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Factors linked to Kawasaki disease and MIS-C in children with prolonged fever: A retrospective cohort study

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Ethics Committee Approval
The study was approved by the ethics committee of the Zeynep Kamil Maternity and Children's Diseases Training and Research Hospital (protocol number: 120, dated May 11, 2022). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Prolonged fever in children presents a diagnostic challenge due to its diverse underlying causes. While infectious diseases historically played a primary role, recent shifts in disease patterns and the emergence of conditions such as multisystem inflammatory syndrome in children (MIS-C) have added complexity. Understanding factors contributing to prolonged fever, particularly the rise in MIS-C and Kawasaki Disease (KD), is vital for accurate diagnosis and timely intervention. This study aimed to identify the etiologies causing prolonged fever in children with temperatures exceeding 38°C for a minimum of 5 days and to examine its relationship with conditions like MIS-C and KD following the coronavirus disease 2019 (COVID-19) pandemic.

Methods: We conducted a retrospective cohort study at a pediatric hospital in Istanbul, Turkey, involving 243 children aged 3 months to 17 years with prolonged fever (>38°C for ≥5 days) between April 2020 and October 2022. We collected data on patient demographics, clinical characteristics, laboratory results, and final diagnoses. The study categorized patients into Group 1 (KD and MIS-C) and Group 2 (other causes). We performed logistic regression analysis to identify factors associated with KD and MIS-C, using hospitalization days and levels of C-reactive protein (CRP), ferritin, and D-dimer. We calculated sensitivity, specificity, and likelihood ratio values and generated ROC (Receiver operating characteristic) curves. The threshold for statistical significance was set at $P<0.05$.

Results: This study encompassed 243 patients with prolonged fever. The primary causes of admission included infection-related illnesses (60.91%, n=148), MIS-C (18.52%, n=45), and KD (10.70%, n=26). Significant differences were observed in lymphocyte count ($P<0.001$), CRP level ($P<0.001$), ferritin level ($P<0.001$), D-dimer level ($P<0.001$), hospitalization days ($P<0.001$), and echocardiographic findings ($P<0.001$) between the groups. Logistic regression analysis revealed noteworthy associations between the presence of KD and MIS-C and hospitalization days ($P=0.001$), elevated CRP levels ($P=0.018$), elevated ferritin levels ($P=0.009$), and elevated D-dimer levels ($P=0.001$). Ferritin exhibited an AUC (Area under curve) of 0.737 ($P<0.001$), and D-dimer demonstrated an AUC of 0.782 ($P<0.001$) in differentiating between the presence of KD and MIS-C.

Conclusion: The prevalence of infectious and inflammatory conditions remains high in cases of prolonged fever, with a noticeable increase in the occurrence of KD and MIS-C since the onset of the COVID-19 pandemic. Notably, ferritin, CRP, and D-dimer levels are valuable indicators for identifying children at elevated risk of developing KD and MIS-C. While data were collected during the epidemic, additional data collection beyond this period would be necessary.

Keywords: prolonged fever, Kawasaki disease, child, multisystem inflammatory syndrome in children

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Introduction

Over four decades ago, initial investigations were undertaken into the underlying causes of persistent fever in children. Various medical conditions, including infections, specific inflammatory disorders, neoplastic diseases, and rheumatological conditions, can manifest with shared fever symptoms [1]. Typically, fever caused by viral infections often affects children without a discernible cause [2]. In developing nations, fever frequently becomes a reason for hospital admissions. Its prevalence ranges from 0.5 to 3% of all pediatric hospitalizations, with the primary challenge linked to prolonged fever being identifying its underlying source [3]. While most fever instances stem from self-limiting viral infections that resolve naturally, the diagnostic approach differs based on the risk associated with distinct age groups [4]. Cases of prolonged fever with uncertain origins present difficulties for medical professionals and patients, often resulting in extended hospital stays [5]. Fever accounts for roughly 30% of visits to primary care facilities and emergency departments for children [6]. Repeated trips to the emergency room correlate with prolonged durations of children's fevers [7]. Parents may experience significant concerns regarding the potential adverse effects of fever, known as "fever phobia" [8].

Kawasaki disease (KD) represents a medium-vessel vasculitis characterized by an unknown origin and is frequently encountered in children less than 5 years old. The primary hallmark of KD is the onset of an acute, prolonged, and persistent fever [9]. As reported by Verdoni et al. [10] in April 2020, instances of KD in Bergamo, Italy, have escalated by a factor of 30 since the inception of the coronavirus disease 2019 (COVID-19) pandemic. Additionally, there has been a rise in conditions resembling KD in connection with COVID-19 [11]. This specific presentation is acknowledged as multisystem inflammatory syndrome in children (MIS-C) by the United States Centers for Disease Control and Prevention (CDC) [12]. The origin of the pediatric hyperinflammatory condition known as MIS-C can be attributed to the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). While sharing certain similarities with KD, MIS-C is a recently recognized disorder lacking definitive diagnostic tests [13]. The diagnosis of MIS-C necessitates the observation of either a recent COVID-19 infection, direct contact with a confirmed COVID-19 case, or positive outcomes from polymerase chain reaction, serology, or antigen tests [14]. Swift identification and appropriate treatment hold paramount importance for both these conditions.

The evolving nature of prolonged fever in children has spurred the necessity for an exhaustive investigation into its underlying determinants. We postulated that persistent fever in children, characterized by temperatures surpassing 38°C for a minimum of 5 days, exhibits links to diverse underlying causes, with infectious diseases traditionally holding the predominant role. Moreover, considering the shifts in disease patterns and the emergence of conditions like multisystem inflammatory syndrome in children (MIS-C) and KD, we foresee heightened intricacy in the etiological landscape of prolonged fever. Our study aimed to pinpoint the contributing factors to prolonged fever in children and to delve into the relationship between this phenomenon and conditions such as MIS-C and KD, particularly in light of the COVID-19 pandemic. Additionally, this study sought to identify the risk factors associated with both KD and MIS-C.

Materials and methods

Study design and participants

This study employed a retrospective cohort design to investigate potential factors contributing to outcomes that manifested spontaneously throughout the study without deliberate interventions. The primary focus of this study was prolonged fever as the outcome of interest, involving an examination of its potential underlying causes within the study's timeframe.

The research took place at a maternal and children's hospital in Istanbul, Turkey, from 10 April 2020 to 31 October 2022. Our well-established training and research hospital, with a legacy spanning 160 years, serves a diverse patient population ranging from 0 to 18 years of age and provides complimentary medical services. Two-hundred-fifty patients, aged between 3 months and 17 years, who had been admitted to the hospital due to prolonged fever exceeding 38°C (lasting for more than 5 days) [15,16] were assessed. After excluding patients with incomplete data, the analysis was conducted on a cohort of 243 individuals.

Data collection and inclusion criteria

Information was extracted from the hospital's electronic health record system, encompassing patient age, gender, clinical attributes, initial laboratory findings, associated symptoms, clinical indications, ultimate discharge diagnosis, and duration of hospitalization. Two researchers independently reviewed and validated the collected data. Fever was defined as an axillary temperature of ≥38°C upon admission. In our classification, fever was denoted by at least one axillary temperature reading ≥38°C upon admission, meticulously documented using a calibrated thermometer.

Episodes of fever led patients to the emergency unit through three distinct pathways: (i) referrals from other medical facilities, (ii) referrals from outpatient cases exhibiting febrile symptoms, and (iii) referrals from other emergency departments. The duration of the hospital stay was calculated from the admission date to the discharge date.

The hospital stay was calculated from the day of admission to the discharge date. Chest radiographs, blood tests assessing C-reactive protein (CRP) levels, total and differential white blood cell counts (WBC), Ferritin, D-dimer, sedimentation rates, urinalysis, blood and stool cultures, as well as cerebrospinal fluid cultures, were requested based on clinical judgment by the pediatrician.

Cardiac assessments were conducted using echocardiographic data, evaluating various outcomes such as irregularities in coronary arteries, valve regurgitation, pericardial effusion, and ventricular configuration and performance. Utilizing the Z-score categorization method detailed in the revised 2017 American Heart Association guidelines, coronary artery anomalies were categorized according to Z-scores for one or more branches, following established criteria [17].

The inclusion criteria encompassed febrile patients of all ages and genders, identified through triage and documented by the attending physician, supported by diagnostic records, clinical

indicators, and symptoms. Records lacking laboratory test results or inadequate patient demographic and clinical details were excluded.

The study's etiologies were classified into distinct categories: infectious diseases, KD, MIS-C, acute undetermined febrile illnesses, malignancy, and a miscellaneous category. The "others" category combined various etiologies due to their limited case numbers. Patients were segregated into specific groups (KD and MIS-C) based on diagnostic criteria delineated by the American Heart Association [17] and the Centers for Disease Control and Prevention (CDC) [18].

Group classification

Patients were divided into two distinct groups. Group 1 encompassed patients diagnosed with classical KD, atypical KD, and multisystem inflammatory syndrome in children (MIS-C), adhering to well-defined diagnostic criteria. On the other hand, Group 2 consisted of patients afflicted by other origins of prolonged fever, including infectious diseases, acute undetermined febrile illnesses, malignancy, and miscellaneous factors. The primary goal of this comparison was to delineate the unique attributes, laboratory indicators, and outcomes linked to these two groups. Ethical approval was secured from the ethics committee of the Zeynep Kamil Maternity and Children's Diseases Training and Research Hospital (protocol number: 120, dated May 11, 2022). Written informed consent was acquired from all patients or their legal guardians while hospitalized. The study adhered to the principles outlined in the Declaration of Helsinki.

Statistical analysis

In this study, statistical analyses were carried out employing the Number Cruncher Statistical System (NCSS) 2007 Statistical Software (Utah, USA). Alongside descriptive statistical methods (mean, standard deviation, median, and interquartile range), the data assessment involved scrutinizing variable distributions using the Shapiro-Wilk normality test. For comparisons between normally distributed variables, an independent t-test was utilized, while the Mann-Whitney U test was applied for comparisons involving qualitative data.

Logistic Regression analysis was conducted to identify factors influencing the presence of KD +MIS-C. Additionally, Areas under the ROC curve were computed to aid in the differential diagnosis of KD +MIS-C presence. The variables' sensitivity, specificity, positive predictive value, negative predictive value, LR (+) values, and cut-off values were determined. Results were evaluated with a significance level of $P<0.05$.

The sample size was calculated using G*Power 3.1, a software application developed by Franz Faul at the University of Kiel, Germany. Setting the Type I error rate to 0.05 and a confidence level of 90%, the analysis determined that a minimum total sample size of 172 was required.

Results

A total of 322 patients were admitted to our hospital due to a fever lasting longer than 5 days, with 250 patients being hospitalized and 243 included in the study. Table 1 presents the baseline characteristics and laboratory results of the participants. All patients were included in the study. Among them were 126 boys (51.85%), with a median age of 39 months (IQR, 19–58 months).

The mean lymphocyte count in Group 1 was statistically significantly lower than in Group 2 ($P<0.001$). Additionally, CRP, Ferritin, and D-dimer levels were significantly higher in Group 1 compared to Group 2 ($P<0.001$, $P<0.001$, $P<0.001$, respectively). Furthermore, the mean hospitalization days in Group 1 were significantly greater than those in Group 2 ($P<0.001$), and the distribution of echocardiographic findings in Group 1 was notably higher than that in Group 2 ($P<0.001$).

The most prevalent cause of fever was infectious respiratory disease (60.91%), predominantly linked to upper (54.61%) and lower (14.18%) respiratory tract infections, as well as acute otitis media (13.48%). Other common reasons for admission included MIS-C (18.52%) and KD (10.70%) (Table 2). Three patients had positive urine culture test results, while only one exhibited positive blood culture results. Cerebrospinal fluid cultures were sterile among the seven patients who underwent

Table 1: Baseline characteristics and laboratory findings.

		All patients		Group 1 n=72		Group 2 n=171		*P*-value
Age (month)	Mean(SD)	42.71 (28.16)		42.79 (29.56)		42.68 (27.66)		0.821‡
	Median (IQR)	39 (19-58)		34 (20-58)		40 (19-59.5)		
Sex	Female	117	48.15%	40	56.34%	77	44.77%	0.101+
	Male	126	51.85%	31	43.66%	95	55.23%	
Hospitalization (days)	Mean(SD)	6.42 (4.58)		9.39 (4.46)		5.2 (4.05)		<0.001‡
	Median (IQR)	5 (3-8)		9 (7-10)		4 (3-6)		
WBC(10^9/L)	Mean(SD)	13.8 (7)		14.24 (7.96)		13.61 (6.57)		0.526*
Neutrophil(10^9/L)	Median (IQR)	8.76 (6.38)		9.56 (6.79)		8.43 (6.19)		0.288‡
	Mean(SD)	7.5 (4.27-12.26)		7.42 (4.64-12.79)		7.55 (3.83-11.84)		
Lymphocyte (10^9/L)	Median (IQR)	3.73 (2.69)		3.45 (2.42)		3.85 (2.79)		<0.001‡
	Mean(SD)	3.05 (2.04-4.74)		2.84 (1.75-4.6)		3.1 (2.24-4.77)		
Platelet(10^9/L)	Mean(SD)	319.17 (141.07)		327 (185.07)		315.94 (118.76)		0.579*
CRP(mg/L)	Median (IQR)	94.32 (77.51)		128.5 (79.73)		80.22 (72.21)		<0.001‡
	Mean(SD)	76.92 (32.8-137)		117.4 (66.7-177.97)		63.98 (23.47-126.52)		
Ferritin(mcg/L)	Median (IQR)	217.98 (313.59)		390.25 (497.23)		137.52 (97.43)		<0.001‡
	Mean(SD)	134.1 (79.85-240)		230.2 (129.3-325)		117.8 (68.97-180.5)		
D-dimer (µg/mL)	Median (IQR)	1.78 (2.5)		3.24 (3.76)		1.08 (0.99)		<0.001‡
	Mean(SD)	1.05 (0.63-1.96)		2.07 (1.06-3.86)		0.8 (0.52-1.2)		
Sedimentation	Median (IQR)	70.96 (34.65)		88.54 (28.25)		60.89 (34.05)		<0.001‡
	Mean(SD)	77 (42.25-98.75)		98 (81-110)		64 (34.5-85)		
Fever (day)	Median (IQR)	7.7 (2.64)		7.62 (1.69)		7.73 (2.94)		0.361‡
	Mean(SD)	7 (6-9)		7 (7-8)		7 (6-9)		
Cardiac involvement	Absent	198	89.59%	52	73.24%	146	97.33%	<0.001+
	Present	23	10.41%	19	26.76%	4	2.67%	
Comorbidities	Absent	239	98.35%	70	98.59%	169	98.26%	0.852+
	Present	4	1.65%	1	1.41%	3	1.74%	

* Independent t-test, ‡ Mann-Whitney U test, + Chi-square test, CRP: C-reactive protein, MPV: mean platelet volume

lumbar puncture. Cardiac involvement was detected in 23 patients (10.41%) through echocardiography. In the MIS-C and KD groups, 26.72% of patients exhibited cardiac involvement. In this subset, seven patients displayed coronary artery abnormalities, six had myocardial dysfunction, twelve had valvular regurgitation, and two exhibited pericardial effusion. In the other group, 2.67% of patients showed cardiac involvement, with two having minimal mitral regurgitation and two having minimal pericardial effusion. Among all patients, 41.6% reported no additional symptoms. The most common additional complaint was cough (11.52%), followed by rashes (8.64%) (Table 3).

Table 2: The final diagnosis of the patients.

		n	%
Final Diagnosis	Kawasaki Disease	26	10.70
	MIS-C	45	18.52
	Infectious Diseases	148	60.91
	Unidentified febrile illness	21	8.64
	Malignancy	2	0.82
	Others	1	0.41
Infectious Diseases	Acute gastroenteritis	5	3.55
	Acute lower respiratory system infectious diseases	20	14.18
	Encephalitis	1	0.71
	Urinary tract infection	6	4.26
	Lymphadenopathy	10	7.09
	Myositis	2	1.42
	Acute otitis media	19	13.48
	Sepsis	1	0.71
	Acute upper respiratory system infectious diseases	77	54.61

Table 3: Additional symptoms on fever of the patients.

		All patients		Group 1 n=72		Group 2 n=171	
Additional symptoms	Abdominal pain	15	6.17%	11	15.49%	4	2.33%
	Coughing	28	11.52%	0	0.00%	28	16.28%
	Sore throat	16	6.58%	4	5.63%	12	6.98%
	Headache	1	0.41%	0	0.00%	1	0.58%
	Skin rash	21	8.64%	13	18.31%	8	4.65%
	Diarrhea	18	7.41%	6	8.45%	12	6.98%
	Joint pain	5	2.06%	1	1.41%	4	2.33%
	Lymphadenopathy	6	2.47%	0	0.00%	6	3.49%
	Eye slip	2	0.82%	1	1.41%	1	0.58%
	Aphthous lesions	6	2.47%	1	1.41%	5	2.91%
	Febrile seizure	2	0.82%	0	0.00%	2	1.16%
	Conjunctivitis	13	5.35%	5	7.04%	8	4.65%
	Joint swelling	1	0.41%	0	0.00%	1	0.58%
	Ragat	1	0.41%	1	1.41%	0	0.00%
	Vomiting	1	0.41%	0	0.00%	1	0.58%
	Myalgia	3	1.23%	0	0.00%	3	1.74%
	Earache, discharge	3	1.23%	0	0.00%	3	1.74%
	No additional symptom	101	41.56%	28	39.44%	73	42.44%

Logistic regression analysis was conducted using variables such as days of hospitalization, lymphocyte count, CRP level, ferritin level, and D-dimer level to identify factors influencing the presence of KD + MIS-C. Hospitalization days (P=0.001), elevated CRP (P=0.018), elevated ferritin (P=0.009), and elevated D-dimer (P=0.001) were statistically significant (P=0.001) (Table 4). In the differential diagnosis of KD + MIS-C, Ferritin and D-dimer levels exceeded the desired threshold (0.700). The AUC values were 0.737 [0.672–0.795] and 0.782 [0.720–0.836] respectively (Table 5, Figure 1). The cut-off values for sensitivity, specificity, positive and negative predictive values and likelihood ratios of laboratory parameters are presented in Table 6.

Table 4: Logistic regression analysis to search factors affecting the presence of KD+MIS-C.

	OR (%95 Cl)	*P*-value
Hospitalization (days)	1.23 (1.11–1.37)	0.001
Lymphocyte (10^9/L)	1.03 (0.88–1.20)	0.752
CRP(mg/L)	1.04 (1.01–1.09)	0.018
Ferritin(mcg/L)	1.05 (1.02–1.06)	0.009
D-dimer (µg/mL)	2.04 (1.47–2.84)	0.001

CRP: C-reactive protein, OR: odds ratio, Cl: confidence interval

Table 5: Receiver operating characteristic curve analysis.

	AUC	SE	95% CI	*P*-value
Lymphocyte	0.564	0.041	0.495–0.632	0.098
CRP	0.680	0.040	0.612–0.742	0.001
Ferritin	0.737	0.038	0.672–0.795	<0.001
D-dimer	0.782	0.036	0.720–0.836	<0.001

CRP: C-reactive protein

Figure 1: Receiver operating characteristic curves and related areas under the curve for determining KD and MIS-C among patients with long fever.

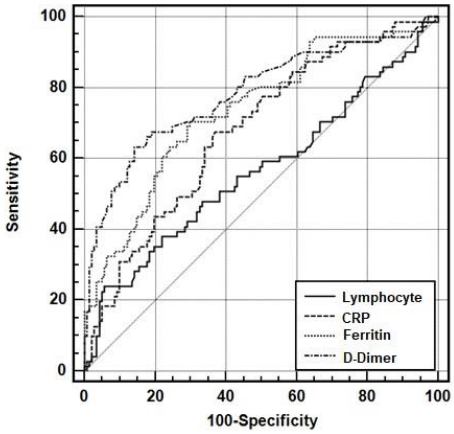

Table 6: The sensitivity, specificity, positive predictive value, and negative predictive value of the parameters.

	Cut-off	Sensitivity	Specificity	PPV	NPV		LR (+)
Lymphocyte	≤1.51	23.94	94.19	63.0	75.0		1.12
CRP	>85.86	67.61	63.95	43.6	82.7		1.88
Ferritin	>154	70.42	70.39	52.6	83.6		2.38
D-dimer	>1.6	63.38	85.71	68.2	82.9		4.44

CRP: C-reactive protein, PPV: positive predictive value, NPV: negative predictive value, LR: likelihood ratio

Discussion

Our research has uncovered that the primary cause of extended fever leading to hospitalization is infectious disease, primarily associated with respiratory tract infections. However, it is important to note that reporting respiratory tract infections has declined at our hospital, a trend attributed to the COVID-19 restrictions implemented [19]. Pediatricians have observed a significant reduction in respiratory viral infections and various infection-related conditions during the COVID-19 pandemic [20].

There has been an increased frequency of cases involving MIS-C and KD after infectious diseases. A study demonstrated that children experiencing febrile illnesses lasting beyond seven days exhibited compromised health-related quality of life [21]. Numerous studies have been published on the origins and evaluation of prolonged fever in children. The predominant cause of fever episodes is non-threatening viral infections that resolve independently without treatment. However, the approach to diagnosis varies depending on the level of risk associated with the child's age [4]. Research indicates that infectious diseases are the leading cause of fever [22,23]. However, there is currently no firmly established predictive significance concerning severe bacterial infection solely based on the prolonged duration of fever before seeking medical care [24,25].

Children often experience fever due to viral infections, even when the precise cause is not readily identifiable [26]. In our investigation, 41.6% of patients displayed no accompanying symptoms. The most prevalent supplementary issue among those who did was coughing, followed by rashes. Mar et al. [27] also noted that an extended fever duration consistently correlated with a sore throat. According to alternate research findings,

approximately 60% of individuals with a sore throat continue to exhibit symptoms beyond the third day [28].

In the study conducted by Klein-Kremer et al. [7], an analysis of fever-related concerns within the participant group revealed that out of 219 individuals (45%), coughing was reported, 148 individuals (30%) experienced vomiting, and 74 individuals (15%) complained of a "runny nose". Following infectious diseases, the prominent causal factors were MIS-C and KD. An entirely novel condition, MIS-C, emerged during the COVID-19 pandemic. This ailment typically manifests after COVID-19 infection and exhibits clinical features, symptomatology, and laboratory characteristics similar to KD. However, it is worth noting that while the two conditions share similarities, they possess distinct diagnostic criteria due to the absence of a singular diagnostic test [14].

As reported by Kim et al. [29], even though there was an increase in the proportion of infants under 1 year of age hospitalized for KD, the prevalence of refractory KD and challenging cases did not significantly increase during social distancing. While MIS-C and KD exhibit marked inflammation and inflammatory vasculopathy, further research is essential to ascertain whether these conditions represent distinct immunopathogenic disorders [30].

Prompt diagnosis and treatment are paramount for both MIS-C and KD. Patients afflicted with both conditions tend to display elevated levels of inflammatory markers [31]. In the acute phase of KD, laboratory indicators such as elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and WBC count will be observed [32]. Leukopenia, rather than an increase in WBC count, is predicted during the acute phase of MIS-C, along with higher CRP and ESR. Troponin, D-dimer, and brain natriuretic peptide levels are frequently elevated. While fibrinogen and ferritin levels are elevated, MIS-C is characterized by more typical increases in D-dimer and ferritin levels [33].

Our study identified statistically significant CRP, ferritin, and D-dimer levels elevations in the MIS-C and KD groups compared to the other groups.

Limitations

Certain limitations of this study must be acknowledged, particularly concerning potential biases that could impact the validity and generalizability of our findings. Firstly, since this study was retrospective and conducted at a single center, it is important to consider the inherent limitations of such a design and the limited external applicability of the results. The study's findings might not offer a fully comprehensive representation of the broader population due to the specific patient pool associated with a single institution.

Secondly, using electronic health records for data collection introduces the potential for information bias. Despite efforts to ensure data accuracy, the study's retrospective nature limits control over data collection, which may lead to potential misclassification of variables.

Furthermore, an inherent limitation of our study design is the absence of a control group. Establishing direct causal relationships between prolonged fever and specific conditions, such as MIS-C and KD, becomes challenging without a comparative group. This limitation restricts our ability to draw definitive conclusions regarding the factors causing these conditions.

Additionally, the study's timeframe during the COVID-19 pandemic might have influenced the results due to changing medical practices. Despite these limitations, this study offers valuable insights into the landscape of prolonged fever in children, illuminating the prevalent causes and associations, particularly in emerging conditions like MIS-C and KD.

In the future, research involving larger multicenter cohorts and longitudinal designs could offer more robust evidence and help address some of the limitations above.

Strengths

This study focused on investigating prolonged fever in a pediatric population, contributing valuable insights into this significant health concern among children. The research involved an in-depth analysis of data from a substantial number of patients, bolstering the statistical robustness and reliability of the findings. The study delved into clinically pertinent outcomes, such as cardiac involvement and diagnostic markers, which are pivotal in making well-informed medical decisions.

Advanced statistical techniques, including logistic regression and ROC curve analysis, were employed to probe the factors influencing the presence of particular conditions. Patients from a maternal and children's hospital with diverse socioeconomic backgrounds were encompassed in this study, amplifying the potential applicability of the discoveries to comparable healthcare settings. By investigating the correlation between prolonged fever and specific conditions, this research addresses gaps in the existing literature, thereby providing valuable insights for clinical practice.

Conclusion

This study imparts valuable insights into the multifaceted nature of prolonged fever in pediatric patients, shedding light on various contributing factors. The prevalence of infectious diseases, KD, and multisystem inflammatory syndrome in children (MIS-C) underscores the evolving landscape of fever etiologies, which the COVID-19 pandemic has further influenced. The study's findings underscore the importance of swift diagnosis and timely intervention, as evidenced by the correlation between elevated inflammatory markers and MIS-C and KD. The distinct immunopathogenesis of MIS-C and KD necessitates ongoing exploration to unravel their nuanced differences.

Looking ahead, collaborative endeavors across various research centers offer the potential to validate and expand upon these revelations, ultimately refining clinical approaches and enhancing patient outcomes. The impact of the pandemic on epidemiology, clinical presentation, and outcomes raises pertinent questions. While data were collected during the epidemic, a need for additional data post-pandemic becomes apparent to comprehensively address these aspects.

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