Table s4. PICO 2: Should serologic testing vs. no testing be performed to detect past or current COVID-19 infection in patients presenting with symptoms consisting with Pediatric inflammatory multi-system syndrome (PIMS)?

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<thead>
<tr>
<th>Study</th>
<th>PIMS Suspicion Criteria</th>
<th>Patients Characteristics</th>
<th>Serology Test/ Results</th>
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<tr>
<td>Perez-Toledo UK Case</td>
<td><strong>PIMS criteria:</strong> The Royal College of Pediatrics and Child Health Guidance for PIMS was used and these include: Child (16 years) presenting with 1 AND 2 AND 3:</td>
<td><strong>N:</strong> 8</td>
<td>1. Elisa</td>
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<td>1. Symptoms: persistent fever, lab results reflecting inflammation (neutrophilia, elevated CRP and lymphopaenia), evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder). Other features include coagulopathy. (This may include children fulfilling full or partial criteria for Kawasaki disease).</td>
<td><strong>Hospitalized:</strong> All patients were hospitalized between 28th April – 8th May 2020.</td>
<td>- Platform: Elisa</td>
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<td>2. Exclusion of any other microbial cause.</td>
<td><strong>Age:</strong> Median age: 9 (7-14 years)</td>
<td>- Antibody type: IgM, IgG, IgA, IgG1-4</td>
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<td>3. SARS-CoV-2 PCR testing may be positive or negative</td>
<td><strong>Gender:</strong> 63% Males</td>
<td>- Antibodies target: Spike protein</td>
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<td><strong>Race:</strong> Mixed</td>
<td>- Approval: NR</td>
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<td></td>
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<td><strong>PCR testing:</strong> All negative</td>
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<td><strong>Past COVID-19 exposure:</strong> NR</td>
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<td><strong>Patients presenting symptoms:</strong> Fever (100%), GI symptom (100%), overlapping hyperinflammation with either typical or atypical Kawasaki disease (87.5%), overlapping symptoms of Hyper-inflammation and toxic shock syndrome (12.5%), and rash (75%)</td>
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<td><strong>Impaired Myocardial Function:</strong> 63% (on Echocardiography)</td>
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<td><strong>PICU admission:</strong> 75%</td>
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<td><strong>Laboratory results:</strong> Median CRP 188 (136-255) mg/L, Median Ferritin 1325 (819-2121) µg/L</td>
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<td><strong>Treatment:</strong> All patients received supportive care (antibiotics, respiratory and cardiovascular support as indicated. Patients received IVIG and/or steroids if they fulfilled either full or atypical Kawasaki disease criteria</td>
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<td><strong>Outcome:</strong> Patients D/C from PICU but remained as in-patients.</td>
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<td>Whittaker UK Case</td>
<td><strong>PIMS criteria:</strong> Patients meeting the UK, CDC, or WHO PIMS criteria without proof of SARS-CoV-2 exposure.</td>
<td><strong>N:</strong> 58 (including 8 patients from Riphagen study)</td>
<td>1. EDI COVID-19 IgG ELISA Kit</td>
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<td><strong>Kawasaki Disease criteria:</strong> American Heart Association criteria; Persistent fever and 4 of 5 mucocutaneous features (erythema and cracking of lips, strawberry tongue and/or erythema of</td>
<td><strong>Hospitalized:</strong> All patients were hospitalized between 23rd March– 26thth May 2020.</td>
<td>- Platform: Elisa</td>
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<td><strong>Age:</strong> Median 9 years (3 months- 17 years)</td>
<td>- Antibody type: IgG</td>
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<td><strong>Gender:</strong> 57% females</td>
<td>- Antibodies target: NR</td>
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<td><strong>Race:</strong> black (38%) or Asian (31%), White (21%), other (10%).</td>
<td>- Approval: NR</td>
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<td>IgG: 40/46 (87%)</td>
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<td>Riphagen UK Case Series</td>
<td>oral and pharyngeal mucosa; bilateral bulbar conjunctival injection without exudate; rash [maculopapular, diffuse erythroderma]; erythema and edema of the hands and feet in acute phase and/or periungual desquamation in subacute phase; and cervical lymphadenopathy [&gt;1.5 cm diameter])</td>
<td><strong>PCR positive:</strong> 15 patients (26%)  <strong>Past COVID-19 exposure:</strong> 45/58 (78%) (PCR or Serology positive)  <strong>Patients presenting symptoms:</strong> Fever (100%), Sore throat (10%), headache (26%), abdominal pain (53%), erythematous rash (52%), conjunctival injection: (45%), lymphadenopathy (16%), mucus membrane changes and cracked lips (29%), swollen hands and feet (16%),  <strong>Severe cases:</strong> PICU admission (50%), AKI (22%), shock requiring Inotropic support (47%), mechanical ventilation (43%):  <strong>Laboratory results:</strong> CRP 229 (156-338) mg/L, Ferritin 610 μg/L (359-1280)  <strong>Treatment:</strong> IVIG (71%), Corticosteroids (64%), IL-1 receptor antagonist (5%), Infliximab (14%)  <strong>Outcome:</strong> Coronary artery aneurysm (14%), Death (2%)</td>
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<td>Verdone Italy Case Series</td>
<td><strong>Study population included in Whittaker study.</strong></td>
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<td><strong>PIMS criteria:</strong> This study included patients presenting Kawasaki-like syndrome in the Italian epicenter of COVID-19,  <strong>Kawasaki Criteria:</strong> Definition based on the 2017 American Heart Association criteria that divides patients into two categories.  1) Classic Kawasaki: fever for ≥5 days + 4 or more clinical criteria including bilateral bulbar non-exudative conjunctivitis, changes of the lips or oral cavity, non-suppurative laterocervical lymphadenopathy, polymorphic rash, erythema of the palms and soles, firm induration of the hands or</td>
<td><strong>N:</strong> 10  <strong>Hospitalized:</strong> Patients diagnosed with Kawasaki disease admitted to the General Paediatric Unit of Hospital Papa Giovanni XXIII (Bergamo, Italy), between Jan 1, 2015, and April 20, 2020.  <strong>Age:</strong> Range (2-16)  <strong>Gender:</strong> 70% boys  <strong>Race:</strong> NR  <strong>PCR testing:</strong> 3/9 positive. (1 not done)  <strong>Past COVID-19 exposure:</strong> 5/10 patients had contact with a suspected or confirmed COVID-19 case.  <strong>Patients presenting symptoms:</strong> Classic Kawasaki (50%), Incomplete Kawasaki (50%)</td>
<td><strong>1. NADAL COVID-19 IgG/IgM Test</strong>  - Time since symptoms onset (4 to 30days)  - Platform: LF  - Antibody type: IgM,IgG  - Antibodies target: NR  - Approval: NR  - IgM: 3/10 (30%)  - IgG: 8/10 (80%)  - IgM or IgG: 8/10 (80%)</td>
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| Toubiana France Case Series | feet, or both) and incomplete types.  2) Incomplete Kawasaki: fever for ≥5 days plus + 2 or 3 of the complete Kawasaki symptoms. | Impaired Myocardial Function: Abnormal echocardiography signs (60%)  
PICU admission: The number of patients admitted to the PICU was not reported, however, 2 patients required inotropes.  
Laboratory results: Elevated CRP (100%), elevated Ferritin (5/9) (55%)  
Treatment: IVIG (100%), Aspirin (20%), Methylprednisolone (80%)  
Outcome: Discharged | |
Age: Median: 7.9 (3.7-16.6)  
Gender: 57% females  
Race: NR  
PCR testing: 38% positive  
Past COVID-19 exposure: Patients’ parents report their kids never went to school, social gatherings, or traveled since lockdown implementation. Recent viral like syndrome (headache, cough, coryza, fever for less than 48 hours) was reported in 9 patients. History of exposure to a suspected COVID-19 case (10/21)  
Duration between viral like syndrome and Kawasaki-like syndrome onset: Median: 45 (range 18-79) days  
Duration between exposure to suspected COVID-19 case and Kawasaki-like syndrome onset: Median: 36 (range 18-45) days.  
Patients presenting symptoms: Patients fulfilled complete (52%) or incomplete Kawasaki definition (48%)  
Impaired Myocardial Function: Aneurysm (0%).  
PICU admission: 81% were admitted to the PICU. Mechanical ventilation (52%), Inotropic agents (71%)  
Laboratory results: CRP (253 (89-363) mg/L.  
Treatment: IVIG (100%), steroids (48%), Aspirin (100%), antibiotics (86%)  
Outcome: Discharged | |
| Serology test:  
1. Architect SARS-CoV-2 Abbott core lab.  
- Platform: CIA  
- Antibody type: IgG  
- Antibodies target: NR  
- Approval: NR  
IgG: 19/21 (90.5%)  
RT-PCR:  
1. bioMerieux SARS-Covid-19 RT-PCR assay  
- Time: within the first 3 days of patient presentation. |
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| Grimaud France Case Series | PIMS criteria: This study doesn’t use any PIMS or Kawasaki disease definition. It includes all patients admitted to the PICU with fever, shock, and a suspected COVID-19 infection. | N: 20  
Hospitalized: All patients (< 18 y.o) admitted to the PICU with shock, fever and a suspected SARS-CoV-2 infection between April 15th and April 27th, 2020.  
Age: median 10 (2.9–15)  
Gender: 50% male  
Race: NR  
PCR testing: 50% positive  
Past COVID-19 exposure: Previous viral like illness or contact with a suspected Covid-19 case wasn’t reported.  
Patients presenting symptoms: None fulfilled the typical Kawasaki disease definition. However, the most common symptoms were: Fever (100%), severe abdominal pain (100%), vomiting (100%). Hypotensive (100%), major systematic inflammation (100%), acute myocarditis (100%) and rash (50%)  
Impaired Myocardial Function:  
PICU admission: 100%  
Laboratory results:  
Treatment: IVIG (100%), Corticosteroids (10%), IL-1 receptor antagonist (5%), anti-IL-6 monoclonal antibody (5%)  
Outcome: All patients were discharged from the PICU. | 1. Euroimmun IgA, IgG  
- Platform: Elisa  
- Antibody type: IgG, IgA  
- Antibodies target: NR  
- Approval: NR  
Serology test results: 15/15 positive. (100%) |
| Feldstein USA Case Series | PIMS criteria: Hospitalized patients (age <21), with fever, laboratory evidence of inflammation, multisystem organ involvement (at least 2 systems involved), with either positive PCR, positive serology, or history of contact with suspected or confirmed COVID-19 cases. | N: 186  
Hospitalized: Patients were hospitalized in 53 hospitals between March 15, 2020, to May 20, 2020.  
Age: median 8.3 years  
Gender: 62% males  
Race: 25% black, 19% white, 31% Hispanic, 5% other race, 22% unknown  
PCR testing: 73/181 (40%) | 1. NR  
- Platform: NR  
- Antibody type: NR  
- Antibodies target: NR  
- Approval: NR  
Positive: 85/131 (65%) |
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| Belhadjer     | PIMS criteria           | No patient met the clinical presentation for classic Kawasaki disease.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | **Past COVID-19 exposure:** 14 patients had symptoms of COVID-19 with median period between COVID-19 symptoms and PMIS symptoms onset was 25 days (range, 6 to 51)  
**Patients presenting symptoms:** Fever (100%), GI symptoms (91%), bilateral conjunctival injection (55%), oral mucosal changes (42%), peripheral extremities changes (37%), rash (59%).  
**Impaired Myocardial Function:**  
**PICU admission:** 80% admitted to PICU, 20% required mechanical ventilation,  
**Laboratory results:** Elevated CRP (91%), elevated ferritin (61%)  
**Treatment:** IVIG (77%), IV steroids (49%), IL-6 inhibitor (8%), IL-1 receptor antagonist (13%)  
**Outcome:** 70% discharged, 2% died, 28% still hospitalized.  
**Serology Test/ Results:**  
1. CIA (not specified)  
   - Platform: CIA  
   - Antibody type: IgG  
   - Antibodies target: NR  
   - Approval: NR  
   IgM: 2/35 (5.7%)  
   IgG: 28/35 (80%)  
   IgA: 25/35 (71.4%)  
| France        | Case Series             | Inclusion Criteria: Patients included are all children admitted to the hospital with signs of multisystem inflammatory state (fever, and elevated CRP) associated with acute heart failure (left ventricular systolic dysfunction), or cardiogenic shock  
**Hospitalized:** Patients admitted to 12 hospitals in France and 1 hospital in Switzerland between March 22, and April 30, 2020. These hospitals are located within the most active COVID-19 areas  
**Age:** Median 10 years  
**Gender:** 51% males  
**Race:** NR  
**PCR testing:** NP swab: 34% positive, fecal PCR:6% positive  
**Past COVID-19 exposure:** 13/35 reported a recent contact with suspected COVID-19 patients (within the past 4 months)  
**Patients presenting symptoms:** Fever (100%), GI symptoms (80%), respiratory distress (65%) rash (57%),  
**Impaired Myocardial Function:** Echocardiogram showed EF <30% (10/35), EF between 30%-50% (25/35), global left ventricular hypokinesia (31/35), coronary artery aneurysm (0/35)  
**PICU admission:** 100%, (2/3 required mechanical ventilation)  
**Laboratory results:**  
|
### Study

**PIMS Suspicion Criteria**

A confirmed case should meet clinical and laboratory criteria, and a suspected case should meet clinical and epidemiological criteria.

Clinical signs: Hospitalized patient aged <21 yo with 1 day or more of subjective or objective fever and either one of the following signs: hypotension, shock, signs of severe cardiac illness, or signs of other severe end-organ damage, or at least two of the following: maculopapular rash, bilateral non-purulent conjunctivitis, signs of mucocutaneous inflammation (hands, feet, or mouth), or GI symptoms, and the absence of a more possible etiology.

Laboratory signs: Elevated inflammatory markers (at least 2 markers elevated), and a positive COVID-19 lab test (PCR within the last 4 weeks, or Serology test anytime).

Epidemiological criteria: Either close contact, with a confirmed or suspected COVID-19 case, and/or travel to a hotspot. Both should be within the previous 6 weeks.

**Patients Characteristics**

- **Treatment:** IVIG (25/35), IV steroids (12/35), IL-1 receptor antagonist (3/35), heparin (23/35)
- **Outcome:** as hospital discharged (28/35)

**Serology Test/ Results**

- **NR**
- **Platform:** NR
- **Antibody type:** IgG
- **Antibodies target:** NR
- **Approval:** NR
- **IgG:** 76/77 (99%)