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CLINICAL AND LABORATORY FEATURES OF EXANTHEMATOUS SYNDROME IN PEDIATRIC PATIENTS WITH COVID-19

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Key words: *COVID-19, children, exanthematous syndrome, skin manifestations, disease severity, inflammatory markers, respiratory complications, multisystem inflammatory syndrome in children (MIS-C).*

ABSTRACT
This study aimed to determine the clinical and laboratory characteristics of exanthematous syndrome in children with COVID-19 and to assess its association with disease severity and complications. A combined retrospective and prospective design was applied, including 19,682 pediatric cases (2020–2022) and 363 hospitalized children aged 0–18 years (2022–2024). Clinical, laboratory, and radiological parameters were analyzed with emphasis on the presence of exanthema. Exanthema was identified in 40.5% of patients and was significantly associated with a more severe disease course, including higher rates of pneumonia, respiratory failure, hypoxemia, and systemic complications. Laboratory findings in these patients indicated intensified inflammatory response, immune dysregulation, and coagulation abnormalities. The results demonstrate that exanthematous syndrome is not merely a dermatological manifestation but reflects systemic pathological processes. Its presence may serve as an accessible clinical marker for early identification of children at risk of severe COVID-19, requiring enhanced monitoring and management.

COVID-19 BILAN KASALLANGAN BOLALARDA EKZANTEMATOZ SINDROMNING KLINIK VA LABORATOR XUSUSIYATLARI

Kalit so‘zlar: *COVID-19, bolalar, ekzantematoz sindrom, teri namoyon bo‘lishlari, kasallik og‘irligi, yallig‘lanish markerlari, respirator asoratlar, bolalarda multisistem yallig‘lanish sindromi (MIS-C).*

ANNOTATSIYA
Mazkur tadqiqotning maqsadi COVID-19 bilan kasallangan bolalarda ekzantematoz sindromning klinik va laborator xususiyatlarini aniqlash hamda uning kasallik og‘irligi va asoratlar bilan bog‘liqligini baholashdan iborat edi. Tadqiqot kombinatsiyalashgan retrospektiv va prospektiv dizayn asosida olib borildi: 2020–2022 yillarda qayd etilgan 19 682 nafar pediatrik holat va 2022–2024 yillarda shifoxonaga yotqizilgan 0–18 yoshdagi 363 nafar bola qamrab olindi. Ekzantema mavjudligiga alohida e’tibor qaratgan holda klinik, laborator va radiologik ko‘rsatkichlar tahlil qilindi. Ekzantema bemorlarning 40,5% ida aniqlanib, kasallikning og‘ir kechishi, jumladan pnevmoniya, nafas yetishmovchiligi, gipoksemiya va tizimli asoratlarning yuqori uchrashi bilan bog‘liq ekani ko‘rsatildi. Laborator natijalar yallig‘lanish javobining kuchayishi, immun disregulyatsiya va koagulyatsion buzilishlarni tasdiqladi. Olingan natijalar ekzantematoz sindrom faqat dermatologik belgi emas, balki tizimli patologik jarayonlarning klinik ifodasi ekanini ko‘rsatadi. Uning mavjudligi og‘ir COVID-19 xavfi yuqori bo‘lgan bolalarni erta aniqlashda muhim klinik marker bo‘lib xizmat qilishi mumkin.

Although COVID-19 in children generally follows a milder clinical course than in adults, cutaneous manifestations remain an important component of its clinical spectrum. Published reviews indicate that dermatological signs associated with SARS-CoV-2 infection include maculopapular, urticarial, vesicular, chilblain-like, and vascular lesions. In pediatric populations, these manifestations may occur both during the acute phase of infection and in association with post-infectious inflammatory responses [1, P.5407–5414; 2, P.1–9]. Previous studies conducted by the author and co-authors have also described the frequency, patterns, and clinical variants of exanthema in pediatric COVID-19, thereby demonstrating the continuity and relevance of the present investigation [6, P.159–160; 7, P.38].

In pediatric infectious disease practice, the presence of a rash presents significant diagnostic challenges, as it necessitates differentiation from measles, scarlet fever, varicella, allergic eruptions, drug-induced reactions, and other viral exanthems.

At the same time, recent evidence suggests that dermatological manifestations in COVID-19 may be associated with endothelial damage, immune dysregulation, vasculitic processes, and systemic inflammation [1, P.5408; 3, P.1–9; 4, P.83–89]. Therefore, the investigation of the clinical and laboratory characteristics of exanthematous syndrome in children with COVID-19 is of considerable importance, not only for differential diagnosis but also for early severity assessment, prediction of complications, and optimization of clinical management strategies.

AIM OF THE STUDY

To determine the clinical and laboratory characteristics of exanthematous syndrome in children with COVID-19 and to evaluate its association with disease severity and the development of complications.

MATERIALS AND METHODS

The study was conducted using a combined retrospective and prospective design. The retrospective component included 19,682 children with laboratory-confirmed COVID-19 who were treated between 2020 and 2022. The prospective component comprised 363 children aged 0 to 18 years who were hospitalized and examined between 2022 and 2024. Inclusion criteria were based on clinical and laboratory confirmation of SARS-CoV-2 infection. The examination protocol included detailed history taking, physical examination, assessment of body temperature, respiratory rate, heart rate, and oxygen saturation, as well as evaluation of respiratory, gastrointestinal, neurological, and cutaneous manifestations. Laboratory investigations included complete blood count parameters (hemoglobin, erythrocytes, hematocrit, leukocytes, neutrophils, lymphocytes, eosinophils, and platelets), as well as measurement of C-reactive protein, interleukin-6, coagulation parameters, and biochemical blood markers. Radiological examinations and computed tomography were performed in patients presenting with signs of lower respiratory tract involvement.

Patients were stratified into moderate, severe, and critical groups based on the clinical course and in accordance with current clinical guidelines for the management of COVID-19 in children. Particular attention was given to the presence or absence of exanthema, as well as to the relationship between exanthema, respiratory impairment, and laboratory indicators of inflammatory activity. Statistical analysis was performed using descriptive methods, relative indicators, and comparative evaluation of clinical and laboratory parameters between groups with and without exanthema.

Table 1

Frequency of clinical manifestations of COVID-19 in the prospective group (n=363)

Indicator	Absolute number	%
Fever	356	98.0
Rhinopharyngitis	330	91.0
Intoxication syndrome	261	72.0
Diarrhea	248	68.2
Sweating	221	61.0
Hyperthermic syndrome	218	60.0
Acute bronchitis	211	58.0
Pneumonia	211	58.0
Respiratory failure	229	63.0
Exanthema	147	40.5
Anosmia	40	11.0
ARDS / bilateral interstitial pneumonia / sepsis / acute renal injury	4–5	1.1–1.3

RESULTS

The retrospective analysis demonstrated that, during 2020–2022, COVID-19 in children predominantly followed a moderate clinical course. The highest incidence was observed among children aged 1–3 years and adolescents aged 15–18 years. Across all years analyzed, moderate forms of the disease predominated, whereas severe and critical forms were observed less frequently.

In the prospective cohort of 363 children, moderate disease was identified in 73% of cases, severe disease in 25%, and critical illness in 2%. The most common clinical manifestations included fever, rhinopharyngitis, intoxication syndrome, diarrhea, sweating, acute bronchitis, pneumonia, and respiratory failure.

Exanthema was documented in 40.5% of patients. Children presenting with exanthema more frequently exhibited a severe course of the disease, more extensive pulmonary involvement, and more pronounced signs of systemic inflammation. In this group, pneumonia, respiratory failure, interstitial lung changes, and inflammatory laboratory abnormalities were observed more often than in children without cutaneous manifestations.

Clinical observations further indicated that exanthema generally developed in association with general infectious symptoms and respiratory manifestations and, in some cases, with gastrointestinal symptoms. In severe cases, exanthema was accompanied by hypoxemia, bilateral pulmonary involvement, and a higher likelihood of systemic complications.

Table 2

Distribution of disease severity in children with and without exanthema

Group	Moderate	Severe	Critical
Children without exanthema (n=216)	80.2%	17.4%	2.4%
Children with exanthema (n=147)	63.0%	36.0%	1.0%

Laboratory analysis demonstrated that children with exanthema exhibited more pronounced inflammatory and hematological alterations. According to the study data, this group showed a tendency toward lower hemoglobin levels, erythrocyte counts, and hematocrit values, accompanied by elevated leukocyte and neutrophil counts, reduced lymphocyte levels, increased erythrocyte sedimentation rate, and a marked rise in eosinophils. These findings indicate a more intense immune-inflammatory response in children presenting with rash. Alterations in coagulation parameters were also more pronounced in children with exanthema. Changes in prothrombin time, international normalized ratio, and fibrinogen levels suggested endothelial dysfunction and involvement of the hemostatic system in the pathogenesis of a more severe disease course. Among comorbid conditions, frequently ill children, grade I–II anemia, chronic ENT pathology, protein-energy malnutrition, allergic predisposition, and certain chronic somatic diseases were identified. Among adverse outcomes and complications in the exanthema group, multisystem inflammatory syndrome in children (MIS-C), sepsis, prolonged post-COVID manifestations, and renal or hepatic dysfunction were observed.

DISCUSSION

The results obtained indicate that exanthema in children with COVID-19 is not merely an incidental symptom but a clinically significant manifestation associated with the nature and severity of the infectious process. The higher proportion of severe forms observed among children with rash suggests that cutaneous manifestations may reflect more pronounced systemic inflammation and more extensive respiratory involvement. These findings are consistent with published reviews on pediatric COVID-19 and MIS-C [2, P.1–9; 3, P.1–9; 4, P. e83–e89]. The present observations are also in agreement with the author's earlier studies on exanthematous syndrome and clinical presentations of COVID-19 in children [6, P.159–160; 7, P.38; 8, P.256–262; 9, P.125–128]. International evidence interprets dermatological manifestations of COVID-19 in children as being associated with immune-mediated mechanisms, vascular injury, endothelial dysfunction, and systemic inflammatory responses [1, P.5408; 4, P.e83–e89]. The coexistence of exanthema with pneumonia, respiratory failure, and coagulation abnormalities observed in the present study further supports this concept.

From a clinical perspective, the presence of rash in a child with COVID-19 should alert clinicians to the possibility of a more severe disease course. Such patients require closer monitoring of oxygen saturation, respiratory function, inflammatory markers, and potential complications affecting the lungs and other organ systems. Present study demonstrates that COVID-19 in children is predominantly characterized by a moderate clinical course; however, a substantial proportion of patients develop severe manifestations associated with respiratory impairment, systemic inflammatory response, and multiorgan involvement. Within this clinical spectrum, exanthematous syndrome was identified in 40.5% of examined children and showed a clear association with more severe forms of the disease.

The findings indicate that exanthema in pediatric COVID-19 should not be regarded solely as an isolated dermatological manifestation. Rather, its presence reflects a broader pathological process involving inflammatory activation, immune dysregulation, endothelial injury, and, in many cases, pulmonary and hemostatic disturbances. Children with exanthema more frequently exhibited pneumonia, respiratory failure, bilateral pulmonary involvement, coagulation abnormalities, and laboratory indicators of intensified inflammatory activity, underscoring the clinical significance of cutaneous manifestations in the overall assessment of disease severity.

The study supports the concept that exanthematous syndrome may serve as an accessible clinical marker for the early identification of children at risk for a more severe and complicated course of COVID-19. From a practical standpoint, the detection of rash in a child with confirmed or suspected SARS-CoV-2 infection should prompt enhanced clinical vigilance, including careful monitoring of respiratory status, oxygen saturation, inflammatory laboratory parameters, and potential systemic complications, including MIS-C and organ dysfunction. Thus, the assessment of cutaneous manifestations should be integrated into routine clinical evaluation in pediatric COVID-19. The findings expand current understanding of the clinical and laboratory profile of exanthematous syndrome and highlight its diagnostic and prognostic value. Further multicenter studies with larger cohorts are required to clarify the role of exanthema in predicting clinical outcomes and to improve evidence-based management strategies for children with COVID-19 and associated skin manifestations.

CONCLUSION

The present study provides a comprehensive analysis of the clinical and laboratory characteristics of exanthematous syndrome in children with COVID-19 and substantiates its significant role within the overall structure of the disease. The findings confirm that, although COVID-19 in pediatric populations is predominantly characterized by a moderate clinical course, a considerable proportion of cases are accompanied by severe manifestations involving respiratory impairment, systemic inflammation, and multiorgan involvement. Within this context, exanthema emerges as a frequent and clinically meaningful component, identified in 40.5% of examined patients.

The results demonstrate a clear association between the presence of exanthema and a more severe course of the disease. Children with cutaneous manifestations more frequently exhibited pneumonia, respiratory failure, interstitial lung changes, and laboratory indicators of intensified inflammatory activity. Hematological and biochemical findings, including alterations in leukocyte and lymphocyte counts, elevated inflammatory markers, and changes in coagulation parameters, indicate that exanthema is linked to pronounced immune-inflammatory responses, endothelial dysfunction, and involvement of the hemostatic system. These observations support the concept that cutaneous manifestations in pediatric COVID-19 reflect not only local dermatological processes but also systemic pathological mechanisms. Furthermore, the study highlights that exanthema typically develops in combination with general infectious and respiratory symptoms and, in more severe cases, is associated with hypoxemia, bilateral pulmonary involvement, and an increased risk of complications such as multisystem inflammatory syndrome in children (MIS-C), sepsis, and organ dysfunction. The presence of comorbid conditions, including anemia, chronic ENT pathology, nutritional deficiencies, and allergic background, may further aggravate the clinical course and contribute to the development of adverse outcomes. Taken together, the findings indicate that exanthematous syndrome should be regarded as an important clinical marker with both diagnostic and prognostic significance. Its detection in children with COVID-19 provides additional information regarding disease severity and may facilitate early identification of patients at increased risk of complications.

The integration of dermatological assessment into routine clinical evaluation is therefore essential for a more comprehensive understanding of the disease course and for improving patient management.

From a practical standpoint, the results of the study substantiate the need for enhanced clinical vigilance in children with COVID-19 presenting with exanthema. The identification of rash should prompt more thorough monitoring of respiratory function, oxygen saturation, and laboratory indicators of inflammation and coagulation, as well as timely assessment for potential systemic complications.

The study also supports the importance of considering exanthema in the differential diagnostic process, given the overlap with other infectious and non-infectious conditions characterized by skin manifestations. These considerations, derived directly from the clinical and laboratory findings presented, emphasize the necessity of incorporating the evaluation of cutaneous symptoms into standardized clinical algorithms for the management of pediatric COVID-19.

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EDITORIAL REVIEW

The submitted article is devoted to the analysis of clinical and laboratory characteristics of exanthemata's syndrome in pediatric patients with COVID-19, which represents a relevant and timely topic in modern pediatric infectious disease research. Despite the generally mild course of COVID-19 in children, the study addresses an important clinical aspect cutaneous manifestation–and their association with disease severity and systemic involvement. Relevance of the study is well substantiated. The author correctly emphasizes the diagnostic challenges posed by exanthema in pediatric practice, particularly in the context of differential diagnosis with other infectious and non-infectious conditions. Given the growing body of evidence on multisystem inflammatory responses in children, including MIS-C, the investigation of dermatological signs as potential markers of disease severity is both justified and clinically important. Scientific novelty of the study lies in the comprehensive evaluation of exanthemata's syndrome not merely as a dermatological manifestation but as an indicator of systemic pathological processes, including immune dysregulation, endothelial dysfunction, and inflammatory activation. The integration of clinical observations with laboratory parameters provides a multidimensional perspective that enhances the understanding of the pathogenesis and clinical significance of skin manifestations in pediatric COVID-19.

Practical significance is evident in the proposed interpretation of exanthema as an accessible clinical marker for early identification of patients at risk of severe disease. The findings have direct implications for clinical practice, particularly in improving diagnostic accuracy, risk stratification, and monitoring strategies in pediatric patients. From a methodological standpoint, the study is based on a combined retrospective and prospective design, which increases the robustness of the analysis. The inclusion of a large retrospective cohort (19,682 patients) and a well-defined prospective sample (363 patients) enhances the reliability of the findings. The clinical and laboratory assessment appears comprehensive, covering key physiological, hematological, and biochemical parameters. However, the manuscript would benefit from a more detailed description of statistical methods, including the use of specific tests and the level of statistical significance, which is currently presented in a generalized form. Among the strengths of the study are the large sample size, the integration of clinical and laboratory data, and the clear demonstration of associations between exanthema and disease severity. The logical structure and consistency with previous publications by the author further support the credibility of the results. At the same time, several limitations should be noted. The absence of detailed statistical analysis and quantitative indicators (e.g., p-values, confidence intervals) somewhat limits the interpretability of the findings. In addition, the study could benefit from a more explicit discussion of potential confounding factors, such as comorbid conditions and treatment variations. The inclusion of multicenter data would further strengthen the generalizability of the conclusions. In conclusion, the article represents a scientifically sound and practically valuable contribution to the field of pediatric COVID-19 research. The study is methodologically adequate, the results are coherent, and the conclusions are well supported by the data. Despite minor methodological limitations, the manuscript meets the requirements of academic publication. Recommendation: The article is recommended for publication in a scientific journal after minor revisions, primarily related to the clarification of statistical methods and enhancement of methodological transparency.