ANDES PEDIATRICA
REVISTA CHILENA DE PEDIATRÍA
www.scielo.cl

Andes pediatr. 2024;95(6):703-710
DOI: 10.32641/andespediatr.v95i6.5177

ORIGINAL ARTICLE

Safety of SARS-CoV-2 vaccine in children with a history of Multisystem Inflammatory Syndrome (MIS-C)

Seguridad de la vacuna contra SARS-CoV-2 en pacientes con antecedentes de Síndrome Inflamatorio Multisistémico (SIM-C)

Karina Saravia Herrera[a,b], Josefa Hojman Jiménez[a,b], Javier Troncoso Bichara[c], Giannina Izquierdo Copiz[a,b], Cecilia Piñera Morel[a,b], Paula Leal Aranda[b], Rodolfo Villena Martínez[a,b]

[a]Departamento de Pediatría y Cirugía Infantil, Campus Sur, Facultad de Medicina, Universidad de Chile. Santiago, Chile.
[b]Hospital de niños Dr. Exequiel González Cortés, Santiago, Chile.
[c]CESFAM Amador Neghme. Santiago, Chile.

Received: March 5, 2024; Approved: Jun 11, 2024

What do we know about the subject matter of this study?

MIS-C involves an exacerbated multisystem inflammatory reaction following exposure to SARS-CoV-2 antigens and is the most severe expression of COVID-19 in pediatrics. Vaccination has been shown to reduce the risk of developing MIS-C. There is no consensus on recommendations to vaccinate patients with a history of MIS-C.

What does this study contribute to what is already known?

Re-exposure to SARS-CoV-2 antigens through SARS-CoV-2 vaccination in children with a history of MIS-C raises the concern of reactivating a hyperimmune response with immunization. Through this retrospective descriptive study, we observed that vaccination against SARS-CoV-2 is safe in recovered MIS-C patients.

Abstract

In May 2020, the WHO warned of the occurrence of a multisystem inflammatory syndrome associated with COVID-19 infection (MIS-C) in the pediatric population. **Objective:** To determine the safety of the SARS-CoV-2 vaccine in Chilean children previously hospitalized due to MIS-C. **Patients and Method:** Descriptive study on patients with history of MIS-C, discharged from the *Hospital Dr. Exequiel González Cortéz* in Santiago, Chile, between March 2020 and December 2022 who later received the SARS-CoV-2 vaccine. The number of doses, date of each vaccination, time interval to diagnosis of MIS-C, and the type of vaccine received in the period studied were reviewed. A questionnaire was administered on symptoms and adverse events presented by patients in the period up to 12 weeks after each vaccination, as well as symptoms suggestive of recurrence of MIS-C. Patients who could not be contacted, did not want to participate, or were not susceptible to vaccination were excluded. **Results:** 50 patients were included, the median age was 5.2 years, 58% were male, and 68% required PICU admission. 82% received at least 1 dose of a SARS-CoV-2 vaccine. The time (me-

Keywords:
MIS-C;
SARS-CoV-2;
COVID-19;
Vaccination;
Adverse Events

Correspondence:
Karina Saravia Herrera
karina.saravia@ug.uchile.cl

Edited by:
Paul Harris Diez

How to cite this article: Andes pediatr. 2024;95(6):703-710. DOI: 10.32641/andespediatr.v95i6.5177

dian) between MIS-C diagnosis and the first dose of the SARS-CoV-2 vaccine was 15 months (0-24). No serious adverse events or recurrence of MIS-C were reported. **Conclusion:** Vaccination against SARS-CoV-2 was safe, regardless of age, clinical manifestation of MIS-C, course, type of vaccine, and interval between illness and vaccination. Thereby, the interval for vaccination after MIS-C could be less than 3 months.

Introduction

During the SARS-CoV-2 pandemic, in May 2020 the World Health Organization alerted about the presentation of pediatric cases with inflammatory clinical manifestations of various systems, which shared characteristics with Kawasaki disease and toxic shock syndrome, but which had in common a history of SARS-CoV-2 infection within the previous six weeks, frequently requiring management in critical patient units (PICU), which was called Multisystem Inflammatory Syndrome in children associated with COVID-19 (MIS-C)[1,2]. In Chile, the Ministry of Health published a protocol for its management and initiated case surveillance, instructing retrospective and prospective notification of all persons between 0 and 19 years of age with MIS-C[3,4]. According to this, the first case in our country occurred in April 2020 and from then until August 2023, 504 cases were reported, with a case fatality of 1%, and a progressive trend to occur increasingly in children under 3 years of age between 2022 and 2023, compared with the beginning of the pandemic[5], which could be temporarily explained by the later start of vaccination in preschool and infant cohorts.

Vaccination against SARS-CoV-2 in Chile began in December 2020, initially prioritizing the population groups at the highest risk of severe COVID-19, decreasing by age, including adolescents between 16 and 17 years of age on dialysis, solid organ transplant recipients, hematopoietic precursor transplant recipients, and/or with autoimmune pathology, using inactivated and messenger RNA platforms. Since 2021, younger age groups and people without comorbidities were incorporated, extending coverage to people between 12 and 17 years of age in June 2021 and between 11 and 6 years of age in September of the same year. As of December 2021, vaccination coverage included those over 3 years of age, with inactivated vaccines, and later in July 2023, the group between 6 and 35 months of age with inactivated vaccines and messenger RNA platform[6,7].

Accumulated scientific evidence has shown that MIS-C means an exaggerated multisystem inflammatory reaction following exposure to SARS-CoV-2 antigens, where the pathophysiology is not fully elucidated, but the participation of proinflammatory cytokines and superantigens has been described, as well as a mechanism called antibody-dependent enhancement where the presence of pre-existing non-neutralizing antibodies may facilitate viral dissemination and tissue damage[8,9].

Recommendations for its management include the use of immunomodulatory therapies, such as systemic corticosteroids and intravenous immunoglobulin[10,11]. For these reasons, re-exposure to SARS-CoV-2 antigens, through vaccination, raised the question of its safety in patients with a history of MIS-C and the hypothesis that they could have some predisposition to repeat the immune response and/or present some serious adverse effect, more frequently than expected in the general population[1,12]. There is little information available to establish international recommendations on vaccination in patients with a history of MIS-C, preferring to defer for a minimum period of three months after having presented MIS-C[13]. The objective of this study was to determine the safety of the SARS-CoV-2 vaccine in pediatric patients who were hospitalized due to MIS-C between March 2020 and December 2022, in a high-complexity pediatric health center.

Patients and Method

General design and patients

Descriptive cross-sectional study of patients under 15 years of age with a history of MIS-C, who were admitted to the *Hospital Dr. Exequiel González Cortés* (HEGC), between May 2020 and December 2022. The epidemiological registry of patients reported with a diagnosis of MIS-C (Epivigila) who were hospitalized at the HEGC in the period described was consulted. Patients who could not be contacted, those who did not agree to participate, and children under 3 years of age were excluded since at the time of the evaluation they were not included in the group recommended for vaccination. A review of the clinical records was carried out to obtain demographic and clinical data on hospitalization due to MIS-C. An *ad-hoc* Excel spreadsheet was used considering the following variables: sex, age at admission, comorbidities, admission to PICU, number of days hospitalized in PICU, total number of days hospitalized, and MIS-C phenotype, as specified by the Chilean Society of Infectious Diseases in the current MIS-C protocol[2].

Vaccination

The National Immunization Registry was reviewed to obtain data on the SARS-CoV-2 vaccine received by each patient, number of doses received, date of each vaccination, time interval from the diagnosis of MIS-C, and type of vaccine received in the period studied. A questionnaire was elaborated to find out clinical signs and symptoms, reported by the guardians, temporally related and eventually attributable to the vaccination received. The questionnaire was applied, inquiring about symptoms and adverse events presented by the patients in the period up to 12 weeks after each vaccination, as well as symptoms suggestive of recurrence of MIS-C (defined as 3 days of fever, gastrointestinal symptoms, skin rash, and bilateral non-suppurative conjunctivitis). Additionally, the guardians of the vaccinated patients were asked about sociodemographic characteristics and the reasons that led them to vaccinate, based on a survey designed and validated in Chile to determine the reasons for vaccination[14].

Statistical analysis

A sample size analysis was performed by convenience, including all patients who met the inclusion criteria. Descriptive analysis methods were applied to quantitative variables using mean (standard deviation) or median (range), depending on the normality of the data. For the descriptive analysis of categorical variables, frequency and percentage were used.

Ethical aspects

The study was approved by the Ethics Committee of the South Metropolitan Health Service. Given the context of the pandemic, both the informed consent and the interviews were carried out digitally, by e-mail, or phone call with the guardian.

Results

During the observation period, 77 patients diagnosed with MIS-C were discharged from the HEGC, of whom 17 could not be located and 10 corresponded to patients under 3 years of age; therefore, data corresponding to 50 patients were analyzed. The median age at admission due to MIS-C was 5.2 years; 58% (n = 29) were male, and 38% (n = 19) had some comorbidity. 68% (n = 34) required admission to the PICU, with a mean length of stay of 5 days and a mean total hospital stay of 8 days. Regarding the clinical presentation, 52% (n = 26) had a shock phenotype (Table 1).

Table 1. Characterization of patients with MIS-C admitted to Dr. Exequiel González Cortés Hospital, between May 2020 and December 2022, vaccines against SARS-CoV-2 received and time intervals with respect to their diagnosis

Characteristic	Value [range]
Sex	Male: 29 (58%)
Age at admission (years)	Median: 5.2 [0 - 13]
Comorbidities	19 (38%)
PICU admission	34 (68%)
Days in PICU	Median: 4 [1 - 19]
Days of total hospitalization	Median: 7 [2 - 25]
MIS-C Phenotype *Kawasaki-like* *Shock* *No Shock – No Kawasaki-like*	 16 (32%) 26 (52%) 8 (16%)
SARS-CoV-2 vaccination	41 (82%)
Differential time between 1st dose of SARS-CoV-2 vaccine and MIS-C (days/months)	Median: 452 / 15 [18 - 867]/ [0 -24]
Differential time between 1st and 2nd dose (days)	Median: 30 [27 - 284]
Differential time between 2nd and 3rd dose (days)	Median: 188 [131 - 392]
Differential time between 3rd and 4th dose (days)	Median: 154 [90 - 174]
Vaccine type 1° dose	nactivated: 38 (92.6%) ARNm: 3 (7.4%)
Vaccine type 2° dose (n = 35. 70%)	nactivated: 32 (91%) ARNm: 2 (9%)
Vaccine type 3° doses (n = 23. 46%)	nactivated: 3 (13%) ARNm: 20 (87%)
Vaccine type 4° doses (n = 4. 8%)	nactivated: 0 (0%) ARNm: 4 (100%)

PICU: Critical patient unit, MIS-C: multisystem inflammatory syndrome associated with COVID-19. SINOVAC was used as the inactivated vaccine and PFIZER as mRNA vaccine.

Regarding post-MIS-C vaccination, 82% (n = 41) received at least 1 dose of SARS-CoV-2 vaccine, 70% received 2 doses, 46% received 3 doses, and 8% received 4 doses. 92% received an inactivated vaccine for the initial schedule and 87% received a messenger RNA vaccine for booster. The median time between MIS-C diagnosis and the first dose of the SARS-CoV-2 vaccine was 15 months (range 0-24); 1 month between the first and second dose, 6.2 months between the 2nd and 3rd dose, and 5.1 months between the 3rd and 4th dose. Regarding the sociodemographic data of the parents or guardians, 88% of the guardians contacted were female, 84% of whom were the mothers of the patients, and 30% were immigrants. 58% reported a two-parent family structure, 60% had no higher education, and 66% reported a paid job (Table 2).

Table 2. Sociodemographic data of tutor of children with a history of MIS-C admitted to the Dr. Exequiel González Cortés Hospital

Sociodemographic data	
Tutor's gender	Female: 44 (88%)
Relationship with the patient	Mother: 42 (84%) Father: 6 (12%) Other: 2 (4%)
Marital status of tutor	Married / Civil Union: 27 (54%) Single: 19 (38%) Separated / Divorced / Widowed: 4 (8%)
Family structure	Single parent: 13 (26%) Biparental: 29 (58%) Extended: 8 (16%)
Tutor's nationality	Chilean: 35 (70%)
Healthcare system	Public: 45 (90%) Private: 5 (10%)
Tutor's educational level	Without higher education: 30 (60%) With incomplete higher education: 3 (6%) With completed higher education: 14 (28%) With postgraduate studies: 3 (6%)
Tutor's Occupation	Unemployed: 17 (34%) Employed: 33 (66%)

MIS-C: multisystem inflammatory syndrome associated with COVID-19

In relation to the motivation for vaccination, 39% reported that it was by medical recommendation, 46% by personal opinion, 10% were influenced by the media, and the remaining 5% did not wish to answer this question. No patient reported being motivated by family or friends.

Regarding the clinical signs suggestive of recurrence of MIS-C post-vaccination, 14.6% reported fever, 24.3% gastrointestinal symptoms, 4.8% exanthema, and 4.8% bilateral non-suppurative conjunctivitis. No patient had mucocutaneous involvement or required hospital readmission (Figure 1). No serious adverse events (death, prolonged hospitalization, and permanent sequelae) were reported, however, 27% reported some medically treated adverse effects, such as headache, pain, pruritus, and induration at the puncture site, requiring outpatient evaluation. No patient was diagnosed with MIS-C following SARS-CoV-2 vaccination.

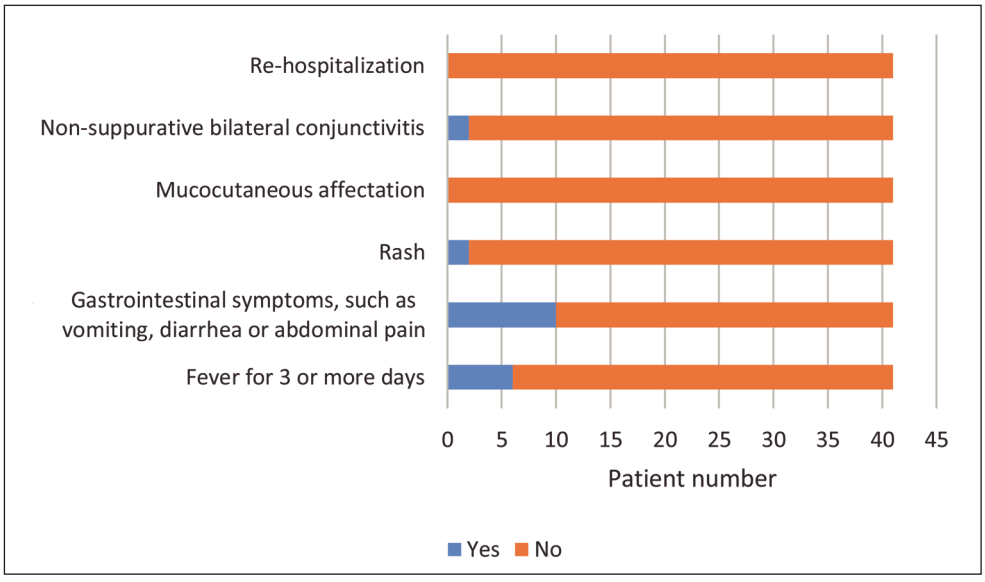

Figure 1. Symptoms suggestive of MIS-C recurrence in children with a history of MIS-C after SARS-CoV-2 vaccination. MIS-C: multisystem inflammatory syndrome associated with COVID-19.

Discussion

MIS-C is one of the most severe clinical manifestations of COVID-19 in pediatrics[8], which is consistent with the high rates of shock and admission to the PICU in the patients in our study and represents a diagnostic and management challenge[6,11]. In Chile, a decrease in the incidence of MIS-C has been reported in the last two years, the highest incidence being observed in 2021 with 4.9 cases per 100,000 inhabitants, compared with 0.2 cases in 2023; however, an increase in cases in unvaccinated children under 3 years of age has been described[5]. Vaccination strategies using inactivated and/or messenger RNA platforms have proven to be safe, immunogenic, and effective in the pediatric population[6,15-18]. The vaccines used in Chile in the pediatric population during the study period included Pfizer-BioNTech (messenger RNA) and Sinovac (inactivated), both with 2-dose schedules, with a 28-day interval between them, including the entire population aged 12 to 17 years (June 21, 2021), then from 6 to 11 years (September 8, 2021), and finally from 3 to 5 years (December 6, 2021), reaching coverage rates of 95% in the population between 6 and 17 years[6], which is consistent with the 70% coverage for 2 doses in our study, where only 5 patients were between 3 and 5 years old, corresponding to 12% of the patients with a history of MIS-C vaccinated.

The scientific information available on vaccination against SARS-CoV-2 in patients with a history of MIS-C is scarce. Hoste et al. surveyed 132 health professionals who provided direct care to patients diagnosed with MIS-C in 32 countries, reporting that most of them did not consider MIS-C as a contraindication for vaccination, but recommended longer intervals to initiate vaccination compared to healthy children[19]. Similarly, the vaccine advisory committee of the Spanish Society of Pediatrics recommends that children with a history of non-vaccination-related MIS-C who have fully recovered, including cardiac function, could be vaccinated against SARS-CoV-2 90 days after recovery[13]. Likewise, the CDC (Centers for Disease Control and Prevention) considers that the benefits of vaccination in persons with a history of MIS-C outweigh the theoretical risk of vaccination-associated MIS-C disease or myocarditis, so they recommend vaccination in patients who had MIS-C who have clinically recovered (including normal cardiac function) and with at least 90 days after the diagnosis of MIS-C[20].

In our study, we were able to report that although the interval between MIS-C and the first vaccination was long, due to the lack of vaccine availability at that time, reactogenicity was similar to that described in the general pediatric population[6], with no reports of MIS-C recurrences or serious adverse events. However, 27% reported some adverse effects medically treated and requiring outpatient evaluation, such as headache, pain, pruritus, and induration at the puncture site. Studies based on surveys of physicians attending patients with MIS-C from 61 countries show that 89% of the cases did not present adverse effects with vaccination against SARS-CoV-2. Regarding recommended vaccination times, 52% were vaccinated after 6 to 12 months[21]. Although this seems to be auspicious in terms of immunization safety, there are still marked differences in vaccination schedules around the world, which makes it difficult to develop a general recommendation.

Besides, a meta-analysis reported that COVID-19 messenger RNA vaccines administered in children significantly reduce the risk of developing MIS-C and that, in addition, the risk of MIS-C because of vaccination is much lower than that following natural SARS-CoV-2 infection[15]. Another study, with 193 children diagnosed with MIS-C seen at two tertiary centers in the US and Italy, of whom 63 were susceptible to vaccination, recommended vaccination within 90 days or more from MIS-C diagnosis. Of the susceptible subgroup, only 15 agreed to immunization and were surveyed for signs and symptoms of reactivation of hyperinflammation, and none presented significant adverse effects or reactivation of MIS-C with vaccination[22]. Similarly, Elias et al. conducted a multicenter study in North American children over 5 years of age previously diagnosed with MIS-C. They obtained a sample of 385 vaccine-susceptible patients, of whom 136 received at least one dose of SARS-CoV-2 vaccine. After surveying their parents, they concluded that most adverse reactions (90%) were mild, mainly related to the puncture site, but none required hospitalization or suffered recurrence of MIS-C[23]. In Spain, Pino et al. conducted a multicenter observational study with patients from hospitals in Catalonia, where 152 children between 4 and 11 years of age were included; of these, 49 children were vaccinated against SARS-CoV-2 after the MIS-C episode, and none relapsed[24]. In Argentina, Curtti et al. published a report analyzing 4 adolescents with MIS-C, who were vaccinated against SARS-CoV-2 (between 6 weeks and 9 months after diagnosis) without the presence of reactivation of symptoms or cardiac alterations[25]. In this sense, the results obtained in our study, in relation to the safety of vaccination, agree with the available literature, regardless of the vaccine platform and/or the number of doses administered.

A preliminary study investigated the safety of the Pfizer-BioNTech (BNT162b2) mRNA COVID-19 vaccine, reporting results of a prospective cohort of 21 patients with a history of MIS-C compared to healthy

controls. They describe that there were no significant differences in adverse event reporting between the two groups, except for puncture site induration, which was higher in the group with a history of MIS-C. The mean number of days between the onset of MIS-C symptoms and the first dose of the vaccine was 380 days. The investigators concluded that the BNT162b2 mRNA COVID-19 vaccine did not induce any MIS-C-like symptoms in any patient[26]. In our study, patients received both inactivated and mRNA vaccines. Similar to what was reported in the previously mentioned study, the mean time between the diagnosis of MIS-C and the first vaccine dose was 381 days, which could represent an important bias when interviewing guardians, given that many might forget or not report the investigated symptomology. Based on currently available data, the interval between MIS-C and vaccination could be less than 3 months, with intervals like those described for other inactivated vaccines. However, despite this limitation, the data collected are consistent with the trend published in the literature.

It is noteworthy that most of the parents who decided to vaccinate did so based on personal opinion rather than on the recommendation of a health professional, which is an important aspect to work on and reinforce in the daily work of pediatricians or health personnel in contact with children and adolescents, in order to support vaccination coverage strategies.

Conclusions

According to this experience, vaccination against SARS-CoV-2 is safe in patients with a history of MIS-C, regardless of age, clinical phenotype of presentation, severity, type of vaccine, and interval between illness and vaccination, with no association with recurrence of MIS-C after immunization. Consensus recommendations should be developed for vaccinating patients after MIS-C, which could be less than 3 months, considering that vaccination against SARS-CoV-2 has a safety profile similar to that of other vaccines administered by programs or campaigns.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflict of interest

RV participated as an investigator in the studies of COVID-19 phase III vaccines in adults for Janssen and phase III in the pediatric population for Sinovac, as well as consultancies for Pfizer. The other authors declare no conflict of interest.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

References

1. World Health Organization (WHO). Multisystem inflammatory syndrome in children and adolescents with COVID-19 (Scientific brief). C2020. [Accedido el 25 diciembre 2022]. Disponible en: https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19
2. Torres JP, Izquierdo G, Acuña M, et al. Multisystem inflammatory syndrome in children (MIS-C): Report of the clinical and epidemiological characteristics of cases in Santiago de Chile during the SARS-CoV-2 pandemic. Int J Infect Dis. 2020;100:75-81. doi:10.1016/j.ijid.2020.08.062
3. Protocolo síndrome inflamatorio multisistémico en niños, niñas y adolescentes con SARS-CoV-2. [internet] Chile: Subsecretaría de Salud Pública/ Subsecretaría de Redes Asistenciales, División de Prevención y Control de Enfermedades/Programa nacional de salud de la infancia. C2020 [Accedido el 25 diciembre 2022]. Disponible en https://www.minsal.cl/wp-content/uploads/2020/07/Protocolo-S%C3%ADndrome-inflamatorio050720.pdf
4. Protocolo de sospecha diagnóstica y manejo del Síndrome inflamatorio multisistémico (SIM-COVID-19) en niños, niñas, adolescentes y jóvenes. [internet] Chile: Subsecretaría de Salud Pública/ Subsecretaría de Redes Asistenciales, División de Prevención y Control de Enfermedades/División de Gestión de la Red Asistencial, Departamento de Ciclo Vital/ Departamento de ges, redes complejas y líneas temáticas. C2021 [Accedido el 25 diciembre 2022] Disponible en https://www.minsal.cl/wp-content/uploads/2021/08/ Sindrome-Inflamatorio-Multisistemico-en-Ninos-Ninas-y-Adolescentes.pdf.
5. Boletín epidemiológico Síndrome Inflamatorio Multisistémico. Agosto 2023. [internet] Chile: Departamento de epidemiología, Ministerio de Salud. C2023 [Accedido el 2 de Septiembre 2023] Disponible en http://epi.minsal.cl/wp-content/uploads/20523/08/SITUACION-EPIDEMIOLOGICA-SIM-10082023.pdf
6. Villena R, Alvarado S, Saldaña A. Experiencia chilena en el comportamiento del SARS-CoV-2 y campaña de vacunación en pediatría. Neumol Pediatr. 2022;17(1):20-5. doi.org/10.51451/np.v17i1.476
7. Actualización de vacunación contra SARS-CoV-2 desde los 6 meses en adelante. Departamento de Inmunizaciones División de Prevención y Control de Enfermedades. Subsecretaría de Salud Pública. 03 de julio 2023. C2023 [Accedido el 2 de Septiembre de 2023]. Disponible en https://www.minsal.cl/wp-content/uploads/2023/07/Actualizacion-de-vacunacion-contra-SARS-CoV-2-desde-los-6-meses-en-adelante.pdf
8. Howard-Jones AR, Burgner DP, Crawford NW, et al. COVID-19 in children. II: Pathogenesis, disease spectrum and management. J Paediatr Child Health. 2022;58(1):46-53. doi:10.1111/jpc.15811
9. La Torre F, Taddio A, Conti C, et al. Multi-Inflammatory Syndrome in Children (MIS-C) in 2023: Is It Time to Forget about It? Children (Basel). 2023 May 31;10(6):980. doi: 10.3390/children10060980. PMID: 37371212; PMCID: PMC10297102.
10. Harwood R, Allin B, Jones CE, 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. Lancet Child Adolesc Health. 2021;5(2):133-41. doi: 10.1016/S2352-4642(20)30304-7. Epub 2020 Sep 18. Erratum in: Lancet Child Adolesc Health. 2021 Feb;5(2):e5. PMID: 32956615; PMCID: PMC7500943
11. Yagnam F, Izquierdo G, Villena R, et al. Síndrome Inflamatorio Multisistémico Pediátrico asociado a COVID-19: características clínicas y manejo en una Unidad de Paciente Crítico Pediátrico. Andes pediatr. 2021;92(3):395-405. doi: 10.32641/andespediatr.v92i3.3333
12. Karatzios C, Scuccimarri R, Chédeville G, et al. Multisystem Inflammatory Syndrome Following SARS-CoV-2 Vaccination in Two Children. Pediatrics. 2022;150(2):e2021055956. doi:10.1542/peds.2021-055956.
13. Síndrome inflamatorio multisistémico pediátrico (SIMP) y vacunas de la covid [Internet]: Comité Asesor de Vacunas de la AEP (CAV-AEP). C2022. [Accedido el 10 de septiembre de 2023]. Disponible en: https://vacunasaep.org/profesionales/noticias/vacunas-covid19-y-sindrome-inflamatorio-multisistemico-pediatrico
14. Leal P, Gaete J, González C, et al. Delays in the vaccination of infants between 2 and 18 months of age: associated factors in Chile. BMC Public Health. 2023;23(1):1882. doi: 10.1186/s12889-023-16769-3. PMID: 37770902; PMCID: PMC10540413.
15. Hamad Saied M, van der Griend L, van Straalen JW, et al. The protective effect of COVID-19 vaccines on developing multisystem inflammatory syndrome in children (MIS-C): a systematic literature review and meta-analysis. Pediatr Rheumatol Online J. 2023;21(1):80. doi: 10.1186/s12969-023-00848-1. PMID: 37550719; PMCID: PMC10405572.
16. Watanabe A, Kani R, Iwagami M, et al. Assessment of Efficacy and Safety of mRNA COVID-19 Vaccines in Children Aged 5 to 11 Years: A Systematic Review and Meta-analysis. JAMA Pediatr. 2023;177(4):384-94. doi: 10.1001/jamapediatrics.2022.6243. PMID: 36689319; PMCID: PMC9871947.
17. Soto JA, Melo-González F, Gutierrez-Vera C, et al. Inactivated Vaccine-Induced SARS-CoV-2 Variant-Specific Immunity in Children. mBio. 2022;13(6):e0131122. doi: 10.1128/mbio.01311-22. Epub 2022 Nov 16. PMID: 36383021; PMCID: PMC9765711.
18. Le Corre N, Abarca K, Astudillo P, et al. Different Safety Pattern of an Inactivated SARS-CoV-2 Vaccine (CoronaVac®) According to Age Group in a Pediatric Population from 3 to 17 Years Old, in an Open-Label Study in Chile. Vaccines (Basel). 2023;11(10):1526. doi: 10.3390/vaccines11101526. PMID: 37896930; PMCID: PMC10611329.
19. Hoste L; MIS-C researchers, Soriano-Arandes A, Buddingh EP, Whittaker E, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Vaccination in Children with a History of Multisystem Inflammatory Syndrome in Children: An International Survey. J Pediatr. 2022;248:114-8. doi.org/10.1016/j.jpeds.2022.05.028. Epub 2022 May 19. PMID: 35598642; PMCID: PMC9119291.
20. Clinical guidance for COVID-19 vaccination [Internet]: Cdc.gov. C2024 [Accedido el 17 de febrero de 2024]. Disponible en: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html
21. Minoia F, Lucioni F, Heshin-Bekenstein M, et al. Approaches to SARS-CoV-2 and other vaccinations in children with a history of multisystem inflammatory syndrome (MIS-C): An international survey. Front Pediatr. 2022;10:1030083. doi: 10.3389/fped.2022.1030083. PMID: 36440337; PMCID: PMC9682234.
22. Wisniewski M, Chun A, Volpi S, et al. Outcomes After SARS-CoV-2 Vaccination Among Children With a History of Multisystem Inflammatory Syndrome. JAMA Netw Open. 2022;5(3):e224750. Published 2022 Mar 1. doi:10.1001/jamanetworkopen.2022.4750. PMID: 35344047; PMCID: PMC8961315.
23. Elias MD, Truong DT, Oster ME, et al. Examination of Adverse Reactions After COVID-19 Vaccination Among Patients With a History of Multisystem Inflammatory Syndrome in Children. JAMA Netw Open. 2023 Jan 3;6(1):e2248987. doi: 10.1001/

jamanetworkopen.2022.48987. PMID: 36595296; PMCID: PMC9857632.
24. Pino R, Antoñanzas JM, Paredes-Carmona F, et al. Multisystem inflammatory syndrome in children and SARS-CoV-2 variants: a two-year ambispective multicentric cohort study in Catalonia, Spain. Eur J Pediatr. 2023;182(4):1897-909. Disponible en doi:10.1007/s00431-023-04862-z
25. Curtti T, Agrimbau Vázquez J, Yori S, et al. Immunization with messenger RNA vaccines against COVID-19 in adolescents with a history of multisystem inflammatory syndrome: a case series. Arch Argent Pediatr. 2023 Jun 1;121(3):e202202757. English, Spanish. doi: 10.5546/aap.2022-02757.eng. Epub 2022 Oct 6. PMID: 36194695.
26. Ludwikowska KM, Popiel A, Matkowska-Kocjan A, et al. COVID-19 mRNA BNT162b2 vaccine safety and B-cell and T-cell reactogenicity among children with a history of paediatric multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS-TS) - preliminary study. Vaccine. 2023;41(13):2289-99. doi: 10.1016/j.vaccine.2023.02.072. Epub 2023 Mar 2. PMID: 36870876; PMCID: PMC9977623.