Short Term Respiratory Outcomes in Children with Antibody Positive Paediatric Multisystem Inflammatory Syndrome: Temporally Associated With SARS-COV-2 (PIMS-TS)

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Abstract:

Paediatric multisystem inflammatory syndrome: temporally associated with SARS-COV-2 (PIMS-TS) is a well described rare but severe COVID-19 related syndrome. PIMS-TS have been reported in children from geographical areas of high COVID-19 infection. Most children with PIMS-TS require management in an intensive care unit with variable respiratory involvement. Adults recovering from COVID-19 infection have been reported to suffer from respiratory morbidity but such outcomes are unknown in children. We present the first report of normal short term respiratory outcomes as measured by spirometry in children with SARS-COV-2 antibody positive, PIMS-TS syndrome managed at a specialist children's hospital in the UK.

Introduction:

The Paediatric Inflammatory Multisystem Syndrome temporally associated with SARS-CoV-2 (PIMS-TS) is now a well-recognised syndrome.[1] The features of PIMS-TS are fever with any, some or all of Kawasaki disease-like features, gastrointestinal symptoms, cardiac dysfunction, and shock. Children frequently require intensive care admission with 20% requiring mechanical ventilation.[2] The management focuses on supportive care with immunomodulation, in some, to treat hyper inflammation and prevent cardiac complications.[2, 3]

Severe COVID-19 infection in adults results in significant respiratory morbidity post recovery. In contrast to adults, although severe respiratory symptoms are less common in children with COVID-19 infection and PIMS-TS, the post recovery respiratory outcomes are unknown. We describe the spirometry results of children with PIMS-TS performed as part of a multidisciplinary clinical monitoring program, from a tertiary children’s hospital in the United Kingdom.

Methods:

Children aged six years and above with a clinical diagnosis of PIMS-TS and a positive IgG antibody to SARS-COV-2 virus admitted to our hospital between 10

April and 29 May 2020 were identified prospectively.[1] Anonymised data were collected from clinical notes and hospital electronic patient records. The cohort included patients whose cardiac and intensive care outcome has been previously described.[4] Spirometry was performed within two weeks of hospital discharge (baseline) and four to six weeks later (follow up).

Spirometry was performed by a physiologist using an EasyOne Air Spirometer (ndd Medizintechnik AG, Switzerland) according to European Respiratory Society guidelines. The data were analysed for quality by a senior physiologist and two respiratory physicians and compared to predicted values based on the Global Lung Initiative 2012 reference equations. Forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and forced expiratory flow at 25-75% of the FVC ($FEF_{25-75\%}$) were measured and the data was recorded as percentage predicted, z score and the actual values. The data were analysed using GraphPad Prism v5 (GraphPad Software, La Jolla, CA, USA). The Wilcoxon matched pair test was used to compare the paired data.

Results:

Eighteen children were admitted fulfilling the criteria for PIMS-TS. 12 (66·6%) were aged above six years, and represent the cohort of children described below.
Of the twelve children, eleven (91·6%) were African/Afro Caribbean, Asian or mixed ethnicity. None had preceding respiratory conditions. Nine children (75%) were admitted to the intensive care unit and two (16·6%) were ventilated for 3·6 and 4 days. All 12 children tested positive for SARS-COV-2 IgG antibody none had positive PCR test for SARS-COV-2 and 10/12 (83.3% had respiratory symptoms. The respiratory features were cough 3/12 (25%), dyspnoea 7/12 (58·3%), and tachypnoea 10/12 (83·3%). Two children had no respiratory symptoms (16·6%). Chest radiographs were performed in 11/12 (91·6%) with pulmonary consolidation reported in seven (58·3%) children (Table 1a).

Ten (83·3%) children were treated with intravenous Immunoglobulin and seven (58·3%) were treated with 2 to 3 weeks of systemic steroids. One patient had

tocilizumab. The median duration of hospital admission was 12·5 days (IQR 9·2-13·7). All 12 children had normal oxygen saturations (>93%) at hospital discharge. Follow up spirometry was performed at a median of 33 days post hospital discharge (IQR 25-42 days) and at a median of 16 days after stopping steroids (IQR 6-22 days). Reproducible, quality spirometry data were available in 11/12 (91·6%); one patient had variable spirometry technique and was excluded from the analysis. Of the 11 patients, two had data either at baseline or follow up only (both normal) leading to nine paired data points.

The spirometry showed normal FEV_1 (>80%) and FVC (>80%) in eight patients at baseline and in all ten at follow up. FEV_1 but not FVC at baseline were lower in 7/12 children treated with systemic steroids compared to 5/12 without, 84% (IQR 71-90) vs. 97·5% (IQR 90-102·8), and 85% (IQR 76-90) vs 96% (IQR 89·5-106·3) respectively (p=0·04, p=0·07) . No difference was found between FEV_1 and FVC at baseline and follow up (p=0·16, p=0·07 respectively). No difference was found between baseline FEV_1/FVC and $FEF25_{-75\%}$ at baseline and follow up, (p=0·2, p=0·09 respectively) (table 1b). Both children who were ventilated had normal spirometry at follow up. None had symptoms of breathlessness at follow up.

Discussion:

This report is the first to describe the short-term respiratory outcomes of a well-defined cohort of children with PIMS-TS and positive SARS-COV-2 antibody. Although 83.3% had respiratory symptoms during admission, all the children had normal spirometry at four to six weeks post discharge from the hospital with eight (80%) having normal spirometry within eight days of discharge from the hospital. PIMS-TS have been postulated to be an immune mediated disease triggered by SARS-CoV-2 infection. The severities of symptoms are varied, but most children present with profound shock and cardiovascular manifestations requiring management in an intensive care setting. Two (16·6%) children who required mechanical ventilation, had normal spirometry at 4-6 weeks. The children who received systemic steroids and immunoglobulin therapy appear to have lower FEV_1/ FVC compared to those who received only immunoglobulin. This is likely to reflect severe disease at presentation prompting treatment with systemic steroids.

Our study is limited by the small number of patients and the absence of spirometry in children before the illness. However, none had prior respiratory symptoms and therefore it is reasonable to speculate normal spirometry in these children before the illness. We did not measure the diffusion capacity or total lung volume during the immediate follow up, but all children had normal spirometry, normal oxygen saturations, and no functional limitation. The infection control policies restricted access to detailed pulmonary function tests. Restrictive lung disease and diffusion abnormalities have been described in adults recovering from severe COVID-19 infection.[5] However, the pathophysiology in PIMS-TS is likely to be different to adult COVID-19 disease.

In summary we report normal spirometry and no respiratory limitation in children with PIMS-TS at four to six weeks post hospital discharge. The severity of the disease or the treatment has no effect on the short-term respiratory outcome which needs confirmation in a larger cohort. The immune mechanism underlying lung sparing effect of the SARS-CoV-2 virus in children needs further exploration.

Contributor statements:

PN, EA, CH, AC conceptualized and designed the study, critically reviewed the manuscript and approved the final manuscript as submitted.

DC, CH wrote the first draft of the manuscript and critically reviewed the manuscript for important intellectual content.

PN, CH, EA, HK, BS wrote the data analysis plan and helped with data analyses and critically reviewed the manuscript for important intellectual content.

DC, PD, CH performed data collection, performed initial analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.

PN, CM, BS, DJ, HK, SW designed the data collection instruments, coordinated and supervised data collection and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Declaration of interests:

We declare no competing interests

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Study approval

The study was classified and registered as service evaluation following assessment using the UK NHS research governance assessment tool (http://www.hra-decisiontools.org.uk/research/). The study was then reviewed by the Research Governance department at our institution (Birmingham Women's and Children's NHS Foundation Trust) and deemed to not require ethical approval (R&D Director's letter of approval available). All patients and/or their parents/legal guardians provided signed informed consent to inclusion of de-identified data in this report.

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