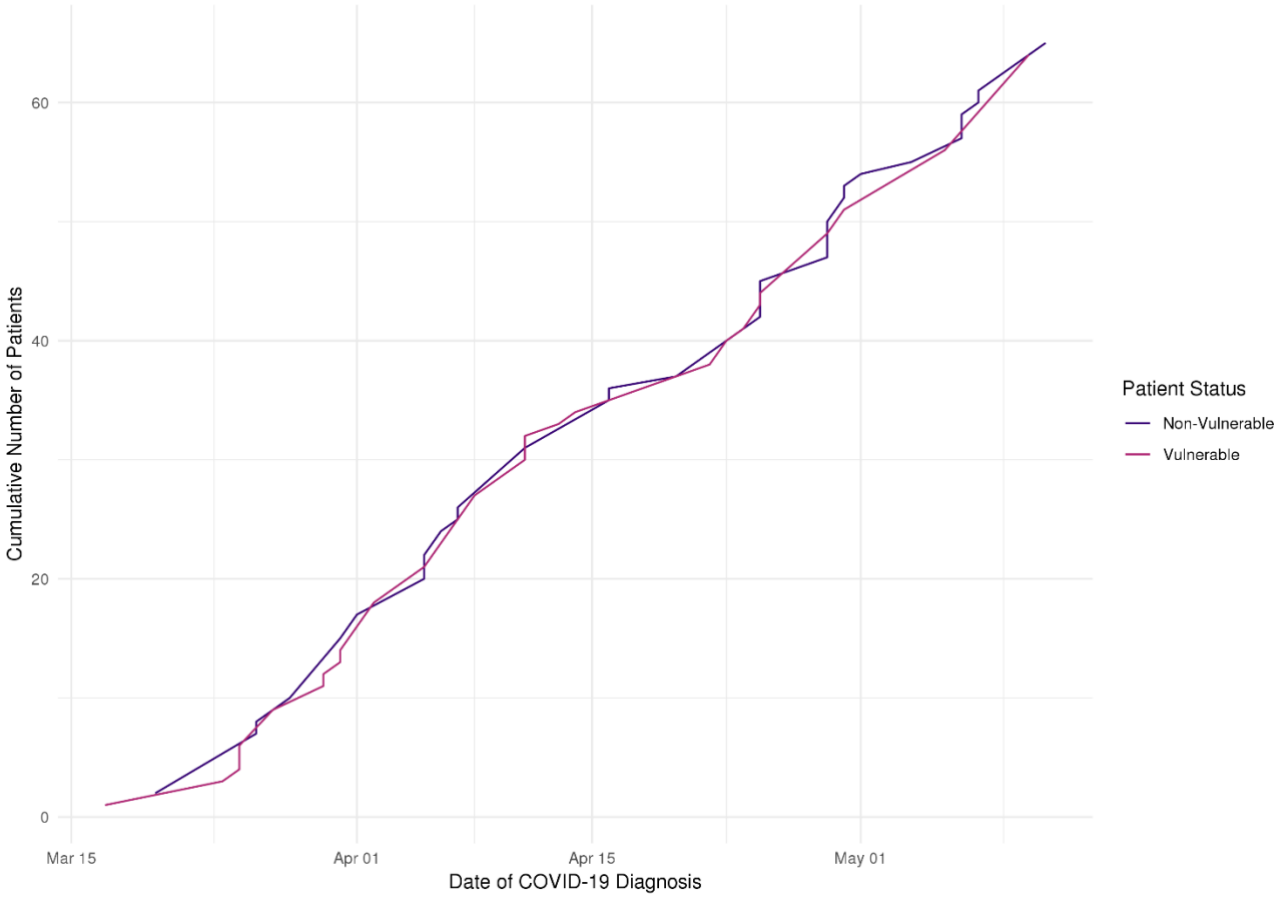

Figure (Bottom). Vulnerability groups for admissions of 65 paediatric patients symptomatic with suspected COVID-19 disease.