ORIGINAL ARTICLES

Quality of life among children with Multisystem Inflammatory Syndrome (MIS-C) at Vietnam National Children's Hospital in 2022: A Case series study

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ABSTRACT

Objectives: Multisystem inflammatory syndrome in children (MIS-C) after COVID-19 can affect children's well-being and adversely impact their quality of life, especially for children in developing countries such as Vietnam. Therefore, this study aims to describe the clinical characteristics and the corresponding quality of life of MIS-C patients admitted to the Vietnam National Children's Hospital (VNCH) in 2022.

Methods: This cross-sectional study utilized a preceding study to collect data regarding MIS-C patients' characteristics, clinical features, and quality of life after treatment. The quality of life was assessed using PedsQL version 4.0 instrument. While mean and standard deviation was used to describe quantitative variables, qualitative variables were shown using frequency and percentage.

Results: There were 245 participants in this study. A majority of participants were male and 8-12 years old. For symptoms, conjunctivitis occurred in most patients, which accounted for more than 70% across all age groups. In terms of quality of life, the mean score of physical aspects were highest among the age groups with the score equal to approximately 96.8 points. Patients who had experienced rash, lymphadenopathy, vomiting, and abdominal pain had low mean scores in all aspects of quality of life.

Conclusions: Children with MIS-C at the VNCH showed similar clinical symptoms with international studies. After being treated, patients with certain MIS-C-related clinical symptoms showed different effects each dimension in quality of life.

Keywords: *MIS-C, COVID-19, children, quality of life.*

INTRODUCTION

COVID-19, a disease caused by SARS-CoV-2, spread rapidly all over the world with an estimated of 776 million cases in July 2024 (1). Although children have shown little acute complications of the COVID-19, several long-term effects were expressed in some children (2). After having COVID-19 for a period of time, usually 2-6 weeks, several pediatric patients started to be admitted to the hospital due to severe hyper-swelling condition in some countries (2). These conditions were later on classified as multisystem inflammatory syndrome in children, denoted by MIS-C (3). Although the definition of MIS-C varies according to the organization, the Centers for Disease Control and Prevention of United States (the U.S. CDC) provided a comprehensive definition

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for this syndrome (3). In particular, a patient is considered a MIS-C case if this patient, at least, were under 20 years of age with body temperature surpassed 38oC for over 24 hours (3). Other requirements for case identification were evidence regarding laboratory results and multisystem manifestations, accompanied by hospitalization and historical evidence of COVID-19 (3). The detailed description of MIS-C has been described elsewhere (4,5). In our study, we applied the definition of MIS-C stated by the U.S. CDC (3).

MIS-C is considered a rare, yet severe condition that can lead to the need for intensive care and even death. This finding was observed in a recent Systematic Reviews and Meta-Analysis of studies from January to July in 2020 (2). The authors found that all patients had fever, predominantly accompanied by abdominal pain and diarrhea (73.7%), vomiting (68.3%), rash (56.2%), and conjunctivitis (51.8%) (2). Approximately 71.0% of these patients were admitted into the Pediatric Intensive Care Unit (PICU) (2). The number of deaths recorded were 11 patients (accounted for 1.7% of the total participants) (2). Recently, a study conducted in Taiwan also found that among participants diagnosed with MIS-C (19 girls and 9 boys), the percentage of patients had fever, skin rash and vomiting were 100%, 64% and 46% respectively (6). There were about 32% of the participants were required to be admitted into PICU (6). Therefore, children's well-being can be severely affected by a series of symptoms after experiencing MIS-C.

The symptoms of MIS-C and the health impact can reduce the quality of life among pediatric patients (7). In fact, a novel study in Spain shown that children with persistent symptoms of post-COVID-19 (such as cognitive conditions, fatigue, myalgia, headache, muscle weakness, and dyspnea) had experienced psychological disorders (about 60% of the total subjects) and emotional/behavioral problems (30%) (8). Another study in the UK observed about 13% of the MIS-C patients had physical impairment and up to 18% of them shown emotional and psychological problems after 6 months (7). Study in Denmark found that MIS-C patients from 13-24 years of age had low physical scores and emotional scores than children who was not positive with COVID-19 (9). Hence, not only did MIS-C affect the patient's physical health, but it may also reduce the patient's quality of life.

In Vietnam, the number of COVID-19 cases stood at approximately 11.6 million patients with about 0.043 million deaths up until July 5, 2024 (10). This situation raised a potential threat of Multisystemic Inflammatory Syndrome to the health of the population, especially children and adolescents (7). Pediatric patients in Vietnam usually prefer major hospitals if they contract a serious disease such as COVID-19. One of the most prestigious hospitals in the Northern Vietnam is the Vietnam National Children's Hospital (VNCH). Moreover, although the symptoms of MIS-C in Vietnam have been described in previous research (11–13), little has been known about the negative effect of this syndrome on the quality of life although international research suggested children with MIS-C had low quality of life (7–9). Therefore, this case series study aims to describe the clinical characteristics and the corresponding quality of life of MIS-C patients admitted to the VNCH in 2022.

METHODS

Research design: Case series study.

Study Subjects: Children (2 to 18 years of age) admitted to VNCH for MIS-C treatment from January 2022 to December 2022.

Study site and time: This study was conducted from December 2022 to January 2023 at VNCH, Hanoi, Vietnam.

Sample size and sampling method: This study focuses on children admitted to VNCH for MIS-C treatment in 2022. MIS-C was diagnosed based on the U.S CDC criterion, which had been described extensively in the previous study (14)ranging from mild features to multi-organ dysfunction and mortality. However, this novel entity has a heterogenicity of data regarding prognostic factors associated with severe outcomes. The present study aimed to identify independent predictors for severity by using multivariate regression models. A total of 391 patients (255 boys and 136 girls. From this pre-selected cohort, patients were selected based on the following criteria: 1) Patients who were able to be reconnected; 2) Patients whose parents agreed to join the research and signed the consent form.

Research variables: We collected information regarding 1) Patients' demographic and admission characteristics; 2) MIS-C symptoms; and 3) Patients' quality of life.

The first information component comprises of age (by month), gender (male or female), ethnicity (Kinh or others), living areas (Ha Noi or others), Weight (Kilogram), Height (Meter), admission to the Pediatric Intensive Care Unit (PICU), length of stay in PICU and total admission period. The Body Mass Index (BMI) was calculated from the Weight and Height of each patient.

For the clinical constituent, MIS-C-signature manifestations were collected. These symptoms include Diarrhea, Vomiting, Abdominal pain, Rash, Conjunctivitis, Cheilitis, Swollen or red hands and feet, Lymphadenopathy, Cough, Shortness of breath, Headache, and Seizures (6)risk factors associated with pediatric intensive care unit (PICU.

Finally, the patients' quality of life was assessed using "Pediatric Quality of Life Inventory – Generic Core Scales" version 4.0, denoted by PedsQL 4.0 (15). This questionnaire categorizes the quality of life into four aspects, namely Physical (8 questions), Emotional (5 questions), Social (5 questions), and School (3 questions for children 2-4 years and 5 questions for children from 5-18 years). Each question was evaluated from 0 to 4, with 0 being "Never" and 4 being "Almost always". After being collected, the scores were rescaled to 100-point scale, with 0=100, 1=75, 2=50, 3=25, 4=0. The mean score of each dimension was calculated if more than half of the questions were answered.

Data collection: This study was extended from the original research by collecting more data on the quality of life (14) ranging from mild features to multi-organ dysfunction and mortality. However, this novel entity has a heterogenicity of data regarding prognostic factors associated with severe outcomes. The present study aimed to identify independent predictors for severity by using multivariate regression models. A total of 391 patients (255 boys and 136 girls. In the original research, data was collected from the Electronic Hospital record (denoted by eHos) for the patient's demographic information, admissions characteristics, and symptoms in the original research (14)ranging from mild features to multi-organ dysfunction and mortality. However, this novel entity has a heterogenicity of data regarding prognostic factors associated with severe outcomes. The present study aimed to identify independent predictors for severity by using multivariate regression models. A total of 391 patients (255 boys and 136 girls. In the present study, the patients

selected from the mentioned phase were followed by trained clinicians to assess the quality of life. The follow-up procedure was conducted as follows. First, the parents of these patients had been informed of this study and then asked to sign the consent form before conducting the PedsQL assessment. Second, the patients' quality of life questionnaire was asked by doctors and answered by the patient's parents (via telephone for non-revisited patients and directive method for revisited patients).

Data analysis: In this study, descriptive statistics were utilized to illustrate the patient's characteristics of patients and their corresponding quality of life score. In particular, while central measurement (the mean and the median) and variation (standard deviation, minimum or maximum value) was used to describe the quantitative data, the qualitative information was shown in the form of frequency and percentage. For the quality of life, the data was clustered into four age-groups according to the PedsQL guidelines, namely 2-4 years, 5-7 years, 8-12 years, and 13-18 years (15). Radar chart was applied to compare the mean score of each dimension of PedsQL among the symptoms.

Data was exported to Microsoft Excel software for standardizing. Afterward, R software version 4.4.1 was used to analyze data.

Ethics approval: This study has been approved by the Ethics Committee at the Vietnam National Children's Hospital (Approval no. VNCH-TRICH-2023-33). Written informed consent from the parents or legal guardians of all participants were collected.

RESULT

Table 1. Characteristics and symptoms of MIS-C participants

	2-4 years	**5-7 years**	**8-12 years**	**13-18 years**
	N = 55 (100%)	N = 67 (100%)	N = 112 (100%)	N = 11 (100%)
Gender				
Male	35 (64%)	41 (61%)	74 (66%)	10 (91%)
Female	20 (36%)	26 (39%)	38 (34%)	1 (9%)
Ethnicity				
Kinh	53 (96%)	67 (100%)	109 (97%)	11 (100%)
Others	2 (4%)	0 (0%)	3 (3%)	0 (0%)
Area				
Ha Noi	21 (38%)	27 (40%)	50 (45%)	5 (45%)
Others	34 (62%)	40 (60%)	62 (55%)	6 (55%)
BMI	17 (± 7.4)	16 (± 4.4)	19 (± 7.4)	23 (± 10)
Admitted to the PICU	25 (45%)	42 (63%)	64 (57%)	10 (91%)
Length of PICU stay	2.3 (± 4.1)	2.6 (± 3)	3.1 (± 3.7)	5.5 (± 4)
Length of Hospital stay	7 (± 3.3)	6.6 (± 2.7)	7.2 (± 3.9)	7.3 (± 3.4)

	2-4 years	5-7 years	8-12 years	13-18 years
	N = 55 (100%)	N = 67 (100%)	N = 112 (100%)	N = 11 (100%)
Clinical manifestation				
Diarrhea	10 (18%)	18 (27%)	32 (29%)	4 (36%)
Vomiting	17 (31%)	27 (40%)	46 (41%)	1 (9%)
Abdominal pain	11 (20%)	35 (52%)	51 (46%)	5 (45%)
Rash	45 (82%)	52 (78%)	81 (72%)	4 (36%)
Conjunctivitis	42 (76%)	53 (79%)	84 (75%)	8 (73%)
Cheilitis	23 (42%)	17 (25%)	33 (29%)	1 (9%)
Swollen or red hands and feet	12 (22%)	4 (6%)	11 (10%)	0 (0%)
Lymphadenopathy	19 (35%)	35 (52%)	42 (38%)	2 (18%)
Cough	19 (35%)	22 (33%)	28 (25%)	1 (9%)
Shortness of breath	1 (2%)	9 (13%)	6 (5%)	3 (27%)
Headache	6 (11%)	15 (22%)	22 (20%)	1 (9%)
Seizures	2 (4%)	1 (1%)	0 (0%)	0 (0%)

A total of 245 participants were legitimate to participate in this follow-up study (Table 1). The number of children were in the range of 8-12 years of age (112 children), followed by 5-7 years (67 children), 2-4 years (55 children), and 13-18 years (11 children). The number of male patients were higher than female across age-groups. Most children were Kinh, but only half of them were from Ha Noi. While the BMI of under-13-year-olds was less than 20, this figure for children 13-18 years stood at 23 (± 10).

Most of the children from 5-18 years of age were admitted to the PICU, while only 45% of the patients 2-4 years of age were admitted to this department. The average length of stay in PICU spanned from approximately 2.3 days (± 4.1 days) among children 2-4 years to about 5.5 days (4.0 days) among patients 13-18 years old. Meanwhile, the average length of hospital stays for the entire admissions period fluctuated around 7 days (a week).

One of the most prevalent clinical symptoms of MIS-C among age groups was conjunctivitis, with the manifested percentage being 76% among children 2-4 years, 79% for 5-7-year-olds, 75% for 8-12-year-olds, and 73% for 13-18-year-olds. On the other hand, while rash was predominantly observed in children under 13 years old, only a smaller proportion of 13-18-year-olds experienced this symptom (accounted for about 36% of the total 13-18-year-olds).

Table 2. The quality of life of MIS-C patients at VNCH in 2022

		2-4 years	5-7 years	8-12 years	13-18 years
Physical	Mean (SD)	93.6 (± 7.9)	96.8 (± 6.7)	93.4 (± 9.6)	92.0 (± 10.1)
	Median [Min, Max]	100 [75.0, 100]	100 [62.5, 100]	100 [50.0, 100]	100 [75.0, 100]
Emotional	Mean (SD)	98.6 (± 3.9)	96.5 (± 8.9)	96.4 (± 7.4)	100 (± 0.0)
	Median [Min, Max]	100 [87.5, 100]	100 [37.5, 100]	100 [50.0, 100]	100 [100, 100]
Social	Mean (SD)	99.5 (± 2.4)	96.3 (± 15.7)	96.5 (± 13.3)	95.5 (± 8.4)
	Median [Min, Max]	100 [87.5, 100]	100 [25.0, 100]	100 [0, 100]	100 [75.0, 100]
School	Mean (SD)	97.0 (± 5.6)	96.2 (± 16.3)	96.9 (± 9.3)	95.5 (± 3.5)
	Median [Min, Max]	100 [75.0, 100]	100 [20.0, 100]	100 [50.0, 100]	95.0 [90.0, 100]

After being treated for MIS-C at VNCH, patients showed a good quality of life throughout the aspect, with over 90 points in all the PedsQL mean score for each dimension (Table 2). Among these dimensions, only physical attributes were different among age groups (p-value = 0.046). In particular, while the mean score of physical aspect of 5-7-year-olds was 96.8 (± 6.7), the corresponding figure for 13-18-year-olds was 92.0 (± 10.1). All 13-18-year-olds showed no emotional issues, with the average emotional score reaching a height of 100 points.

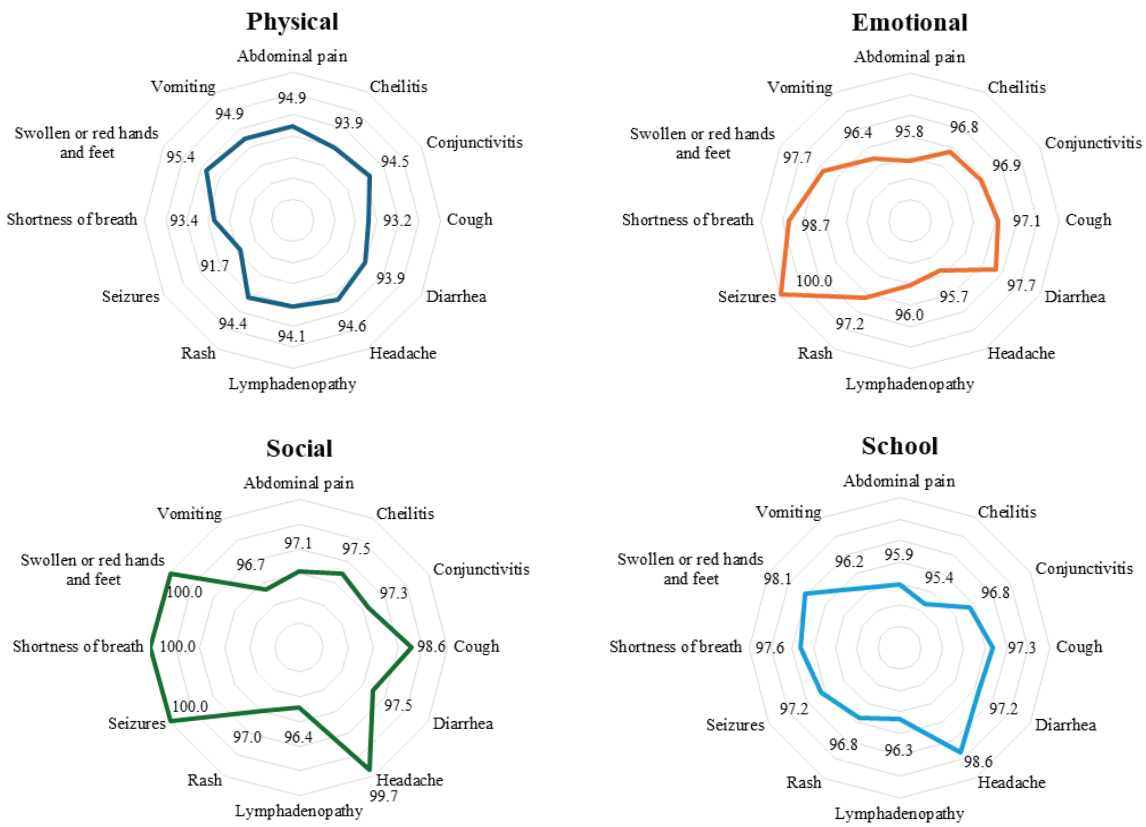

Figure 1. Average mean score for Quality-of-life sub-dimension by symptoms

Figure 1 shows the mean score of each aspect in quality of life corresponding to the symptoms of MIS-C patients. For physical dimension, the lowest mean score was found among patients who had experienced Seizures (91.7 points). Meanwhile, the mean emotional score among children with Seizures was highest of their category. Social scores were high among children who had experienced cognitive symptoms (such as seizures or headache), but low in children with vomiting or lymphadenopathy symptoms. For the school dimension, the lowest score could be observed in children with Cheilitis and other Gastrointestinal issues (including vomiting and abdominal pain). When comparing to children with other symptoms, children with rash had relatively high physical scores, but low scores in psychological domains, including emotional, social, and school.

DISCUSSION

In Vietnam, although there has been an extensive body of literature on the prevalence of MIS-C and the corresponding clinical and laboratory features (11–13), few studies have reported the quality of life among patients who had MIS-C and experience the adverse clinical effects of this disease. The quality of life attracted less attention due to the late expression. For example, a study conducted in 46 children in London found that 13% of MIS-C patients had mild physical issues after a year of follow-up (7). The corresponding results for emotional, social and school scale were 14%, 11% and 5% respectively (7). Therefore, it is crucial to assess the quality-of-life post-MIS-C for patients to assure their overall health outcomes. Our study is one of the first study in Vietnam to report the quality of life of patients who had been treated MIS-C. The result of this study is expected to raise awareness regarding the long-term effect of MIS-C as a part of overall impact of COVID-19.

Our study found that MIS-C patients were predominantly boys. This feature might be due to the fact that pro-inflammatory cytokines in males were more likely to be higher than females (16). These cytokines – "A type of protein that is made by certain immune and non-immune cells and has an effect on the immune system" (17) – is part of the criteria to distinguish MIS-C patients (4). Therefore, higher in pro-inflammatory predictors may push the number of male patients admitted for MIS-C.

For symptoms, the results in our study found that conjunctivitis and skin rash were observed in most participants. However, gastrointestinal symptoms had been the dominant features among 76 patients with MIS-C in a study in Ho Chi Minh city, with approximately 75% of them experiencing abdominal pain, 74% experiencing vomiting, and 73% having loose tools (11). Among MIS-C patients, the most common clinical characteristics may include vomiting, abdominal pain, skin rash, and conjunctivitis (6). Therefore, our findings, and the preceding research, are still in line with the international evidence.

For quality of life, we chose PedsQL to assess the patient's Quality of Life. In fact, there has been many instruments developed to assess the quality of life for children (18). These instruments can be generic or disease specific (18). Due to the novelty of MIS-C, we prioritized the questionnaire that can be applied to the generic population. These questionnaires may include the Infant Toddler Quality of Life questionnaire (ITQOL), the Warwick Child Health and Morbidity profile (WCHMP), the Functional status II (R), the TNO-AZL Preschool Children Quality of Life questionnaire (TAPQOL), the DISABKIDS, and the PedsQL questionnaire (15,19–23). However, only PedsQL had the longest age range (from 2-18 years old) with sufficient aspects regarding quality of life. Therefore, this questionnaire was chosen for our study.

We discovered participants who had experienced rash had relatively low emotional, social and school dimension score compared to children with other symptoms of their respective aspect. In fact, a study concluded that skin disorder in children may affect children's personal perceptions (24). Their self-esteem may be severely affected by the misinterpretation that some skin-related issues, including rash, may infect others (24). This may also explain why children with invisible symptoms such as headache had low scores in emotional aspect, but not in social and school (Figure 1). However, further discovery is needed to fully explain this phenomenon to not only enhance the physical health of MIS-C patients but also their psychological well-being.

In this study, we encountered some challenges. Firstly, only 245 cases out of 391 cases of MIS-C in VNCH were selected into this study (14). Moreover, only children in VNCH took part in this research. Therefore, we could not report the prevalence of the MIS-C patients' quality of life for a geographical area (such as district or province). Secondly, most parents were interviewed through telephone, which may introduce bias due to miscomprehension. In particular, the quality-of-life average scores were relatively high across the aspects. This indicated that parents who answer the questions through telephone often give "never" respond to the symptoms. However, we have minimized this risk by training doctors/clinicians/reviewers to understand deliver the questionnaire thoroughly. Thirdly, the quality of life was assessed solely based on the self-perception of the parents. Future studies need to perform standardized physical and psychological tests to provide a comprehensive result.

CONCLUSION

Our study was conducted on 245 patients admitted to the VNCH for MIS-C treatment. The dominant clinical symptoms were rash and lymphadenopathy among the patients. The PedsQL instrument was used to assess patients' quality of life. Children 5-12 years of age had higher physical mean score compared to 13-18-year-olds. Children who had experienced signature MIS-C symptoms (such as rash, lymphadenopathy, vomiting, and abdominal pain) showed lower mean score across the psychological dimensions of PedsQL (emotional, social, and school) compared to children who had experienced other symptoms.

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