Comparison laboratory data between children with Kawasaki Disease and COVID-19

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Research Article

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Abstract

Background:

The 2019 coronavirus disease (COVID-19) has been an emerging, rapidly evolving situation in China since late 2019 and has even become a worldwide pandemic. The first case of severe childhood novel coronavirus pneumonia in China was reported in March 2020 in Wuhan. The severity differs between adults and children, with lower death rates and decreased severity for individuals under the age of 20 years old. Increased cases of Kawasaki disease (KD) have been reported from New York City and some areas of Italy and the U.K., with almost a 6-10 times increase when compared with previous years. We conducted this article to compare characters and laboratory data between KD and COVID-19 in children.

Methods:

We obtained a total of 24 COVID-19 children from the literature review and 234 KD cases from our hospital via retrospective chart review.

Results:

We found that patients with KD had higher levels of white blood cell (WBC), platelet, neutrophil percentage, C-reactive protein (CRP), procalcitonin, Aspartate Aminotransferase (AST), and body temperature, while patients with COVID-19 had higher age, hemoglobin levels, and lymphocyte percentage. After performing multiple logistic regression analysis, we found that age, WBC, platelet, procalcitonin, and AST provide identical markers for distinguishing COVID-19 from KD in children.

Conclusion:

In this COVID-19 pandemic period, clinicians should pay attention to children with COVID-19 infection when high WBC, platelet, procalcitonin, and AST values are present in order to provide precision treatment with intravenous immunoglobulin (IVIG) for KD or multisystem inflammatory syndrome in children (MIS-C).

Background

The novel coronavirus has been reported as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been designated as COVID-19 (coronavirus disease 2019). (1) So far, according to a systemic review (2), children have comprised only 1-5% of total diagnosed cases of COVID-19. Common presenting symptoms of COVID-19 include cough, pharyngeal erythema, headache, and fever. (3) Because the symptoms or clinical characteristics in patients with COVID-19 and patients with Kawasaki disease (KD) have considerable overlap, identification of laboratory markers that may be indicative of COVID-19 disease would be highly helpful in an acute care setting.

KD is a systemic vasculitis syndrome with five major clinical criteria of symptoms (the 1-2-3-4-5 rapid memory method) including one mouth (fissure lips and/or strawberry tongue), two eyes (bilateral non-purulent conjunctivitis), three fingers check neck lymph node enlargement (>1.5cm in diameter, usually unilateral), four limbs changes (induration, redness and/or desquamation), and five days of fever as with as polymorphism skin rash. (4) Some KD patients also have respiratory tract or gastrointestinal tract symptoms like cough, rhinorrhea, sore throat, headache, vomiting, diarrhea, abdominal pain, and joint pain. (5, 6) The clinical symptoms of COVID-19 somewhat overlap with those patients of KD. The Bacillus Calmette-Guérin (BCG) vaccine scar reaction was reported with regard to KD mostly in routine vaccination countries like Taiwan, China and Japan. (7) In addition to its specific effect against tuberculosis,
the BCG vaccine has beneficial non-specific (off-target) effects on the immune system that protect against a wide range of other infections and is also routinely used to treat bladder cancer (8) or as a functional survey for T cell of delayed-type hypersensitivity. Some reports have suggested that vaccination with BCG may also have a role in protecting individuals against COVID-19. (9, 10)

Skin rash over the toe area has been reported by dermatologists, indicating some similar symptoms between COVID-19 and KD in vasculitis. (11) Other symptoms like the loss of smell or taste in COVID-19 may overlap with hearing loss in KD patients. The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) proposed “that anosmia could be added to the list of screening tools for possible COVID-19 infection”. (12) Skin rash, headache, sore throat, rhinorrhea, diarrhea, abdominal pain, and cough are the shared symptoms between KD and COVID-19. The aim of this article is to compare differences between childhood patients with KD and COVID-19 to provide clinical information for precise treatment.

**Materials And Methods**

A retrospective analysis was conducted on the medical records of patients admitted to the Shenzhen Baoan Women's and Children's hospital in China from 2017 to 2020. All the children were under the age of 18 years old. KD diagnosis was given according to the American Heart Association (AHA) criteria with at least four of the following five clinical manifestations: bilateral bulbous conjunctival congestion, fissure lips or oral cavity changes, hand and foot symptoms, dysmorphism skin manifestations, and cervical lymph node enlargement. (13, 14) We excluded incomplete or atypical KD. (15) We collected a total of 24 children patients (8+10+6) with age less than 18 years old, with COVID-19 diagnosis, and with laboratory data available online from PubMed. (16-18) Laboratory data of white blood cell count/differential count (WBC/DC), C-reactive protein (CRP), procalcitonin (PCT), Aspartate Aminotransferase (AST), age, and gender were all enrolled for analysis. The aim of this report was to identify laboratory markers to help clinicians distinguish KD from COVID-19 during this pandemic period and review the disease characteristics.

**Statistics**

The data in this study were analyzed with median values, with quartile, Q1, and Q3) being used for measurement data, and n and percentage used for enumeration data. We adopted the non-parametric Mann-Whitney U rank sum test for comparison between the two groups. The Chi-square test was used for counter measurement. The receiver operating characteristics (ROC) curve method was used to differentiate between groups. The best cut-off points for accurate diagnosis were based on the highest sensitivity value plus the specificity identified by the ROC curve and the cutoff values are as followed (age: 59months, WBC: 9.71*10^9/L, platelet: 273*10^9/L, PCT: 0.13ng/L, AST: 21.71U/L). Multivariate logistic regression was applied to analyze the influencing factors that showed significance in univariate analysis. Statistical significance was defined as a p-value of less than 0.05. SPSS 13.0 statistical software was used for all analyses.

**Results**

We enrolled 234 KD patients and 24 COVID-19 patients for analysis. As shown in Table1, lymphocyte percentage (p=0.012) and Hb levels (p<0.001) were significantly higher in patients with COVID-19 than KD children. Meanwhile, the WBC (p<0.001), neutrophil percentage (p<0.001), platelet counts (p<0.001), CRP (p<0.001), procalcitonin (p<0.001), and AST levels (p=0.019) were significantly lower in patients with COVID-19 when compared with that of KD. Meanwhile, the cut-off value of WBC and CRP were 9.71(10^9/L) and 38.57 (mg/L), respectively. There was no significant difference in regarding the levels of ALT between patients with KD and COVID-19 (p=0.513).
After performing multiple logistic regression, we found that age, WBC, platelet counts, procalcitonin, and AST levels showed significant difference between patients with KD and COVID-19 (p<0.05). The comparison of disease characteristics is shown in Table 2. The etiology of KD remains unknown, but COVID-19 is caused by the human coronavirus. Diagnostic criteria for KD include five major symptoms and fever for more than five days, but the clinical symptoms or signs in COVID-19 are non-specific or even asymptomatic or without fever. Furthermore, KD has a male predominate characteristic, and the global prevalence of KD is higher in those of Asian descent than in European or in Americans descent. (19) While the prevalence of COVID-19 is higher in Americas than Europe and Asia.

Discussion

The COVID-19 pandemic has already reached over 80.8 million infections and caused over 1,760,000 deaths till December 2020. While the exactly prevalence of COVID-19 in children is still unknown, mounting evidence has highlighted that the clinical severity of COVID-19 in children and young adults appears significantly milder compared to older individuals with comorbidities. (20, 21) COVID-19 was also reported to induced the Kawasaki-like disease, the multisystem inflammatory syndrome in children (MIS-C), a novel syndrome linked to SARS-CoV-2. In this study, we compared the difference between children patients with COVID-19 (not MIS-C) and KD (not including KD shock syndrome, KDSS) and demonstrated that higher WBC, platelet, procalcitonin, and AST provide laboratory markers for distinguishing COVID-19 from KD. We further revealed that KD patients have lower age and higher characteristics of fever than COVID-19 children. Other laboratory data including lactate dehydrogenase (LDH), D-dimer, creatine kinase (CK) and serum creatinine were also increased in children with COVID-19. According to the statement of American Heart Association (AHA) (13, 22), LDH, D-dimer, CK and serum creatinine didn't in the list of supplementary criteria of suspected incomplete KD. However, LDH, CK, serum creatinine and D-dimer levels were reported to be higher in KD patients and associated with IVIG resistance or coronary artery lesions formation. (23-26)

The golden period for IVIG treatment in KD patients is around five to nine days after disease onset; therefore, early awareness of KD is very important both for clinicians and parents. However, the challenge for clinicians in pediatric emergency departments is early identification of KD because KD shares many clinical signs with other febrile illnesses in childhood. (27) Furthermore, with "stay at home" orders and trepidation related to COVID-19 infection, many parents now hesitate or fear seeking in-person consultation for their children. Harahsheh et al., raised the concern of a future surge in the prevalence of CAAs caused by the potential for missed or late diagnosis and treatment of KD in children. (28)

In 1974, Tomisaku Kawasaki first described 50 cases of KD in English language. (29) The etiopathogenesis of KD remains unknown even today, and many studies have failed to identify a pathogen responsible for KD or any identified pathogens could not be repeated between studies. (30) Furthermore, growing evidence has demonstrated that KD may be the result of a combination of infection, genetics, environment and immunity. (31) In addition to standard diagnostic criteria, KD patients may experience a variety of nonspecific clinical features, including uveitis, aseptic meningitis, gastrointestinal symptoms, maculopapular rash, impaired liver function, and anemia. (7, 32, 33) Hepcidin-induced iron deficiency was reported to be related with transient anemia and disease outcomes in KD patients but anemia was not found in children with COVID-19. Neutrophil percentage was higher in KD patients than COVID-19 while lymphocyte percentage showed higher in COVID-19 children than KD indicating viral immune response in COVID-19.

In the most severe cases of KD, patients may develop hemodynamic instability, known as KD shock syndrome (KDSS), and secondary hemophagocytic lymphohistiocytosis fulfilled the criteria of macrophage activation syndrome (MAS). (34) Surprisingly, several lines of study have suggested that COVID-19 children have presented significantly unwell across Europe and the US with a novel syndrome linked to SARS-CoV-2 (MIS-C). (35, 36) This rare syndrome of COVID-
19, children shares common features with other pediatric inflammatory conditions, including KD, staphylococcal/streptococcal toxic shock, macrophage activation syndrome, and sepsis. (36)

In 2005, Esper et al. identified a novel human coronavirus tested by RT-PCR, designated New Haven coronavirus (HCoV-NH), in the respiratory secretions of eight of 11 children with KD versus one of 22 controls. (37) Notably, Jones et al., reported a six-month-old infant diagnosed with KD and treated with IVIG and aspirin and positive screening of COVID-19 in Italy. (38) Thereafter, Verdoni et al., reported a case series of a 30-fold increased incidence of Kawasaki-like disease at the Italian epicenter of the COVID-19 epidemic. (39) The patients who showed evidence of an immune response to the COVID-19 virus were older, had a higher rate of cardiac involvement, and macrophage activation syndrome features. (39) Consistently, in Whittaker et al.’s study, pediatric MIS-C patients were generally older than those with KD or KDSS and had higher WBC, and CRP, as well as more profound lymphopenia and anemia. (40) The COVID-19 epidemic has also been associated with a high incidence of a severe form of KD (41). They also identified that the Kawasaki-like disease described here remains a rare condition, probably affecting no more than one in 1000 children exposed to COVID-19. (39) The very limited COVID-19 children (N=24) included in this study is the limitation and weakness of this study. However, the association between KD and COVID-19 still warrants further investigation. In the era of the COVID-19 pandemic, multisystem inflammatory presentations of COVID-19 children and typical KD patients will be more challenging for clinicians and pediatricians in the future.

Conclusion

In conclusion, a younger age, male predominate, with higher levels of WBC, platelet, procalcitonin, and AST provide identical markers for distinguishing KD patients from COVID-19 in children. In this pandemic period of COVID-19, clinicians should pay more attention to children with COVID-19 infection while laboratory data showing high WBC, platelet, procalcitonin, and AST levels to provide treatment with IVIG for KD. Likewise, children with KD should also be screened for COVID-19 infection.

Declarations

Ethics Approval and Consent to Participate: This study was conducted in accordance with the Declaration of Helsinki. It was approved by the ethics committee of Shenzhen Baoan Women's and Children's Hospital, Shenzhen, Guangdong, China. (IRB No. LLSCKS 2020-5-02-KS) and Chang Gung Medical Foundation, Chang Gung, Taiwan (IRB: 202000966B1). Due to the retrospective nature of this study, informed consent did not have to be obtained from the parents/legally authorized representatives of the participants. The ethics committees of Shenzhen Baoan Women's and Children's Hospital, Shenzhen, Guangdong, China and Chang Gung Medical Foundation, Chang Gung, Taiwan both waved the informed consent.

Consent for publication

Not applicable

Availability of supporting data

The dataset containing results from this article are available from the corresponding author (HC Kuo) upon request.

Conflicts of interests

The authors declare that they have no conflicts of interest to declare in relation to this article.
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Authors' contributions

YSH, YHH and HCK designed the study. YSH, YHH, SFL and HCK conceived the study. YSH, YHH, SFL and HCK extracted the data for the study. YCT and SFL revised the article. All authors read and approved the final version of the manuscript.

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Not applicable.

Abbreviations

| Abbreviation | Description                                    |
|--------------|------------------------------------------------|
| COVID-19     | The 2019 coronavirus disease                   |
| KD           | Kawasaki disease                               |
| WBC          | White blood cell                               |
| CRP          | C-reactive protein                             |
| AST          | Aspartate Aminotransferase                     |
| IVIG         | Intravenous immunoglobulin                     |
| MIS-C        | Multisystem inflammatory syndrome in children  |
| SARS-COV-2   | Severe acute respiratory syndrome coronavirus 2|
| PCT          | Procalcitonin                                  |

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33.
2. Zimmermann P, Curtis N. COVID-19 in Children, Pregnancy and Neonates: A Review of Epidemiologic and Clinical Features. Pediatr Infect Dis J. 2020;39(6):469-77.
3. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr. 2020.
4. Kuo H-C. Preventing coronary artery lesions in Kawasaki disease. Biomedical journal. 2017;40(3):141-6.
5. Singh S, Gupta A, Jindal AK, Gupta A, Suri D, Rawat A, et al. Pulmonary presentation of Kawasaki disease-A diagnostic challenge. Pediatr Pulmonol. 2018;53(1):103-7.
6. Baker AL, Lu M, Minich LL, Atz AM, Klein GL, Korsin R, et al. Associated symptoms in the ten days before diagnosis of Kawasaki disease. J Pediatr. 2009;154(4):592-5 e2.
7. Tseng HC, Ho JC, Guo MM, Lo MH, Hsieh KS, Tsai WC, et al. Bull's eye dermatoscopy pattern at bacillus Calmette-Guerin inoculation site correlates with systemic involvements in patients with Kawasaki disease. The Journal of dermatology. 2016;43(9):1044-50.

8. Pettenati C, Ingersoll MA. Mechanisms of BCG immunotherapy and its outlook for bladder cancer. Nat Rev Urol. 2018;15(10):615-25.

9. Klinger D, Blass I, Rappoport N, Linial M. Significantly Improved COVID-19 Outcomes in Countries with Higher BCG Vaccination Coverage: A Multivariable Analysis. Vaccines (Basel). 2020;8(3).

10. Escobar LE, Molina-Cruz A, Barillas-Mury C. BCG vaccine protection from severe coronavirus disease 2019 (COVID-19). Proc Natl Acad Sci U S A. 2020;117(30):17720-6.

11. Sachdeva M, Gianotti R, Shah M, Lucia B, Tosi D, Veraldi S, et al. Cutaneous manifestations of COVID-19: Report of three cases and a review of literature. J Dermatol Sci. 2020.

12. Lechien JR, Hopkins C, Saussez S. Sniffling out the evidence; It's now time for public health bodies recognize the link between COVID-19 and smell and taste disturbance. Rhinology. 2020.

13. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association. Circulation. 2017;135(17):e927-e99.

14. Burns JC GM. Kawasaki syndrome. Lancet. 2004;364:533-44.

15. Rossomando V, Baracchini A. Atypical and incomplete Kawasaki disease. 1997;49(9):419.

16. Cai J, Xu J, Lin D, Yang Z, Xu L, Qu Z, et al. A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.

17. Sun D, Li H, Lu XX, Xiao H, Ren J, Zhang FR, et al. Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study. World journal of pediatrics : WJP. 2020.

18. Liu W, Zhang Q, Chen J, Xiang R, Song H, Shu S, et al. Detection of Covid-19 in Children in Early January 2020 in Wuhan, China. N Engl J Med. 2020;382(14):1370-1.

19. Wang CL, Wu YT, Liu CA, Kuo HC, Yang KD. Kawasaki disease: infection, immunity and genetics. Pediatr Infect Dis J. 2005;24(11):998-1004.

20. Balasubramanian S, Rao NM, Goenka A, Roderick M, Ramanan AV. Coronavirus Disease (COVID-19) in Children - What We Know So Far and What We Do Not? Indian Pediatr. 2020.

21. Dong Y, Wang L, Burgner DP, Miller JE, Song Y, Ren X, et al. Infectious diseases in children and adolescents in China: analysis of national surveillance data from 2008 to 2017. BMJ. 2020;369:m1043.

22. Newburger JW, Takahashi M, Gerber MA, Gewitz MH, Tani LY, Burns JC, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation. 2004;110(17):2747-71.

23. Fukunishi M, Kikkawa M, Hamana K, Onodera T, Matsuzaki K, Matsumoto Y, et al. Prediction of non-responsiveness to intravenous high-dose gamma-globulin therapy in patients with Kawasaki disease at onset. J Pediatr. 2000;137(2):172-6.

24. Kong WX, Ma FY, Fu SL, Wang W, Xie CH, Zhang YY, et al. Biomarkers of intravenous immunoglobulin resistance and coronary artery lesions in Kawasaki disease. World journal of pediatrics : WJP. 2019;15(2):168-75.

25. Lee SM, Lee JB, Go YB, Song HY, Lee BJ, Kwak JH. Prediction of resistance to standard intravenous immunoglobulin therapy in Kawasaki disease. Korean Circ J. 2014;44(6):415-22.
26. Fernandez-Cooke E, Barrios Tascon A, Sanchez-Manubens J, Anton J, Grasa Lozano CD, Aracil Santos J, et al. Epidemiological and clinical features of Kawasaki disease in Spain over 5 years and risk factors for aneurysm development. (2011-2016): KAWA-RACE study group. PLoS One. 2019;14(5):e0215665.

27. Hao S, Jin B, Tan Z, Li Z, Ji J, Hu G, et al. A Classification Tool for Differentiation of Kawasaki Disease from Other Febrile Illnesses. J Pediatr. 2016;176:114-20 e8.

28. Harahsheh AS, Dahdah N, Newburger JW, Portman MA, Piram M, Tulloh R, et al. Missed or Delayed Diagnosis of Kawasaki Disease During the 2019 Novel Coronavirus Disease (COVID-19) Pandemic. J Pediatr. 2020.

29. Kawasaki T, Kosaki F, Okawa S, Shigematsu I, Yanagawa H. A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. Pediatrics. 1974;54(3):271-6.

30. Kuo HC, Liang CD, Wang CL, Yu HR, Hwang KP, Yang KD. Serum albumin level predicts initial intravenous immunoglobulin treatment failure in Kawasaki disease. Acta Paediatr. 2010;99(10):1578-83.

31. Del Principe D, Pietraforte D, Gambardella L, Marchesi A, Tarissi de Jacobis I, Villani A, et al. Pathogenetic determinants in Kawasaki disease: the haematological point of view. J Cell Mol Med. 2017;21(4):632-9.

32. Huang YH, Kuo HC, Huang FC, Yu HR, Hsieh KS, Yang YL, et al. Hepcidin-Induced Iron Deficiency Is Related to Transient Anemia and Hypoferraemia in Kawasaki Disease Patients. Int J Mol Sci. 2016;17(5).

33. Huang YH, Hsu YW, Lu HF, Wong HS, Yu HR, Kuo HC, et al. Interferon-gamma Genetic Polymorphism and Expression in Kawasaki Disease. Medicine (Baltimore). 2016;95(17):e3501.

34. Yang HF, Fan HC. Kawasaki disease shock syndrome and macrophage activation syndrome. Paediatr Int Child Health. 2018;38(4):310.

35. Balasubramanian S, Nagendran TM, Ramachandran B, Ramanan AV. Hyper-inflammatory Syndrome in a Child With COVID-19 Treated Successfully With Intravenous Immunoglobulin and Tocilizumab. Indian Pediatr. 2020.

36. Mahase E. Covid-19: concerns grow over inflammatory syndrome emerging in children. BMJ. 2020;369:m1710.

37. Esper F, Shapiro ED, Weibel C, Ferguson D, Landry ML, Kahn JS. Association between a novel human coronavirus and Kawasaki disease. J Infect Dis. 2005;191(4):499-502.

38. Jones VG, Mills M, Suarez D, Hogan CA, Yeh D, Bradley Segal J, et al. COVID-19 and Kawasaki Disease: Novel Virus and Novel Case. Hosp Pediatr. 2020.

39. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020;395(10239):1771-8.

40. Whittaker E, Bamford A, Kenny J, Kafourou M, Jones CE, Shah P, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. JAMA. 2020.

41. Abrams JY, Godfred-Cato SE, Oster ME, Chow EJ, Koumans EH, Bryant B, et al. Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2: A Systematic Review. J Pediatr. 2020.

Tables

Table 1: Comparison laboratory between children with COVID-19 and Kawasaki Disease
|                          | COVID-19 \(N=24\) | Kawasaki disease \(N=234\) | Univariate P value | Multivariate P value | Multivariate (B) | 95% Confidence interval |
|--------------------------|----------------------|-----------------------------|---------------------|----------------------|-------------------|-------------------------|
| Age (month)              | 54 (16, 105)         | 20 (12, 35.5)               | 0.290               | 0.012                | -1.965            | 0.140 0.030 0.651       |
| Male gender (%)          | 12 (50%)             | 143 (61.1%)                 | 0.290               | -                    |                   |                         |
| White blood cell count \(*10^9/L\) | 6.59 (3.87, 9.57) | 14.25 (10.11, 17.52) | <0.001              | 0.025                | 1.858             | 6.409 1.267 32.415      |
| Neutrophil %             | 47.51 (28.59, 58.8)  | 60.71 (49.62, 74.29)        | <0.001              | -                    |                   |                         |
| Lymphocyte %             | 35.31 (20.5, 50.88)  | 26.88 (16.99, 38.93)        | 0.012               | -                    |                   |                         |
| Platelet \(*10^9/L\)     | 207 (156.75, 301.25) | 353.5 (278.75, 449.5)       | <0.001              | 0.03                 | 1.728             | 5.627 1.178 26.886      |
| Hemoglobin (g/L)         | 122 (113, 134.75)    | 108.5 (100, 115)            | <0.001              | -                    |                   |                         |
| C-reactive Protein (mg/L)| 10.85 (5.82, 30)     | 65.59 (33.34, 115.55)       | <0.001              | -                    |                   |                         |
| Procalcitonin (ng/L)     | 0.07 (0.048, 0.095)  | 0.44 (0.16, 1.33)           | <0.001              | 0.001                | 2.890             | 17.985 3.219 100.493    |
| AST (U/L)                | 31.5 (20.35, 40)     | 35.99 (29.0, 51.75)         | 0.019               | 0.009                | 3.150             | 23.333 2.166 251.365    |
| ALT (U/L)                | 18.5 (13.7, 44.63)   | 20.2 (13.45, 44.63)         | 0.513               | -                    |                   |                         |
Data were present as medium with (quartile, Q1, Q3)

AST: Aspartate Aminotransferase
ALT: Alanine Aminotransferase

Multivariate (B): Coefficients of variables in Multivariate analysis. OR odds ratio, CI confidence interval
Male gender was analyzed by Pearson Chi-square test and others were analyzed by Mann-Whitney U test.

Table 2: Different characteristics between Kawasaki disease (KD) and COVID-19

|                                | Kawasaki disease (KD)                                      | COVID-19                                      |
|--------------------------------|-----------------------------------------------------------|----------------------------------------------|
| Etiology                       | Unknown                                                   | Human corona virus                           |
|                                | (corona virus may be one of the triggers of KD)           |                                              |
| Symptoms                       | 5 major symptoms                                          | Upper respiratory tract symptoms (non-specific or even asymptomatic) |
|                                | (fissure lips and/or strawberry tongue, bilateral non-purulent conjunctivitis, neck lymphadenopathy, limbs induration and polymorphic skin rash) |                                              |
| Fever (> 38°C)                 | 100%                                                      | 60-70%                                       |
| Treatment                      | IVIG + aspirin                                            | anti-IL6, hydroxychloroquine, remdesivir...etc. |
|                                |                                                            | (effect not with conclusion yet)             |
| Age                            | 85% < 5 years-old                                         | 2% < 19 years-old                           |
| Gender                         | Male > female, 1.5 folds                                  | Male≒Female                                 |
| BCG vaccine                    | Scar indurations                                          | May have protective role                     |
| Prevalence                     | Asia > America > Europe                                   | Europe, America > Asia                       |

°C: centigrade of body temperature
IVIG: intravenous immunoglobulin
IL6: interleukin 6
BCG: Bacillus Calmette–Guérin

5 major symptoms (1-2-3-4-5) of Kawasaki disease: 1 mouth (fissure lips and/or strawberry tongue), 2 eyes (bilateral non-purulent conjunctivitis), 3 fingers to check neck lymph node enlargement (neck lymphadenopathy), 4 limbs changes (induration or desquamation) and 5 days fever with skin rash (polymorphic skin rash).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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