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**Interim guidance  
on Kawasaki disease and acute  
multisystem inflammatory syndrome  
in children and adolescents  
in the current emergency scenario  
of SARS-CoV-2 infection**

ISS COVID-19 Rare Diseases Working Group

Version of May 21, 2020



# Interim guidance on Kawasaki disease and acute multisystem inflammatory syndrome in children and adolescents in the current emergency scenario of SARS-CoV-2 infection

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## **ISS COVID-19 Rare Diseases Working Group**

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The available scientific evidence indicates that the clinical course of SARS-CoV-2 infection that occurs in pediatric patients has very low lethality rates (0.06% in the age group 0-15 years). However, recent European and US publications describe an acute multisystem inflammatory syndrome in children and adolescents, associated with positivity for SARS-CoV-2 or to the presence of antibodies antiSARS-CoV-2, the precise classification of which is currently in process. This syndrome seems to share some clinical features with KD, such as an aberrant inflammatory response and some therapeutic options (immunoglobulins, steroids, anti-cytokine drugs). The syndrome, however, could be distinguished from KD by other peculiarities, represented by the age of the affected subjects, severe multisystemic involvement, prevalent myocardial and / or gastrointestinal involvement. The document highlights that, at the moment, even in the absence of a European shared case definition, a correlation between SARS-CoV-2 infection and the onset of the syndrome is plausible, even if there is limited evidence of the causal link. It also stresses the absence of strong epidemiological evidence of an increased incidence of KD, as well as the absence of increased risk of disease recurrence and the absence of increased susceptibility to SARS-CoV-2 infection in patients with previous KD during the COVID-19 pandemic.

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# SARS-CoV-2 infection in children

The real prevalence of SARS-CoV-2 in the pediatric population, as well as in the adult population one, is not known. However, the currently available scientific evidence indicates that the SARS-CoV-2 infection occurs in children with less severe clinical course compared to adults. In fact, children generally have a good prognosis and lethality is much lower than adults.

An analysis was published in China on 2,135 diagnosed or suspected SARS-CoV-2 cases of infection in children, reported to the Chinese Center for Disease Control and Prevention in the period between January 16th and February 8th, 2020. Among all examined cases, 112 patients (5.2%) developed a severe form of the disease with the rapid onset of dyspnoea, hypoxia, fever, cough and gastrointestinal symptoms, including diarrhea. Other 13 children (0.6%) were critically ill and soon showed acute respiratory distress or respiratory failure syndrome; in these cases, shock, encephalopathy, myocardial damage or heart failure, coagulopathy and acute renal were reported.

A review of the literature published in April 2020 confirmed these observations, adding the evidence of accentuations of the bronchial texture and “frosted glass” opacity on CT scan examination, also in some asymptomatic children (2).

In April 2020, the U.S. Centers for Disease Control and Prevention (CDC) published a study regarding the period between 12th February and 2nd April, in which 2,572 (1.7%) of the 149,760 SARS-CoV-2 positive analyzed cases was younger than 18 years old, (3). From the available informations, in 73% of SARS-CoV-2 positive children, at least one of the clinical symptoms underlying the diagnostic suspicion (fever, cough and dyspnoea) was present, while in adults this percentage was 93% (3). The same document reported a rate of hospitalization in an estimated range between 5.7% and 20%, and hospitalization in intensive care in a range between 0.6% and 2%. The hospitalization rate was higher among children younger than one year of age (estimated range 15% -62%) while in the upper age group the estimated range was 4.1-14%. For 295 pediatric cases, health information was available regarding both hospitalization and concomitant diseases. About 77% (28 out of 37 cases) of hospitalized patients had one or more concurrent pathologies, while, among the remaining 258 patients who did not require hospitalization, 30 (12%) had other pathologies (3).

In a group of 41 Spanish pediatric patients with confirmed SARS-CoV-2 infection, 60% (25 cases) needed to be hospitalized: of these 4 cases were hospitalized in intensive care and other 4 needed assisted ventilation (4).

According to the European Surveillance System, TESSy, children represented a very low percentage among 193,351 COVID-19 cases confirmed in Italy until 13th May 2020; in the age range between 0-10 years, the reported cases were 1.1% and 1% in the range between 10-19 years (5).

In Italy, data from the Istituto Superiore di Sanità (ISS) report that until 14th May 2020, among the 29,692 people who died positive to SARS-CoV-2 infection, 3 cases were detected in the age group of 0-19 years (6).

The lethality index of COVID-19 is therefore equal to 0.06% in the age group of 0-15 years, compared to the index of 16.9% in the age group of over fifteen-year-old. The 3 children who died in Italy were affected by severe pathologies (metabolic disease, heart disease, cancer). In a recent publication, the presence of pre-existing pathologies did not highlight a more serious or unfavorable course of the SARS-CoV-2 infection in the evaluated pediatric patients (7).

In a series of 100 children with SARS-CoV-2 positive swab who was admitted to Emergency Room in 17 Italian hospitals, only 52% of the feverish patients presented the other two COVID-19 indicative symptoms (cough and dyspnoea). 38% of the children needed hospitalization, 9 of whom needed respiratory support (6 with pre-existing diseases). All 100 children of the series were cured (8).

These data seem reassuring about pediatric COVID-19 outcomes. However, great care should be taken when children below one year of age manifest symptoms of the infection. Studies performed on pregnant mothers with SARS-CoV-2 infection have investigated the relationship between maternal immunity and protection of the infant from infection, without however reaching conclusive results (9). The finding of indicative symptoms such as fever, difficulty in breathing, cough, gastrointestinal symptoms and sleepiness, in newborns of a SARS-CoV-2 positive mothers, must alert parents and pediatricians.

Therefore, the actual available scientific evidence indicates that the SARS-CoV-2 infection manifests in a more benign clinical trend in children than in adults.

However, recent publications from various countries, mainly from Europe and USA, describe an acute multisystem inflammatory syndrome in children and adolescents with some characteristics of Kawasaki disease (KD) associated with other specific peculiarities. This prompted the national and international medical-scientific community to carry out studies and insights concerning both the definition from the nosological point of view and the welfare aspects; in addition, the European Center for Disease Prevention and Control (ECDC) recently published a Rapid Risk Assessment on this topic.



# Kawasaki disease

## General characteristics, epidemiology and etiopathogenesis.

Kawasaki disease is a systemic vasculitis of small and medium-sized vessels, that mainly affects children aged between 1 and 5 years, and whose prognosis depends essentially on the involvement of the coronary arteries.

Kawasaki disease (KD) has an incidence in Italy of around 14 per 100,000 / year in children younger than 5 years of age, with a number of cases of around 450 / year based on the discharge of the Diagnosis Related Groups (DRG) from hospitals (10).

This value is similar, or slightly higher, than other in European countries, but much lower than in Asian countries.

Epidemiological data suggest an infectious etiology, although the causative agent has not yet been identified. Associations with various infectious agents have been reported, both viral (enterovirus, adenovirus, rinovirus, coronavirus and also Epstein-Barr) and bacterial (e.g. group B streptococci) (11). At present, a causal association with SARS-CoV-2 infection is not established (7). In particular, the incidence in recent months of KD in Italy has not yet been established, **and it is not possible to verify whether the number of affected subjects has increased in conjunction with the COVID-19 epidemic.**

Genetic factors certainly increase susceptibility to KD, as indicated by its particularly high incidence in children of Asian ethnicity (12, 13). Therefore, KD is believed to be an aberrant multifactorial and secondary inflammatory response to an infection in genetically predisposed individuals (14,15). The release of proinflammatory cytokines such as interleukin (IL) -1 $\beta$ , IL-6 and tumor necrosis factor (TNF) - $\alpha$  is directly related to fever, involvement of the mucous membranes and skin peeling, both in toxic shock syndrome and in KD.

Interestingly, the clinical features of KD overlaps with some infectious diseases, such as adenovirus or scarlet fever infections. In addition, KD seasonal epidemic curves during winter and spring are similar to those of some viral diseases.

## Clinical features and diagnosis

The diagnosis of KD is clinical and based on the presence of fever associated with characteristic clinical manifestations. The internationally accepted criteria identify cases of KD on the basis of fever ( $> 38^{\circ}\text{C}$ ) lasting at least 5 days, in absence of possible alternative diagnosis, and in presence of at least four of the following clinical signs: alterations of the extremities (redness of the palms and / or soles of the feet, whit or without edema), polymorphic exanthema, bilateral non-exudative conjunctivitis, alterations of the oral cavity (eg with "strawberry" tongue) and unilateral laterocervical lymphadenopathy.

There are typical forms of KD (with fever and at least 4 signs or "clinical diagnostic criteria"), incomplete forms (with fever and less than 4 "clinical diagnostic criteria") and atypical forms characterized by fever and symptoms that are generally less frequently detected such as arthritis and / or arthralgias, aseptic meningitis, hepatitis, mastoiditis, vomiting, diarrhea, abdominal pain.

KD can be divided into three stages:

- **acute phase** (duration 1-2 weeks): presence of fever and other acute signs of the disease (which may not be present at the same time);
- **subacute phase** (lasting up to the 4th week): begins after the resolution of the fever and other initial signs. It can be associated with skin peeling of the fingers and toes, increased platelets, possible development of coronary aneurysms;
- **convalescence phase** (duration from week 5 to 8): from the disappearance of all the clinical signs of the disease to the normalization of the inflammatory indexes.

The course of the disease in children with KD is highly variable in relation to the possible coronary involvement, which represents the major complication of the disease and determines its prognosis. Both untreated and adequately treated patients can develop coronary artery arteries with rates up to 15-25% in untreated patients, while the percentage decreases (maximum 5%) in the cases treated within 7-10 days from onset of fever. Coronary involvement can evolve rarely towards the appearance of coronary aneurysms; 65-70% of aneurysms and, especially the small ones, resolve in 1-2 years after onset.

In cases of persistent aneurysms, these can decrease over time, or remodel with consequent stenosis, occlusions or tortuosity, often with serious consequences. The main cause of death in KD is in fact acute myocardial infarction caused by the obstruction of a coronary artery (11, 16-18).

Finally, cases of very severe KD with characteristics similar to toxic shock are described, called Kawasaki Shock Syndrome (KSS) (19).

## Treatment

Early treatment with high-dose intravenous immunoglobulins has been associated with a reduction up to a <5% in the risk of coronary involvement, and is recommended in national (17, 18) and international (11) guidelines. To this is associated an anti-inflammatory treatment with acetylsalicylic acid at a dosage of 30-50 mg / kg / day. In a refractory case (up to 15%), after a first cycle of intravenous immunoglobulins, various therapeutic choices may follow, including a second infusion of intravenous immunoglobulins, steroids, or alternative drugs including biological drugs such as TNF inhibitors or anti-cytokines (anti-IL-1 ) (20).

# Acute multisystem inflammatory syndrome in children and adolescents during the SARS-CoV-2 outbreak

In recent weeks, several reports of clinical forms with some characteristics similar to KD and positivity for SARS-CoV-2 or presence of antibodies to SARS-CoV-2 raised the interest.

## General characteristics, epidemiology and etiopathogenesis

On 15<sup>th</sup> May 2020, the ECDC published a Rapid Risk Assessment on pediatric multisystem inflammatory syndrome and SARS-CoV-2 infection (7), reporting 230 suspected cases in the European Union and the United Kingdom, with two deaths. The affected subjects (aged in average 7-8 years, and up to 16 years) are generally older than those with classic KD. These patients presented with severe multisystem involvement, sometimes requiring intensive care.

The real number of these subjects is still under evaluation, as well as the precise nosological classification of this condition, currently called *acute multisystem inflammatory syndrome*.

Both Italian and English data show that the development of these clinical forms followed 2-4 weeks after the peak of SARS-CoV-2 infection, suggesting an immunomediated pathogenesis and a direct effect of the virus.

## Clinical features

This syndrome is characterized by frequent myocardial and / or gastrointestinal involvement. There are also high fever ( $\geq 38^{\circ}\text{C}$ ), signs of shock, abdominal pain; conversely, interstitial pneumonia seems not to be present, while macrophage activation syndrome may be present.

Laboratory tests indicate increased phlogistic indexes, neutrophilia, lymphopenia, anemia and thrombocytopenia, hypoalbuminemia, increased ferritin, C-reactive protein, IL-6, D-dimer, and natriuretic peptide type B (BNP).

Regarding the therapeutic aspects, the best treatment is not known date. Intravenous immunoglobulins, steroids, and sometimes an IL-1  $\beta$  and  $\alpha$  (anakinra) cytokine receptor antagonist have been used.

The experience of the Bergamo Hospital shows that most patients need adjuvant therapy with systemic corticosteroids. Despite the aggressiveness of the form, all of the 10 children treated in the published Italian case study responded promptly to this therapy, recovered and were discharged without demonstrable outcomes (21).

## Risk assessment in relation to the infection with SARS-CoV-2 carried out by the ECDC

The evidences set out by the ECDC Rapid Risk Assessment report (7) define that the evidences supporting the association between pediatric acute inflammatory multisystem syndrome and SARS-CoV-2 infection are:

- the countries reporting the highest number of cases of this syndrome are those with a higher prevalence of COVID-19: United Kingdom, Spain, USA and Italy;
- cases detected in countries with different geographical locations;
- the consecutio temporum between COVID-19 outbreaks and the diagnosis of cases of pediatric multisystem inflammatory syndrome, observed 2-4 weeks after the peak of the infection;
- the biological plausibility that a viral infection can activate an inflammatory disease with some similarities with KD, through an altered immune response.

However, ECDC also notes that the evidence for a causal relationship between COVID-19 and this syndrome is still limited.

It is important to point out that the report highlights the absence of a **European** shared case definition at the moment, and recommends the definition of common criteria in Europe for the detection of the cases, allowing to diagnose the multi-systemic inflammatory syndrome and its follow-up.

The conclusions of the report are that:

- the probability of contracting multisystem inflammatory syndrome is very low,
- and on the other hand, that the impact of the syndrome on the subject's health is high.

Hence, based on the evidence available to date, the ECDC concludes that the risk for the general pediatric population to contract the multi-system inflammatory syndrome associated with COVID-19 is low (7).

## Case definitions proposed by national and international agencies

The “case definition” represents a fundamental element for the purposes of the nosological framework, indispensable for correct registration and epidemiological analysis of cases, effective clinical management of patients, as well as for research on pathogenesis, including risk factors.

As already mentioned, the ECDC notes the lack of case definition shared at European level and underlines its importance and urgency (7).

At the same time, three case definitions proposed by the Royal College of Paediatrics and Child Health (22), CDC (23) and the World Health Organization (WHO) (24) have recently been presented to the scientific community.

These case definitions converge on some signs and symptoms (e.g. fever, shock) and laboratory tests (e.g. PCR, lymphopenia, fibrinogen and procalcitonin) and on the exclusion criterion once other diagnoses have been made. On the other hand, they also differ about e.g. age, positivity to SARS-CoV-2 infection, clinical severity of the disease such as to induce hospitalization, as well as in the definition of the pathology.

The Royal College of Paediatrics and Child Health of the United Kingdom defines the disease as “Paediatric multisystem inflammatory syndrome temporally associated with COVID-19” (22). The case definition is based on signs and symptoms (fever, shock, respiratory and renal, gastrointestinal or neurological disorders) and on biomarkers including in particular phlogistic markers (neutrophilia, elevated C-reactive protein and lymphopenia). The criteria may also include some features of KD. The diagnostic process involves the exclusion of infectious forms (streptococcus, staphylococcus, enterovirus); the PCR test for SARS-CoV-2 can be positive or negative. As regards the treatment, being this a nosological entity on which the evidence is still to be defined, the use of drugs such as antivirals or immunomodulators must

be evaluated by a multidisciplinary team that includes pediatricians, immunologists, rheumatologists and infectious disease specialists.

On 14th May 2020, US CDC issued an “Official Health Advisory” on “Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19)” (23).

In this document, the case definition includes the simultaneous presence of the following criteria:

- age <21 years; fever ( $\geq 38^{\circ}\text{C}$  for  $\geq 24$  hours); phlogistic markers; clinical severity of the disease that requires hospitalization; involvement of multiple organs ( $\geq 2$ , in particular the heart, kidney, respiratory, gastrointestinal, nervous, skin and / or hematological systems);
- absence of plausible alternative diagnoses;
- present or recent positivity to SARS-CoV-2 infection detected by RT-PCR, serology or antigen test; or exposure to COVID-19 within 4 weeks before symptoms' development.

Some patients may also have some KD features that have to be reported if they meet the case definition of MIS-C. MIS-C should be considered in all pediatric deaths with evidence of SARS-CoV-2 infection (23).

On 15th May 2020, WHO published a scientific report on “Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19” (24), indicating a definition of a preliminary case that includes the co-presence of the following criteria:

- the age group 0-19 years with fever > three days
- two of the following symptoms:
  - a) skin rash or bilateral non-purulent conjunctivitis or signs of mucocutaneous inflammation (mouth, hands or feet);
  - b) hypotension or shock;
  - c) myocardial dysfunction, pericarditis, valvulitis or coronary anomalies (including ultrasound findings, elevated troponin / NT-proBNT)
  - d) evidence of coagulopathy (by PT, PTT, elevated d-Dimers)
  - e) acute gastro-intestinal disorders (diarrhea, vomiting or abdominal pain)
- high phlogistic markers such as C-reactive protein or procalcitonin
- absence of obvious microbial cause of inflammation, including bacterial sepsis and streptococcal or staphylococcal shock syndrome.
- evidence of COVID-19 infection (RT-PCR or positive serology or antigenic test) or probable contact with patients with COVID-19.

## Specific recommendations

### Kawasaki disease

**Diagnostic suspicion:** children with fever ( $\geq 38$  °C) and in the presence of diagnostic criteria (bilateral conjunctivitis without secretions, redness of lips and oral mucosa, alterations of hands and/or feet with redness of the palms and soles with or without edema, rash and unilateral enlargement of the cervical lymph nodes), which may not all be present at the same time.

**Diagnosis:** it is recommended that the child with these clinical symptoms is quickly evaluated by a pediatrician and brought to the hospital, favoring the national reference centers, to carry out clinical and laboratory tests. If the diagnosis is confirmed, appropriate drug therapy should be initiated within the time frame indicated by the guidelines.

**Treatment:** appropriate drug therapy includes intravenous immunoglobulins (authorized and proven effective treatment), within 7-10 days from the onset of the fever; acetylsalicylic acid: at anti-inflammatory dosage for 48 hours, then at antiplatelet dose. Diagnostic delay and consequent therapeutic delay can be responsible for very serious complications such as coronary artery aneurysms (up to 15-25% of untreated cases). Appropriateness and timeliness of the diagnosis significantly affect the child's prognosis. There is currently no evidence that KD treatment should be changed during the COVID-19 pandemic period according to existing guidelines.

**Correlations:** there is no large-scale epidemiological evidence of an increase in the incidence of KD both nationally and internationally during the COVID-19 pandemic. Furthermore, there are no evidences or reports to date indicating that during the pandemic, patients with previous KD are exposed to greater risk of SARS-CoV-2 infection, or of KD relapse.

### Acute multisystem inflammatory syndrome in children and adolescents

**Diagnostic suspicion and diagnosis:** the patient with diagnostic suspicion should be referred promptly to the hospital. The diagnosis must be suspected in case of high fever ( $> 38^{\circ}\text{C}$ ) lasting several days, signs of shock, myocarditis, signs of macrophage activation and gastro-intestinal involvement, possibly associated with other classic symptoms of KD in children and young people, also older than the KD group.

**Treatment:** in the published cases, treatment has been based on intravenous immunoglobulin in all patients, in association with corticosteroids in most cases, in addition to supportive care. In case of refractoriness, cytokine receptor antagonists such as anakinra can also be considered.

**Correlations:** based on the ECDC assessment, a correlation between SARS-CoV-2 infection and the onset of the syndrome is plausible (7). A more accurate evaluation will be possible by a wider case collection based on solid and shared diagnostic criteria.

## **National active surveillance**

In order to contribute to the development of medical-scientific knowledge on incidence, pathogenesis, therapies and prognosis and to provide useful information to improve assistance to patients and their families, it is recommended to start active national surveillance, through the registration of new national cases. Case definition must be the essential basis for a national register of adequate quality.

At national level, the registration of cases must comply with the indications of European and international organizations and include a well-defined data set aimed to collecting signs, symptoms and other clinical data, laboratory data, response to treatment and subsequent follow-up both in KD and in multisystemic acute inflammatory syndrome in children. Their systematic and regular collection over time and with national coverage will be able to provide medical-scientific information for the understanding of the nosology and pathogenesis of these pathological forms.

It is appropriate and desirable, that the national registry is centralized and managed by the Istituto Superiore di Sanità, to ensure the quality and compliance with the law.

# General recommendations

## Physical spacing and personal protective equipment (PPE)

Physical spacing measures and individual daily prevention behaviors represent a fundamental tool for people in all age groups. Asymptomatic patients, patients with mild symptoms or with different symptoms than the most frequent ones in COVID-19 infection (fever, dyspnea, cough) can have an important role in the transmission of the virus (3).

## Health worker protection

The subjects most at risk of contracting SARS-CoV-2 infection are primarily healthcare professionals; to fully guarantee their health and safety, it is necessary to implement preventive non-pharmacological interventions in order to preserve them and prevent the transmission of the virus.

The most effective prevention measures to be applied in the health sector include:

- to frequently practice hand hygiene with soap and water or preferably with alcohol-based solutions / gels, to allow hand hygiene at the patient's bed at all recommended times (before and after contact, before aseptic maneuvers, after contact with biological liquids, after contact with surfaces close to the patient);
- to avoid closed contact by keeping the distance of at least one meter from other people in the absence of adequate PPE, in particular from those with respiratory symptoms. This behavior must also be respected during work breaks. To use the PPE appropriately and to keep adequate awareness and training on their use, regarding dressing, undressing and elimination, bearing in mind that, according to as current knowledge, the main SARS-CoV-2 transmission occurs is through droplets and contact, with the exception of specific aerosols generating maneuvers and procedures;
- to avoid touching your eyes, nose and mouth with your hands; to respect the respiratory label (e.g., coughing or sneezing in your elbow);
- to use appropriate PPE; to refer to the indications on their correct use in case of assistance to suspected / probable / confirmed case assistance and in relation to the work context, the job and the type of work. It should be noted that PPE must be considered as an effective measure for the protection of the health care worker only if inserted within a wider set of interventions that includes administrative, procedural, environmental, organizational and technical controls in the health care context;
- to always make the patient with suspected / probable / confirmed COVID-19 wear a surgical mask while receiving direct assistance from the operator;
- to limit the access to only indispensable companions, inviting them to hand hygiene and the use of a mask;
- to adopt clinical screening of admissions or hospitalized patients to facilitate rapid identification of suspected cases. The screening activities must consider that symptoms differ significantly in the child and adolescent compared to those of the adult. Furthermore, the clinical screening it would be necessary considering "atypical" peculiar symptomatic manifestations which over time, on the basis of the case study, could be proven to be caused by and / or associated with SARS -CoV-2 infection;



- to clean and to adopt the correct hygiene measures in closed environments are key points in preventing the spread of SARS-CoV-2. Therefore, to limit contact transmission, it is necessary to restrain exposure and to sanitize the surfaces and environments, in addition to hand hygiene and use of PPE;
- to pay attention to respect the functional separation between areas of care for suspected/ probable/ confirmed COVID-19 patients and areas of non-COVID-19 patients (dirty areas, clean areas) (25).

## **National Helpline for Rare Diseases of the ISS (Telefono Verde Malattie Rare)**

The current health emergency due to the SARS-CoV-2 epidemic has involved, in various respects, also people with rare diseases and their families: for example, the continuity of care of the National Health Service, that has been invested by a new and unexpected commitment, and by numerous questions regarding the grade of susceptibility to infection of people with specific rare diseases. In fact, health information has fundamental importance for the prevention and management of diseases. In the field of rare diseases, one of the main communication and information tools of the ISS is the National Helpline for Rare Diseases (Telefono Verde Malattie Rare, TVMR), established in 2008. The service, available at the free number 800.89.69.49, uses the telephone counseling to guide citizens and professionals to paths and resources on the national and international territory, conveying scientific knowledge and good practices and stimulating empowerment processes. The telephone lines are active on the national territory from Monday to Friday from 9:00 to 13:00. The service is also available from abroad via email ([tvmr@iss.it](mailto:tvmr@iss.it)), and dedicates an email box to deaf people ([tvmrlis@iss.it](mailto:tvmrlis@iss.it)).

Since 2012, TVMR has been a member of the European Network of Rare Disease Help Lines (ENRDHLs), promoted by EURORDIS, the federation of non-governmental associations focused on patients, which represents 862 patient organizations in 70 countries. Since 2017 TVMR has been the promoter and coordinator of the Italian Network of Listening & Information Centers for Rare Diseases (R.I.C.A.Ma.Re), with the participation of several regional institutional information points. Finally, TVMR contributes to update and make information that are useful for citizens with rare diseases and professionals, accessible and usable, through the inter-institutional portal [www.malattierare.gov.it](http://www.malattierare.gov.it). This government portal intends to offer a collection of all the reference points for rare patients, ranging from treatment centers to regional information points, to the Italian Federation of Rare Diseases (UNIAMO), to the numerous patient associations, to the European Reference Networks, in order to disseminate information on the topic of rare diseases in an integrated way with the TVMR.

TVMR's commitment is therefore to inform citizens accurately and appropriately with respect to the most recent updates on scientific knowledge, as well as to provide a link with all the Social-Health Care Centers and Associations of patients, including "Rari Ma Speciali OdV", that are present on the national territory.

## **Role of the Association for Kawasaki disease “Rari Ma Speciali OdV”**

“Rari Ma Speciali OdV” is the Association of KD patients in Italy. The purpose of the Association is to spread knowledge on KD, and to support families and scientific research on the disease, by adopting a synergistic work approach with institutions, scientific societies and patient associations from other countries.

During the SARS-CoV-2 epidemic and in the following emergency related to the possible association with the KD, “Rari Ma Speciali OdV” is acting at the forefront to properly informing families and is collaborating with scientific institutions and societies to get updated and validated information.

The association's commitment is to disseminate this document through the main communication channels and through discussions with families, both nationally and internationally. In this particular moment in which the international community is facing the same situation, the sharing with the network of associations from other countries is essential to have a correct communication and a common approach towards families with KD.

All information on the disease, activities and contacts are available on the Association's website: [www.malattiadikawasaki.it](http://www.malattiadikawasaki.it).

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