Kawasaki-like syndrome linked to COVID-19 in children is a new condition

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A study on children suffering from severe inflammatory symptoms shows the condition is new and distinct from Kawasaki disease.

In April, researchers in the UK and several European countries with high numbers of COVID-19 cases recognised a new inflammatory syndrome

in children that was similar to Kawasaki disease, a rare syndrome known to affect young children.

Now in a paper published today in the *Journal of the American Medical Association* researchers have identified the main symptoms and clinical markers of the new syndrome. This will help clinicians diagnose and treat the condition and researchers to understand it further and find new treatments.

The study, led by Imperial College Academic Health Science Centre (AHSC) researchers, involved clinicians and academic partners in hospitals across England, including Great Ormond Street Hospital (GOSH) and the Evelina London Children's Hospital, as well the Kawasaki Disease Research Center at the University of California San Diego.

The condition, which the researchers have named Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS), was studied in 58 children admitted to eight hospitals in England.

The condition is believed to be extremely rare, but there are concerns about long-lasting coronary damage. Less than 200 cases have been reported in England with a range of symptoms and severity and most children have already recovered.

Lead author Dr. Elizabeth Whittaker, from the Department of Infectious Disease at Imperial College London and a consultant in paediatric infectious diseases and immunology at Imperial College Healthcare NHS Trust, said: "The new condition, PIMS-TS, is extremely rare but it can make a child very ill, so it's important to characterise the disease properly so we can provide close monitoring and the best treatment.

"For any parents worried about their children, I would urge them to follow their usual instincts—whatever would normally prompt you to visit your GP or A&E with your child still applies here."

Dr. Julia Kenny, consultant in paediatric infectious diseases and immunology at Evelina London, said: "Our analysis has shown that this is indeed a new condition. Untreated, there is a risk of severe complications in very unwell children, but with early identification and treatment the outcome is excellent, with the children we are reviewing after discharge completely well.

"For clinicians, it's important that we build collaborative research to quickly improve our understanding of the condition and provide the best evidence-based treatment for our patients."

PIMS-TS appears to be more likely to affect older children than Kawasaki disease (average nine years old versus four years old respectively) and presents more often with abdominal pains and diarrhoea alongside the common features such as persistent fever. It also appears to affect a higher proportion of Black and Asian patients.

Blood tests also show different results, with PIMS-TS patients showing more markers of inflammation and cardiac enzymes, which suggest the heart is under strain.

Kawasaki disease is known to damage the coronary artery in such a way that as the child grows the artery does not, leading to a reduction in the amount of blood that can reach the heart. Immune therapy is known to help alleviate these problems, so has been used on patients with PIMS-TS as well, although the team say differences in the two diseases mean this needs to be investigated further and treatment should be carefully monitored.

Lead researcher Professor Michael Levin, from the Department of Infectious Disease at Imperial College London, said: "The new disease presents in a number of ways and can have serious complications. However, the more we learn the better prepared we are to intervene and prevent worse outcomes. For example, patients who develop shock and cardiac failure have a different pattern of blood tests that may help to identify the at-risk group for targeted treatment."

While the team cannot say for certain that PIMS-TS is caused by COVID-19, 45 of the 58 children had evidence of current or past COVID-19 infection, and the researchers say the emergence of a new inflammatory condition during a pandemic is unlikely to be a coincidence.

The majority of children with indications of infection had antibodies for the new coronavirus, suggesting PIMS-TS happens after infection, potentially as a result of an immune system overreaction.

For this reason, the researchers also say understanding more about PIMS-TS could help a more general understanding of COVID-19 and its effects, even in adults. Because PIMS-TS is so distinct, it is easy to study individuals with high inflammation, which may be harder to identify in the general population.

The researchers are collaborating with teams across Europe and the USA that are also studying the new condition in the hopes of rapidly learning more about PIMS-TS and COVID-19. For example, if the condition is caused by an immune system overreaction, this could have implications for the use of vaccines.

Dr. Alasdair Bamford, consultant and specialty lead in paediatric infectious diseases at Great Ormond Street Hospital, said: "An important next step will be to review this data in the context of other studies being

published from around the world. This will help inform management guidelines and to further refine the case definition. Recruitment of children into observational studies and clinical trials will be key to creating an evidence base for the best treatment."

This research is an example of the work carried out by Imperial College Academic Health Science Centre, a joint initiative between Imperial College London and three NHS hospital trusts. It aims to transform healthcare by turning scientific discoveries into medical advances to benefit local, national and global populations in as fast a timeframe as possible.

More information: Elizabeth Whittaker et al, Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2, *JAMA* (2020). DOI: 10.1001/jama.2020.10369

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