IJBAF, August, 2021, 9(8): 57-72

ISSN: 2320 – 0774

International Journal of Biotechnology and Allied Fields (IJBAF)

www.ijbaf.com

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MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) SEQUENTIAL IMPLICATION WITH COVID-19: BLAST NOW AND THEREAT AHEAD

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ABSTRACT

It is important to accept the study and clinical sequence of the multisystem inflammatory syndrome in children (MIS-C) and its sequential connotation with coronavirus illness 2019 (COVID-19). This manuscript provides up-to-date knowledge about MIS-C. The possible consequences of this new syndrome are reviewed and discussed from a public health perspective. Laboratory signs of inflammation, a contribution from multisystem organs, and signs of contagion with the unvarnished critical respiratory syndrome coronavirus 2 (SARS-CoV-2) with an emphasis on reverse transcriptase-polymerase chain reaction (RT-PCR), antibody tests, or contact with people with COVID-19. Doctors distribute the facts in an immutable manner. Immunomodulation therapies use intravenous immunoglobulins and glucocorticoids, as well as interleukin-6 or 1RA inhibitors. This article illustrates the monthly progress and reported cases of MIC around the world. Information about this rare, albeit hypothetically fatal, syndrome is rapidly emerging. In this review, we refer to current statistics on case significance, patient demographics, clinical topographies, and crucial laboratory results. The Multisystem inflammatory syndrome in broods that accompanies SARS-CoV-2 has been geared towards serious and fatal illnesses in healthy kids and adolescents. At best, care should be taken without neglecting kids to get into trouble.

Keywords: Infection, syndrome, Kawasaki Disease, Interferon, COVID-19

INTRODUCTION

Multisystem inflammatory syndrome in children (MIS-C), which is also known as pediatric fiery multisystem syndrome (PIMS/PIMS-TS) **[1]**, is an unusually complete contagion concerning tenacious pyrexia and life-threatening tenderness following contact with SARS-CoV-2, the sepsis responsible for COVID-19 **[2]**. It is characterized by medical difficulties such as inadequate bloodstream in the body (shock) and organ transpiration. A threatening signal is impenetrable tenacious pyrexia with undecorated indications of subsequent experience with COVID-19. Quick recommendations to pediatric professionals are indispensable, and they are necessary to pursue crucial medical support. Furthermore, exaggerated broods will require intensive attention **[3]**.

All exaggerated broods have a tenacious pyrexia with different clinical complications. The first indications repeatedly comprise severe belly discomfort with diarrhoea and vomiting. Muscle agony and common weariness are recurrent, and short blood pressure is also common. Indications can also comprise pink eye, rashes, distended lymph nodes, puffy hands/feet, and "strawberry tongue". Numerous cerebral instabilities are also imaginable. A cytokine storm may take place, in which the child's distinctive protected system phases an extreme and unrestrained inspiring reaction **[4]**. Cardiac failure is communal and Clinical impairments can comprise impairment of the myocardium, respiratory distress, critical kidney injury, and improved blood coagulation **[5]**. Coronary artery aberrations can progress.

Though it has remained conjectured that the circumstances are interrelated to COVID-19, it has also been accentuated that the probable linkage is neither conventional nor well-unstated. A progressive reminder of the SARS-CoV-2 contagion and the clinical advent of the condition is possible **[6]**. Promote categorization of the condition is necessary to categorize threat causes and assist in recognizing destiny. It is indistinct whether this evolving condition has a similar etiology to Kawasaki disease (KD) (a state antecedent to the arrival of SARS-CoV-2, which is presently understood to be prompted by a dissimilar viral manager). Though some instances look like toxic shock conditions, there is no indication that *staphylococcal or streptococcal* contaminants are intricate and the part of comorbidities is indistinct. Enhanced appreciative will have possible suggestions for clinical supervision.

Genome-wide suggestion readings are probable to afford perceptions of contact and probable biological apparatus.

This fatal sepsis has been evidenced terminal in under 2% of stated instances. Initial acknowledgment and quick expert consideration are necessary. Anti-inflammatory management has remained used, with good reactions being documented for intravenous immunoglobulin (IVIG), with or deprived of corticosteroids **[7]** and oxygen is frequently required. Compassionate care is vital for handling clinical impediments. The maximum number of kids who take professional hospital care subsists.

Information about this recently designated syndrome is developing quickly. Its experimental features may seem slightly like KD, a rare disease of unidentified derivation that is characteristically in young broods who have swollen blood vessels all over their bodies. It may have features of other provocative reflective circumstances of childhood, such as noxious shock and macrophage activation syndrome **[8]**. It seems to be a different syndrome, however, and older broods tend to be overbearing.

This evolving complaint has been distinguished slightly inversely by the World Health Organization (WHO). Although the situation is supposed to monitor the viral sepsis of SARS-CoV-2, antigen or antibody tests are not permanently positive **[9]**. Separation of substitute causes, which include bacterial and other sepsis, is essential in diagnosing variance.

Collections of new instances were testified 2-6 weeks after native ridges in viral communication. The disease is said to be triggered by an inhibited biological means in broods in need of security. The European Centre for Disease Prevention and Control (ECDC) has rated the threat to broods in Europe as an overall “low” based on a “very low” probability that a child will develop this “high” disease impact. In terms of ethnicity, the condition looks to bother more children of African, Afro-Caribbean, and Hispanic ancestry. KD affects more kids of East Asian ancestry. Preliminary information examined broods in countless fragments of Europe and the US, and it was impossible to tell how far the disorder had gone undetected. The outcome of instances in numerous other countries around the world **[10]**. A comparable disease known as MIS in adults (MIS-A) has rarely occurred in grownups. Typical cases of COVID-19 in broods were comparatively rare, possibly because it is generally a milder disease. Initial sepsis is usually related to little or no signs. After the lung stage, which can be life-threatening in

grownups, is usually mild or non-existent. Although the instances of broods with unadorned indications are unmatched, they can rarely lead to intense attention. Mortality was unpredictable. There was indecision as to whether the disorder was limited to broods and the suitability of without grownups from case descriptions has been examined. Erratic information about a serious illness known as "MIS-Ups" (MIS-A), which also results in an ICU **[11]**.

In April 2020, only a few broods with signs of COVID-19/SARS-CoV-2 disclosure came from experimental structures of glasses that met the KD diagnostic guidelines, occasionally supplemented by shock. KD is an unpredictable syndrome that affects mainly young broods (there have been isolated reports of primary adulthood). It is a systemic vasculitis in which blood vessels throughout the body become reddened and cause a determined pyrexia. Recovery is usually spontaneous, but some broods will experience future advances in coronary artery aneurysms in the heart. Indications of noxious shock (a syndrome produced by microbial toxins) occur irregularly, an indication that is sometimes referred to as "Kawasaki shock syndrome" and is classified according to systolic hypotension or private insertion numbers. Although the exact origin of the KD has not been identified, it is conceivable that it could result from a sepsis that triggers an autoimmune and/or auto-inflammatory reaction in broods with hereditary tendencies **[12]**. An exact diagnostic test for KD is not available and its approval is based on numerous sets of laboratory and clinical findings, namely, tenaciouspyrexia, generalized rashes, distended lymph nodes, conjunctivitis, mucosal variations, and hand/foot swelling.

GLOBAL THEREAT

Instances of KD with simultaneous transmission of SARS-CoV-2 in broods in Europe and the US were verified on April 7, 2020, when the American Academy of Paediatrics disseminated information about a case of classic KD in a girl of six months. Confirmed positive for COVID-19 in California **[13]**. In this situation, COVID-19 did not seem to have any major clinical impact. The instances in 2020 are listed below.

On April 25, concerns increased, particularly in the UK, about a group of kids of different ages who have a condition called MIS that requires intensive care, all of which show overlapping structures of noxious shock and atypical KD with blood restrictions in Kids, Particulars. The eight reports that helped call this attention (not all

of them with definitive revelation of COVID-19) were slowly published in The Lancet, where the authors shortened the clinical description to multi-organ contributing hyper inflammatory syndrome as a condition. Similar case books exist among doctors in Europe, plus some that seemless clinically simple. The EU prevention and premature response system highlighted suspected instances in Austria, Germany, and Portugal that had confirmed a positive result for SARS-CoV-2. In Bergamo, at the heart of the COVID-19 epidemic in Lombardy, a collection of 20 KD instances looked to be inconsistent with the number normally documented there over the three-year course. In France, the government stated on April 29, 2020, that around 15 broods were hospitalized in Paris with signs of KD, surveillance that encouraged the Association of the National Monitoring Program for Current KD instances **[14]**.

On May 1, 2020, the RCPCH published an initial case delineation based on the assessment of recognized incidents in the UK, supplemented by clinical surveillance. Two weeks later, on May 15, the WHO and CDC separated two more initial fall lines. The ECDC did not restrict a "quick risk assessment" of the situation on behalf of the European Union. In the weeks that followed, other medical organizations, including the NIH, the American College of Rheumatology, and the American Academy of Paediatrics, did not restrict further clinical management. On May 4, the New York Department of Health and Mental Hygiene arranged for broods with the disorder to be recognized in New York hospitals that had previously held 15 such issues. On May 9, the New York Governor announced a collaboration with the CDC to advance national efforts to identify and respond to the newly recognized childhood disease **[15]**.

As of May 12, around 230 suspected issues had been conveyed in the EU, EEA and the UK (up to 100 instances were testified in the UK in the following days, more than 135 in France, 20 in the Netherlands, 10 in Switzerland and 10 in Germany). In the US, more than 200 instances were suspected in mid-May, around 145 of them in New York; 186 confirmed instances were ultimately diagnosed in 26 states between March 15 and May 20. As of May 11, 2020, five deaths had been described (1 in France, 1 in the UK, and 3 in the US). The case series and related reviews of the new disease were rapidly published in peer-reviewed medical journals from across the nation-state, including the UK, Italy, Spain, France, and Switzerland, France, and throughout the US, including

New York. The evolving observations recommended a somewhat greater variety in the severity of the indications than initially thought. The proposal of a new clinical panel during a pandemic also fuelled the scientific discussion of their conceivable KD discrepancy and the likely role of COVID-19 **[16]**.

As of July 15, 342 child-confirmed reports of MIS-C (with 6 deaths) had been documented in the US from 36 states plus Washington DC. The majority (71%) of the broods were still Hispanic/Latin American or non-Hispanic Blacks, and the CDC emphasized the need to study the minutiae of such a domain. As of July 29, a total of 570 instances and 10 deaths had been testified in 40 states, Washington DC, and New York City **[17]**.

No full reports were documented outside the EU, EEA, UK, and US by dawn, and no suspected reports were observed in East Asia or Southeast Asia (or Australia or New Zealand). The lack of foreseeable reports in China, and additionally, in Asian countries that had previously been forced to experience a COVID-19 epidemic, led to speculation about the possibility of significant development of the virus or a different susceptibility in different population groups. News of the first MIS-C case diagnosed in Peru was announced on June 2, 2020 **[18]**.

In Brazil, reports of MIS-C testified in So Paulo and the precursors of a possible study in Para. In the province, more progenies were admitted with unadorned night-time expressions of COVID-19 as part of paediatric intensive care. In Chile, 42 reports of MIS-C had been registered nationwide as of June 28, with 27 in the capital Santiago **[19]**.

In Russia, 13 broods (5 in intensive care) were preserved in Moscow's Morozov Kids' Hospital because of MIS in mid-June, including a 2-year-old girl with COVID-19 sepsis who received a preliminary verdict from the suspicious KD on the 23rd. In Iran, a case report (which first succumbed in May) revealed unadorned MIS-C in a 5-year-old girl who had access to shock and was found primarily with KD, and more instances of the new disease were documented **[20]**.

In India, a suspicious MIS-C case was described in late May involving a child who had access to a COVID-19 hotspot in Kerala. One interpretation of the reports advised clinicians to have a high level of suspicion about the diagnosis and to follow WHO and CDC definitions to facilitate the timely documentation and treatment of reports. In July, suspicious reports were highlighted and

described in Mumbai, Delhi, Chennai and elsewhere **[21]**.

In Pakistan, at least 24 progenies are said to have had similar evidence as in Kawasaki in Lahore, up to the age of 30. In Kazakhstan, 14 reports were found as of August 20 (among 2,357 kids recognized as infected). Reports have been documented in Israel, plus an accessible child with an unvarnished central nervous system contribution and complement deficiency **[22]**.

In Algeria, the main documentation was in June. In Egypt, on July 10, the facilities denied rumours of the survival of instances of Kawasaki-like disease in the country **[23]**.

In South Africa, between June 4 and July 24, the first 23 presumptuous offspring were detained in Cape Town, the provisional epi-centre of the national COVID-19 epidemic. In Ecuador, the Ministry of Health announced the occurrence of 46 possible instances on July 19. In Costa Rica, a national health organization testified in late August that three kids had been diagnosed with MIS-C. Reports of MIS-C have also been documented in many other Latin American countries, as well as Argentina, Bolivia, Colombia, Cuba, the Dominican Republic, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Uruguay, and Venezuela. The first die-hard PIMS-TS case in Australia (from Victoria) was broadcast on September 4, along with news of other suspected instances that are currently being evaluated **[24]**.

In South Korea, an update was testified in November of two established instances that were discovered on October 5 (and the survival of a case from the end of April). A similar situation has been documented in some grownups. In June, a mature case of Kawasaki-like MIS-SARS-CoV-2 sepsis was found in a 54-year-old woman from Israel with an ancient autoimmune disease who had uveitis in both eyes. (Another suspected adult case was covered by the Israeli national press.)

A case of a 36-year-old American woman with reliable clinical MIS-C topographies was testified in New York. A reliable diagnosis with PMIS was also accomplished in a British-born man of Somali descent (21 years old). A case report circulating in The Lancet of a contactable man (45y) in New York with highly threatening MIS-C characteristics called for full attention to "a potential MIS-C-like situation in grownups". Additional information from MIS regarding adult COVID-19 knowledge.

In October, the CDC confirmed the disease and named it "MIS in Adults" (MIS-A). Inquiries about conceivable associations

between MIS-C and convinced, unadorned occurrences of COVID-19 in grownups have increased. Neurological symptoms in broods considered in London in mid-2020 often complicated "both the central and peripheral nervous systems," according to an unqualified statement from the American Academy of Neurology dated April 13, 2021.

MECHANISM

The pathogenesis is unknown. SARS-CoV-2 could play one of many roles; it could additionally act directly or indirectly as an environmental activator for the disorder (in a certain way, pointing to another activator). As with KD, antibody-dependent augmentation has been projected as a possible means through which antibody progression could facilitate viral access to host cells **[25]**.

Epidemiological considerations suggest a post-sepsis invention that may overlap with the course of virus-assimilated invulnerable reactions. It has been suggested that the disorder could be caused by cytokine outbreaks that became persuaded by COVID-19. The ability of coronaviruses to differentiate between type I and type III interferon wedge reactions could help clarify an impaired cytokine outbreak in toddlers whose defence system rejects the virus repeat regulator SARS-CoV-2 or with a preliminary high viral load is numb. A possible prominent chain of processes leading to a hyper-immune reaction could comprise timely viral activation of macrophage initiation, followed by stimulation of helper T cells, which are decisive for cytokine release, stimulation of macrophages, neutrophils, and monocytes with activation of B cells and plasma cells, and antibody production **[26]**.

The extent to which the pathophysiology resembles that of other paediatric sedimentation syndromes with similar clinical features has not been identified. Clinical intersections with syndromes with different causes (KD, toxic shock, macrophage initiation syndrome, and secondary hemophagocytic lymphohistio-cytosis) can be clarified by body defence initiation and dysregulation of similar initiation pathways. In any of these syndromes, a storm of cytokines causes many organs to fail. The recurrent gastrointestinal manifestations and sensitivity of the mesenteric lymph nodes are consistent with the accepted view that SARS-CoV-2 is mimicked by enterocytes **[27]**.

The association of Kawasaki-like disease with COVID-19 might suggest that SARS-CoV-2 can cause systemic vasculitis by attaching to angiotensin-converting enzyme 2

(ACE2), the protein that the virus uses to target endothelial tissue cells. Although it is recognized that primary sepsis is achieved by the initiation of grave myocardial damage, the presence of myocarditis could also be related to systemic hyper-irritation caused by a disorganized post-sepsis immune response. SARS-CoV-2 was recommended to primarily influence immune-mediated heart damage through immune complexes or increased T28 cell responses.

The consideration of pathophysiology is an essential research focus. Questions about the basic molecular mechanisms that lead to disease after the disclosure of SARS-CoV-2 include the identification of genetic predisposing factors; any association with certain viral variants; and any molecular decoration capable of causing autoimmune/auto inflammatory reactions. Another key question is whether the molecular mechanisms that trigger auto-immune/auto-inflammatory responses in toddlers with PMIS and grownups with severe COVID-19 (consisting of the onset of high levels of IL-6) are similar or different **[28]**.

A likely relationship with KD is under discussion. It is well known that one of the main hypotheses for the pathogenesis of KD also comprises a hyper sedative response to viral contamination (such as from a new RNA virus) in some hereditary toddlers and that SARS-CoV-2 is now being added to the list of "affected active viruses. Hopes have been expressed that reviewing the new disorder could help understand the hidden inventions behind KD **[29]**.

PART OF THE STING CONDUIT

Although the initial stage of the SARS-CoV2-mediated MIS-C pathogenesis remains largely undetected, the extrapolation of information from the pathological means of SARS-CoV suggests a possible role for the STING channel (interferon-gamma stimulator). The STING protein, programmed by TMEM173 (transmembrane protein) and articulated in alveoli, endothelial cells, and the spleen, can be stimulated by DNA debris from host cells and contaminates mitochondrial DNA as well as RNA viruses. The activation of ACE-2 mediated by SARS-CoV-2 was also initiated to positively regulate this passage. As a result, after the activation of NF-ß and IRF-3, there is an enormous release of interferon ß and cytokines. This is essential for STING-associated vasculopathy with onset in childhood (SAVI) as the indicators are characterized by pyrexia, bronchial damage, swelling of the capillaries, myositis, dermatological indicators, accrual necrosis,

and arterial aneurysms. TMEM173 amid numerous cultural subsections, possibly interpreting differences in clinical performance and severity of disease indicators **[30, 31]**.

CLINICAL COURSE

The clinical course tends to be simpler than that of KD. A child's disorder can quickly deteriorate in value, even with encouraging laboratory conclusions. Many toddlers develop shock and heart failure and require intensive care. Supplemental oxygen is required repeatedly and ventilation is used occasionally. A maximum number of toddlers who will receive competent, multidisciplinary, live care. In addition to shortness of breath, heart muscle damage, serious kidney damage, and coagulopathy (thrombophilia) can be major problems that may require destructive supportive care. In some instances, continuous cardiac arrhythmias have caused hemodynamic collapse and the need for extracorporeal membrane oxygenation (ECMO) **[32]**.

Deaths were documented in a smaller minority (less than 2%) of the testifiedinstances. Occasionally, mortality followed the difficulties of the ECMO. Nearly toddlers who are not protected from COVID-19 also seem to have less unadorned Kawasaki-like diseases. Ventricular function often recovers before discharge from the hospital (often after 6-10 days). Coronary artery aneurysms can progress even without the advent of Kawasaki-like features. Their entrance and severity are inexact. So far, they have been documented in 7% of the testified instances. The long-term forecast is indeterminate.

DIAGNOSIS

The diagnosis is made through a specialized clinical evaluation. The analytical feelings may be heightened by the mysterious, stubbornpyrexia and are clinically related to symptoms after experience of COVID-19. People should see a doctor right away, as the child's illness can quickly subside. The first post from paediatricians is usually in the emergency room. Initial detection and multidisciplinary appointments with paediatric specialists (intensive care medicine, sepsis, cardiology, haematology, rheumatology, etc.) are essential. The inspections may comprise blood tests, chest x-rays, echocardiography, and ultrasound of the belly. General practitioners have been advised to consider this disorder in toddlers who have some or all of the KD geographies or toxic shock conditions **[33]**. The main symptoms are shown graphically in **Figure 1**.

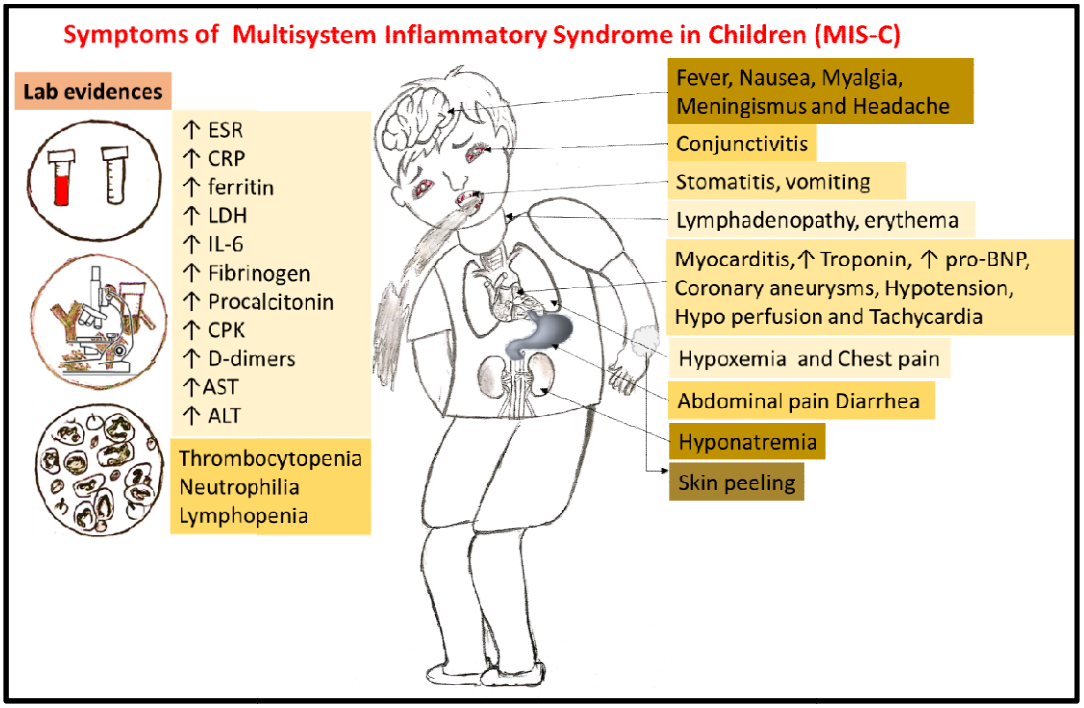

Figure 1: Pictorial representation of MIS in children

DIFFERENTIAL DIAGNOSIS

It is important to rule out non-sepsis and infectious surrogate sources of sedimentation disorders, plus bacterial sepsis, staph and streptococcal shock, and taints allied with myocarditis such as enterovirus. (Co-sepsis with other pathogens, including human *metapneumovirus* and various other microbes, can occasionally occur.) Other hypothetically unrelated causes of bellyagony are appendicitis and mesenteritis. The conclusion of the discrepancy with KD can be encouraging, provided that a diagnostic test is not available for one of the disorders **[34]**.

It is currently not recognized that the newly clear disorder overlaps with KD shock syndrome. As a result, quick diagnosis and timely management of real KD are essential to avoid disability. Because of the obstinate pyrexia, it was necessary to maintain a high level of distrust of KD in all toddlers, but especially in those who were cooler than 1-year-old.

CONCLUSION

MIS-C is still an unusual challenge accompanying the COVID-19 pandemic, and the readings support the idea that SARS-CoV-2 could act as an activating or immunomodulatory problem in the

pathogenesis of MIS-C. The Multi-systemic inflammatory syndrome in toddlers is accompanied by SARS-CoV-2, which leads to a severe and life-threatening taint in healthy toddlers and adolescents.

ACKNOWLEDGMENT

Nil

CONFLICT OF INTEREST

All the authors have declared that they do not have any conflict of interest.

FUNDING

Nil.

REFERENCES

[1] Schlapbach LJ, Andre MC, Grazioli S, Schöbi N, Ritz N, Aebi C, *et al*. Best Practice Recommendations for the Diagnosis and Management of Children With Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2 (PIMS-TS; Multisystem Inflammatory Syndrome in Children, MIS-C) in Switzerland. Frontiers in pediatrics. 2021; 9: 396.

[2] Davies P, Evans C, Kanthimathinathan HK, Lillie J, Brierley J, Waters G, *et al*. Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study. The Lancet Child & Adolescent Health. 2020; 4(9): 669-77.

[3] Ramcharan T, Nolan O, Lai CY, Prabhu N, Krishnamurthy R, Richter AG, *et al*. Paediatric inflammatory multisystem syndrome: temporally associated with SARS-CoV-2 (PIMS-TS): cardiac features, management and short-term outcomes at a UK tertiary paediatric hospital. Pediatric cardiology. 2020; 41(7): 1391-401.

[4] Chinthaginjala H, Ahad HA, Sumanth G, Shaik M, Dasari RR. Hunting Hantavirus: A Quick Guide for Healthcare Professionals before It Invades the Globe unlike COVID-19. International Journal of Pharmaceutical and Phytopharmacological Research. 2020: 1-6.

[5] Ahad HA, Haranath C, Roy D, Dharani BS, Raghav R, Dasari SR. A Quick Reference to The Diagnosis Test for COVID-19: Guide to Every Healthcare Professional in Global Emergencies. International Journal of Pharma Sciences and Research, 2020; 11 (4): 58-64.

[6] Kumar YB, Ahad HA, Haranath C, Sumanth G, Pasupuleti DS, Reddy SS. Platelet Rich Plasma Therapy: A quick

note for every health care professional.(2020). Int J Life Sci Pharma Res. 10(5): P84-9.

[7] Harwood R, Allin B, Jones CE, Whittaker E, Ramnarayan P, Ramanan AV, *et al*. A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. The Lancet Child & Adolescent Health. 2020.

[8] Sadiq M, Aziz OA, Kazmi U, Hyder N, Sarwar M, Sultana N, *et al*. Multisystem inflammatory syndrome associated with COVID-19 in children in Pakistan. The Lancet Child & Adolescent Health. 2020; 4(10): e36-e7.

[9] Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. European journal of pediatrics. 2021: 1-16.

[10] Penner J, Abdel-Mannan O, Grant K, Maillard S, Kucera F, Hassell J, *et al*. 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: a retrospective cohort study. The Lancet Child & Adolescent Health. 2021; 5 (7): 473-482.

[11] Meredith J, Khedim C-A, Henderson P, Wilson DC, Russell RK. Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 [PIMS-TS] in a patient receiving infliximab therapy for inflammatory bowel disease. Journal of Crohn's and Colitis. 2021; 15(4): 687-91.

[12] Ahad HA, Haranath C, Tarun K, Krishna JV, Kumar GA, Teja AS. Vitiating Ebola Outbreak: A Brief Guide to the Humanity. Research Journal of Pharmaceutical Dosage Forms and Technology. 2021 Apr 1; 13(2): 153-6.

[13] Rowley AH. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nature Reviews Immunology. 2020; 20(8): 453-4.

[14] Valverde I, Singh Y, Sanchez-de-Toledo J, Theocharis P, Chikermane A, Di Filippo S, *et al*. Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated

with COVID-19 infection in Europe. Circulation. 2021;143(1):21-32.

[15] Suzuki J, Abe K, Matsui T, Honda T, Yasukawa K, Takanashi J-i, *et al*. Kawasaki Disease Shock Syndrome in Japan and Comparison With Multisystem Inflammatory Syndrome in Children in European countries. Frontiers in Pediatrics. 2021; 9: 206.

[16] Bautista-Rodriguez C, Sanchez-de-Toledo J, Clark BC, Herberg J, Bajolle F, Randanne PC, *et al*. Multisystem inflammatory syndrome in children: an international survey. Pediatrics. 2021; 147(2): e2020024554.

[17] Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, *et al*. Multisystem inflammatory syndrome in children in New York State. New England Journal of Medicine. 2020; 383(4): 347-58.

[18] Coll-Vela L, Zamudio-Aquise MK, Nuñez-Paucar H, Bernal-Mancilla RR, Schult-Montoya SC, Ccorahua-De La Paz M, *et al*. COVID-19-associated multisystem inflammatory syndrome in children: case series at a pediatric hospital in Peru. Revista peruana de medicina experimental y salud publica. 2020; 37(3): 559-65.

[19] de Farias EC, Piva JP, de Mello ML, do Nascimento LM, Costa CC, Machado MM, *et al*. Multisystem inflammatory syndrome associated with coronavirus disease in children: a multi-centered study in Belém, Pará, Brazil. The Pediatric infectious disease journal. 2020; 39(11): e374-e6.

[20] Jiang L, Tang K, Levin M, Irfan O, Morris SK, Wilson K, *et al*. COVID-19 and multisystem inflammatory syndrome in children and adolescents. The Lancet Infectious Diseases. 2020; 20(11): e276-e288.

[21] Jain S, Sen S, Lakshmivenkateshiah S, Bobhate P, Venkatesh S, Udani S, *et al*. Multisystem inflammatory syndrome in children with COVID-19 in Mumbai, India. Indian Pediatrics. 2020; 57(11): 1015-9.

[22] Khan KS, Ullah I. SARS-CoV-2 causes Kawasaki-like disease in children: Cases reported in Pakistan. Journal of medical virology. 2021; 93(1): 20-1.

[23] Ozsurekci Y, Gürlevik S, Kesici S, Akca UK, Oygar PD, Aykac K, *et al*. Multisystem inflammatory syndrome in children during the COVID-19 pandemic in Turkey: first report from

the Eastern Mediterranean. Clinical rheumatology. 2021: 1-11.

[24] Webb K, Abraham DR, Faleye A, McCulloch M, Rabie H, Scott C. Multisystem inflammatory syndrome in children in South Africa. The Lancet Child & Adolescent Health. 2020; 4(10): e38.

[25] Rowley AH, Shulman ST, Arditi M. Immune pathogenesis of COVID-19–related multisystem inflammatory syndrome in children. The Journal of clinical investigation. 2020; 130(11): 5619-21.

[26] Kabeerdoss J, Pilania RK, Karkhele R, Kumar TS, Danda D, Singh S. Severe COVID-19, multisystem inflammatory syndrome in children, and Kawasaki disease: immunological mechanisms, clinical manifestations and management. Rheumatology international. 2020: 1-14.

[27] Carter MJ, Shankar-Hari M, Tibby SM. Paediatric Inflammatory Multisystem Syndrome Temporally-Associated with SARS-CoV-2 Infection: An Overview. Intensive Care Medicine. 2020: 1-4.

[28] Bahrami A, Vafapour M, Moazzami B, Rezaei N. Hyperinflammatory shock related to COVID-19 in a patient presenting with multisystem inflammatory syndrome in children: first case from Iran. Journal of paediatrics and child health. 2020. 57(6): 922-925.

[29] Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, *et al*. Acute heart failure in multisystem inflammatory syndrome in children in the context of global SARS-CoV-2 pandemic. Circulation. 2020; 142(5): 429-36.

[30] Lin AE, Basson CT, Goldmuntz E, Magoulas PL, McDermott DA, McDonald-McGinn DM, *et al*. Adults with genetic syndromes and cardiovascular abnormalities: clinical history and management. Genetics in Medicine. 2008; 10(7): 469-94.

[31] Manolis AS, Manolis TA. Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-Cov-2 Infection (PIMS-TS): Kawasaki-Like Multisystem Inflammatory Syndrome in Children (MIS-C) During the COVID-19 Pandemic with Predominant Myocarditis: Kawasaki-Like Multi-system Inflammatory Syndrome in Children (MIS-C) During the

COVID-19 Pandemic. Rhythmos. 2020; 15(3): 42-6.

[32] Minen F, Hands C, Mustafa MR, Pienaar A, Lillie J. Thrombophilia in pediatric patients with multisystem inflammatory syndrome in children secondary to coronavirus disease 2019 supported on extracorporeal membrane oxygenation. ASAIO Journal. 2021; 67(1): 7-11.

[33] Soma VL, Shust GF, Ratner AJ. Multisystem inflammatory syndrome in children. Current opinion in pediatrics. 2021; 33(1): 152-8.

[34] Liu Y, Jesus AA, Marrero B, Yang D, Ramsey SE, Montealegre Sanchez GA, *et al*. Activated STING in a vascular and pulmonary syndrome. New England Journal of Medicine. 2014; 371(6): 507-18.