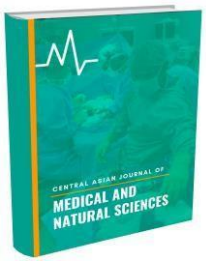

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Article

Clinical and Immunological Aspects of Sepsis in Children with Primary Immunodeficiencies (PID): A Retrospective Analysis in The Setting of The Tashkent City Children's Clinic

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Abstract: Sepsis continues to be one of the major morbidities and mortalities among paediatric patients, especially in children with a primary immunodeficiency (PID). These patients are characterised by high susceptibility to severe infections, atypical clinical manifestations, and high probability of rapid progression of disease due to congenital defects of the immune system. The current research intends to examine clinical and immunological characteristics of sepsis in children with PID in terms of retrospective data analysis of cases treated in the Tashkent City Children's Clinic. A retrospective study was performed through the medical records of children diagnosed with PID and sepsis within a fixed study period. Clinical data and laboratories, immunological parameters, causative pathogens, treatment methods and outcomes were assessed. The features of immune dysfunction, such as the defects in humoral and cellular immunity, and their correlation with the progression and severity of sepsis, were singled out. The review showed that children with PID tend to exhibit severe and frequent septic events, late diagnosis, and length of stay. The prevalent ones were the persistent leukopenia or lymphopenia, low levels of immunoglobulins, and the lack of an inflammatory response. Opponent pathogens and Gram-negative bacteria were often verified as causative agents. Despite the intensive antimicrobial and supportive treatment, the threat of complications and the adverse outcomes were still very great in comparison with immunocompetent children. These results demonstrate the need to undertake early identification of PID in the septic child, timely immunological evaluation, and adopt a personalised treatment plan. Awareness of diagnosis and optimal multidisciplinary care can help improve the prognosis and decrease mortality in the susceptible population of such patients.

Keywords: Sepsis, Primary Immunodeficiency, Children, Clinical Features, Immunological Disorders, Retrospective Analysis

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1. Introduction

Sepsis is a life-threatening condition due to the dysregulated host response to the infection and is one of the significant health issues in the context of paediatric practice worldwide. Although antimicrobial therapy and intensive care have been made more advanced, sepsis remains among the main causes of death among children all over the world and in the most vulnerable groups, particularly [1]. Early diagnosis and prompt management are essential, but in children, the clinical manifestation of the disease is not always specific, and it can thus be difficult to identify and treat as early as possible.

Children with primary immunodeficiencies (PID) are particularly at high risk of acquiring severe and recurrent infections, including sepsis. Primary immunodeficiencies represent a heterogeneous collection of inherited conditions that

involve a malfunction of one or more of the elements of the immune system (humoral immunity, cellular immunity, phagocytic activity, or complement pathways) [2]. These malfunctions reduce the effectiveness of the body in providing sufficient immune response to the pathogens, which increases the vulnerability to opportunistic and invasive infections.

PID children have a different clinical course of sepsis as compared to immunocompetent patients. The infections tend to manifest themselves at a young age in this population, quickly develop, and have unusual symptoms, delayed inflammatory reactions, and adverse prognoses [3]. In addition, routine lab indicators of infection and inflammation can not be as reliable because of the underlying defects in the immune system, which makes it even more difficult to diagnose in the early stages. Consequently, children with PID often get diagnosed with sepsis at a very late stage when the dysfunction of their organs has already occurred.

The immunological deviations are significant in the pathophysiology and grades of sepsis among PID patients. Spontaneous decreases in immunoglobulin levels, lymphopenia, defective generation of cytokines, and deficiency of the innate immune responses play a role in the insufficiency of clearance of the pathogen and systemic inflammation [4]. Moreover, the prognosis is further deteriorated by the exposure to broad-spectrum antibiotics repeatedly, leading to the development of antimicrobial resistance, fungi or opportunistic infections.

Although there is clinical significance to this issue, there is a paucity of data regarding clinical and immunological features of sepsis in PID children, especially in developing nations. Answers to the issues may be offered by retrospective investigations in specialised paediatric Centres, which can help determine the patterns of the disease, the difficulties of diagnosis and results of treatment in a mind-boggling group of patients [5]. An improved comprehension of these factors is necessary to enhance the processes of early detection, tailored treatments, and improved morbidity and mortality rates of children with primary immunodeficiencies with sepsis.

2. Materials and Methods

This observational retrospective research was carried out in one of the Tashkent City Children's Clinics, a tertiary-level paediatric medical centre, specialised in the treatment of children with complex infectious and immunological diseases. The subjects that were studied were medical records of paediatric patients diagnosed with sepsis, but with known primary immunodeficiencies (PID) during a specific period of observation. Paediatric sepsis criteria were used to identify sepsis based on the internationally accepted criteria of sepsis, considering the clinical features and laboratory indicators specific to the age and signs of organ dysfunction [6].

Selection of patients has been done on inclusion and exclusion criteria. Children aged between 0 to 18 years were included, and they had a confirmed diagnosis of PID and immunological tests and had developed sepsis in the hospital. Patients whose immunodeficiencies were secondary, whose medical records were not complete, or those with sepsis due to non-surgical complications were not analysed. All eligible patients were entered in the demographic data, including age, sex, and age at first clinical manifestation.

The hospital records were used to extract clinical data, which were presented in terms of the presenting symptoms, source of infection, the severity of sepsis, hospital stay, requirement of intensive care, and the clinical outcomes. The parameters studied in the lab included complete blood counts, inflammatory indices, including C-reactive protein and procalcitonin, biochemical indices of organ dysfunction, and microbiological culture findings. Immunological diagnosis centred on serum immunoglobulin levels, lymphocyte subsets, as well as available functional immune tests, which enables one to characterise the underlying immune defects [7].

Microbiological records were checked in order to determine the causative organisms and their antimicrobial susceptibility patterns. Blood cultures and available cultures of other sterile sites had been analysed. Special interest was put on the prevalence of

opportunistic organisms and multidrug-resistant pathogens, which are often related to the immunocompromised paediatric population [8]. The antimicrobial therapy, immunoglobulin replacement, and supportive methods of treatment were also considered in terms of their dependency on the progression and outcomes of the disease.

Standardised extraction forms were utilised to collect information and achieve consistency, as well as reduce bias. The statistical analysis was done in the form of descriptive statistics, where the categorical variables were summarised in terms of frequencies and percentages, and the continuous variables were summarised by using medians and ranges. Suitable comparative analyses were used to determine associations between immunological abnormalities and clinical severity. The retrospective nature of the study led to the absence of missing data; however, the careful review of the records omitted the imputation procedure.

The local institutional review board provided ethical approval for the study, and the confidentiality of the patients during the research process was strongly ensured. The chosen study design is also consistent with the current guidelines on retrospective clinical research in the field of paediatric immunology and sepsis and offers credible information about the actual clinical practice and its outcomes in the high-risk population of patients [9].

3. Results

The retrospective study involved the children with primary immunodeficiencies confirmed during hospitalisation at the Tashkent City Children's Clinic and who developed sepsis. The majority of the cases were children who were less than five years old, which would mean that the disease would have manifested early, and children would be vulnerable to the disease. Sepsis represented the first severe clinical event in a significant proportion of patients that resulted in the identification and diagnosis of underlying immunodeficiency, which corresponds to prior trends in paediatric immunology [10]. This was a result of the contribution of X-linked immunodeficiency disorders, as a slight majority of male patients were observed.

Clinically, most patients came in having been severely sepsis, which often deteriorated to septic shock and dysfunction of multiple organs. Some of the most frequent reasons to be admitted to the paediatric intensive care unit were respiratory failure, cardiovascular instability, and altered consciousness. In most cases, standard indicators of systemic inflammation were not so intense, which led to late clinical suspicion and diagnosis. The duration of the hospital stay was significantly increased, especially in patients with combined immunodeficiencies and severe immune abnormalities.

The lab analysis indicated that there were serious abnormalities in haematological and immunological parameters. Regular lymphopenia and leukopenia were typical, including those with T-cell or combined defects of the immune system. The common finding in children with humoral immunodeficiencies was the reduced levels of serum immunoglobulins, predominantly IgG and IgA. C-reactive protein and procalcitonin, which are inflammatory biomarkers, showed a heterogeneous pattern; in some patients, these biomarkers were not associated with the clinical severity of sepsis, which restricts their diagnostic and prognostic capabilities [11].

Microbiological results indicated that Gram-negative pathogens are predominant, with Klebsiella pneumoniae, Pseudomonas aeruginosa and Acinetobacter species being most commonly isolated in the blood cultures. Gram-positive organisms such as Staphylococcus aureus were also detected, and opportunistic infections were found more in patients with severe combined immunodeficiency. The prevalence of multidrug-resistant microorganisms was recorded as high, and this made it difficult to manage using antimicrobials and led to an adverse outcome [12].

Although aggressive treatment was used, such approaches as a broad-spectrum antimicrobial treatment, replacement by immunoglobulin and intensive supportive care were implemented, the complication rates were still very high. ARDS, renal failure and secondary infections were common. Children with primary immunodeficiencies and

sepsis were considerably more likely to die than the general paediatric population, and patients with severe immune defects had the lowest outcome. The findings suggest that the degree of immunological malfunction has a strong relationship with the severity of sepsis, and therefore, the immune condition is of utmost importance in defining the disease progression and the prognosis [13,14].

4. Discussion

The results of this retrospective study indicate how complicated and severe sepsis can be in children with primary immunodeficiencies. The findings corroborate the assumption that sepsis is common at an early age in this group of patients, and it might be the initial life-threatening manifestation of an underlying immune disorder. The note complies with the world statistics, suggesting that the late diagnosis of primary immunodeficiencies is one of the causes of serious infectious morbidity and unfavourable results [15].

Among the main observations during the study, the abnormal clinical and laboratory manifestations of sepsis in children with immunodeficiency can be identified. In contrast to immunocompetent patients, classical inflammatory responses were often attenuated or delayed, and this created problems with diagnosis. A number of studies have highlighted the fact that the conventional biomarkers, including C-reactive protein and procalcitonin, can be relatively insensitive in patients with severe immune dysfunction, which is congruent with the mixed laboratory results in this study [16]. This highlights the importance of increased clinical observation and prompt immunological assessment in children who present with acute or chronic infections.

The presence of Gram-negative and opportunistic pathogens in the majority of cases seen in this study demonstrates the compromised capacity of children having primary immunodeficiencies to prevent invasive and nosocomial infections. The multidrug-resistant organisms were also associated with high rates, further complicating antimicrobial management, which has continued to be demonstrated in immunocompromised paediatric patients all over the world [17]. Such microbiological properties not only extend hospitalisation, but also lead to the possibility of failure of treatment and secondary complications.

Mortality and complication rates were still great despite the application of intensive care support, broad-spectrum antimicrobials, and immunoglobulin replacement therapy. The observation emphasises the low efficacy of standard sepsis treatment approaches when implemented without regard to the background defect in immunity. Recent sources accentuate that personalised treatment strategies, such as early immunomodulatory therapy and individualised antimicrobials, can also enhance the outcomes of children with inborn errors of immunity with sepsis [18].

The close correlation between the extent of immunological deficiency and the adverse outcomes in this article is a strong support of the importance of the immune status as a prognostic variable. Primary immunodeficiencies can be diagnosed early by means of focused screening, genetic investigation, and immunology, which may make it possible to prevent situations, including prophylaxis of antimicrobials and timely immunoglobulin substitution, and this approach could decrease the occurrence and severity of septic episodes [19]. On the whole, the conclusions of the current research underpin the necessity of the multidisciplinary approach and awareness of primary immunodeficiencies in paediatric sepsis to enhance the survival and long-term outcomes.

5. Conclusion

Sepsis among children who have primary immunodeficiencies is a serious and life-threatening clinical syndrome that is characterised by high morbidity and mortality. The results of the research indicate that the underlying defect in the immune system is a major determinant of the clinical manifestation, laboratory features, microbiological profile, and prognosis of sepsis among paediatric patients. Premature disease, unusual clinical presentation, and impaired inflammation response are often associated with late diagnosis

and improper treatment. The findings highlight the fact that children with primary immunodeficiencies are especially exposed to high-risk infections by opportunistic and multidrug-resistant pathogens. Regular diagnostic markers and general measures of sepsis management might prove to be inadequate in the population without taking into account the underlying immunological condition. The close correlation between the degree of immune defect and adverse prognosis speaks of the paramount role of prompt diagnosis and thorough immunological evaluation of children with severe or repeated infections. The early detection of primary immunodeficiencies, along with personalised treatment, including specific antimicrobial therapy, replacement and immunisation with immunoglobulins, and multidisciplinary care, can enhance the clinical outcomes and minimise complications. Increasing diagnostic awareness in clinicians as well as the incorporation of immunological assessment in the pediatric sepsis guidelines are necessary steps in the optimisation of care. Comprehensively, individualised and immunobiased management of sepsis is essential in enhancing the survival and the post-discharge prognosis of children with primary immunodeficiencies.

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