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ADVERSE EFFECTS OF ANTI-TUBERCULOSIS CHEMOTHERAPY IN CHILDREN AND ADOLESCENTS: CLINICAL CHALLENGES AND MANAGEMENT STRATEGIES

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ABSTRACT

Tuberculosis remains a major global health problem, particularly among children and adolescents, who represent a vulnerable population with unique physiological and immunological characteristics. Anti-tuberculosis chemotherapy is highly effective in controlling the disease; however, it is frequently associated with a wide range of adverse drug reactions that may negatively affect treatment adherence, therapeutic outcomes, and quality of life. Children and adolescents are especially susceptible to undesirable effects due to age-related differences in drug metabolism, organ immaturity, and long-term exposure risks. This article aims to analyze the spectrum, frequency, and clinical significance of adverse events associated with anti-tuberculosis chemotherapy in pediatric and adolescent patients. Special attention is given to hepatotoxicity, gastrointestinal disturbances, allergic reactions, neurotoxicity, and hematological complications. The paper also discusses risk factors contributing to the development of adverse effects, including treatment duration, drug combinations, nutritional status, and comorbid conditions. Furthermore, strategies for early detection, monitoring, prevention, and management of chemotherapy-related complications are reviewed.

Introduction. Tuberculosis (TB) remains one of the most significant infectious diseases worldwide, continuing to pose serious medical and social challenges despite advances in diagnosis and treatment. According to global health reports, children and adolescents constitute a substantial proportion of newly diagnosed tuberculosis cases, particularly in regions with high disease burden. The clinical course of tuberculosis in pediatric populations differs from that in adults, requiring specific diagnostic and therapeutic approaches.

Anti-tuberculosis chemotherapy is the cornerstone of TB treatment and has proven effectiveness in achieving disease control and reducing transmission. Standard treatment regimens involve the prolonged use of multiple anti-tuberculosis drugs, which increases the risk of adverse drug reactions. While chemotherapy significantly improves survival and cure rates, its undesirable effects represent a major challenge in pediatric and adolescent patients. These adverse events may lead to treatment interruption, poor adherence, prolonged therapy, or long-term health consequences.

Children and adolescents are especially vulnerable to chemotherapy-related adverse effects due to age-specific physiological characteristics, including immature liver and kidney function, differences in drug absorption and metabolism, and ongoing growth and development. Moreover, the long duration of therapy, polypharmacy, nutritional deficiencies, and the presence of comorbid conditions further increase the likelihood of undesirable reactions. Common adverse effects include hepatotoxicity, gastrointestinal disorders, allergic manifestations, neurotoxicity, and hematological abnormalities, which may vary in severity from mild and transient to severe and life-threatening. Understanding and timely management of adverse events are essential to improving treatment safety, adherence, and overall outcomes in children and adolescents undergoing tuberculosis therapy.

The occurrence of adverse events not only compromises patient safety but also negatively affects treatment adherence and overall therapeutic outcomes. Early identification, proper monitoring, and timely management of chemotherapy-related complications are therefore essential components of effective tuberculosis care in children and adolescents. A comprehensive understanding of the types, frequency, and risk factors of adverse effects is crucial for optimizing treatment regimens and improving patient quality of life.

This article focuses on the problem of undesirable effects associated with anti-tuberculosis chemotherapy in children and adolescents, highlighting their clinical features, underlying risk factors, and approaches to prevention and management. The analysis aims to contribute to improved safety and effectiveness of tuberculosis treatment in this vulnerable population.

Materials and Methods

This study was conducted as a retrospective observational investigation involving children and adolescents diagnosed with tuberculosis and treated with anti-tuberculosis chemotherapy in specialized healthcare institutions. The study included patients aged between 1 and 18 years who received standard anti-tuberculosis treatment during the observation period. Only cases with complete clinical, laboratory, and treatment-related data were selected for analysis in order to ensure the reliability of the findings.

Anti-tuberculosis chemotherapy was administered in accordance with national and international treatment guidelines. The therapeutic regimens consisted of first-line anti-tuberculosis drugs, including isoniazid, rifampicin, pyrazinamide, and ethambutol, while second-line agents were used in selected cases based on drug resistance, intolerance, or insufficient therapeutic response. The duration of treatment ranged from six to eighteen months depending on disease severity, localization, and clinical progression.

Data on adverse events were collected through a detailed review of medical records, focusing on patient complaints, clinical examinations, and laboratory investigations performed throughout the treatment period. Undesirable effects were identified and categorized according to the affected organ systems, with particular attention to hepatotoxicity, gastrointestinal disturbances, allergic reactions, neurological complications, and hematological changes. The severity of adverse reactions was evaluated using clinical criteria and laboratory thresholds and classified as mild, moderate, or severe.

Demographic characteristics, clinical features, treatment duration, and laboratory parameters, including liver function tests and complete blood counts, were analyzed before the initiation of chemotherapy and during follow-up. Descriptive statistical methods were applied to assess the frequency and distribution of adverse effects among the study population. The results were expressed as absolute values and percentages and subsequently presented in tables and illustrated using graphical representations to facilitate interpretation and comparison.

The study was carried out in compliance with ethical standards and the principles of the Declaration of Helsinki. Patient confidentiality was strictly maintained, and all collected data were anonymized prior to analysis. Ethical approval was obtained from the appropriate institutional review board.

Results

The study analyzed adverse drug reactions in children and adolescents aged 1–18 years who received anti-tuberculosis chemotherapy. Undesirable effects were recorded in a substantial proportion of patients, confirming that chemotherapy-related adverse events remain a significant clinical issue in pediatric and adolescent tuberculosis treatment. The type and frequency of adverse reactions varied depending on age, treatment duration, and the combination of anti-tuberculosis drugs used.

Overall, hepatotoxic reactions were the most frequently observed adverse effects, accounting for more than one-third of all recorded events. These reactions were characterized by elevated liver enzyme levels and clinical manifestations of liver dysfunction and were predominantly associated with isoniazid-, rifampicin-, and pyrazinamide-containing regimens. Gastrointestinal disturbances, including nausea, vomiting, abdominal pain, and loss of appetite, represented the second most common group of adverse reactions and were mainly observed during the early phase of treatment. Allergic reactions, such as skin rashes and pruritus, occurred less frequently but required careful clinical observation due to the risk of therapy interruption. Neurological complications, including peripheral neuropathy and headache, were primarily detected in adolescents and were associated with prolonged isoniazid exposure. Hematological abnormalities, such as anemia and leukopenia, were observed in a smaller number of patients but were clinically relevant. The distribution of adverse drug reactions by organ system is summarized in **Table 1**.

Table 1. Distribution of adverse effects of anti-tuberculosis chemotherapy in children and adolescents

Type of adverse effect	Number of cases (n)	Percentage (%)
Hepatotoxic reactions	38	34.5
Gastrointestinal disturbances	31	28.2
Allergic reactions	18	16.4
Neurological complications	13	11.8
Hematological abnormalities	10	9.1
Total	**110**	**100**

Age-related analysis revealed clear differences in the severity of adverse drug reactions. Mild reactions were more commonly observed in younger children, whereas adolescents demonstrated a higher proportion of moderate and severe adverse effects. Severe reactions were rare in early childhood but increased markedly during adolescence. This age-dependent distribution of adverse reaction severity is illustrated in **Figure 1**, which shows a progressive shift toward clinically significant reactions with increasing age.

Figure 1. Severity of adverse drug reactions by age group

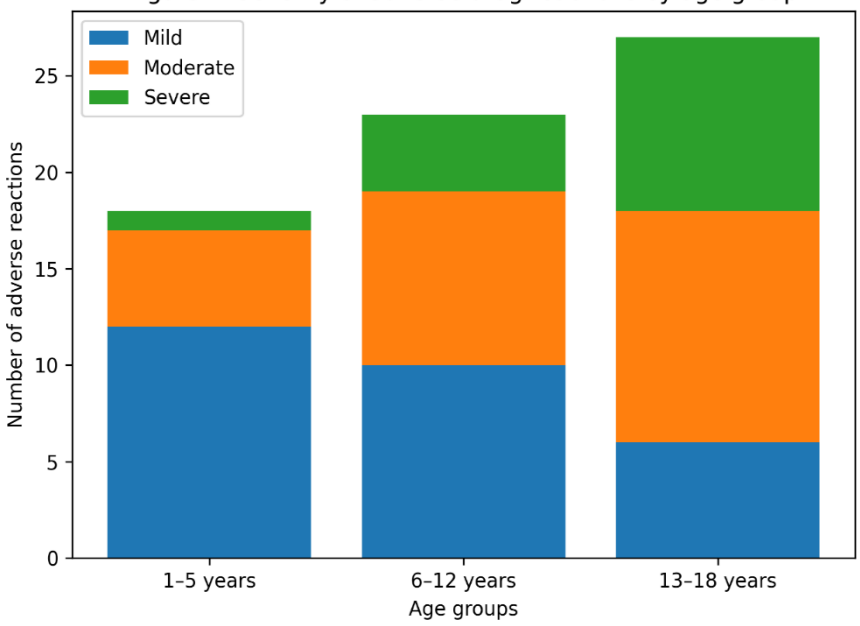

Figure 1. Severity of adverse drug reactions by age group in children and adolescents receiving anti-tuberculosis chemotherapy.

In addition, the relationship between the duration of chemotherapy and the incidence of adverse effects was evaluated. Patients who received treatment for longer periods exhibited a higher cumulative number of adverse drug reactions. This increase was particularly evident for hepatotoxic and neurological complications, suggesting a cumulative toxic effect associated with prolonged exposure to anti-tuberculosis drugs. The trend of increasing adverse effects with longer treatment duration is demonstrated in **Figure 2**.

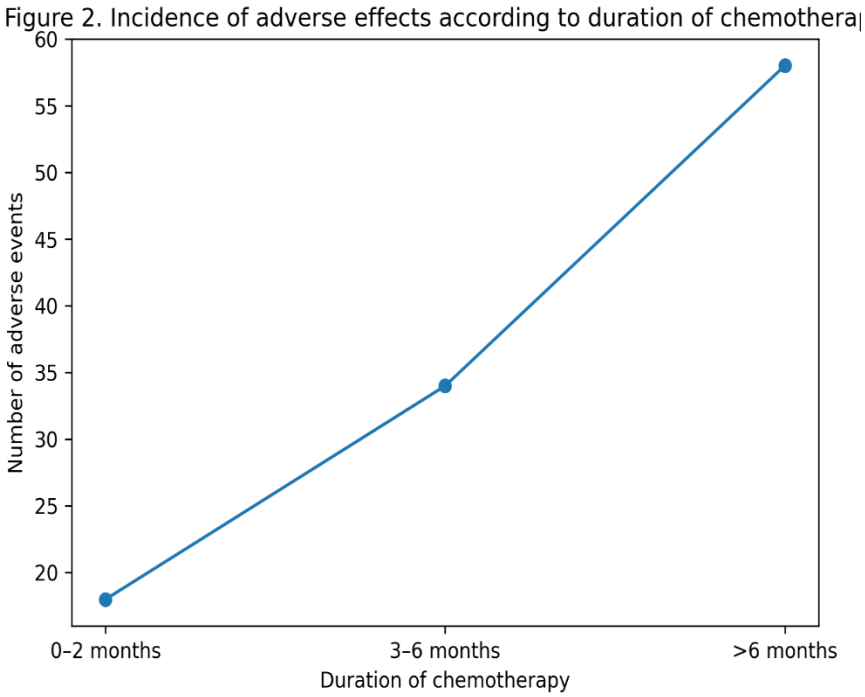

Figure 2. Incidence of adverse effects according to the duration of anti-tuberculosis chemotherapy.

In summary, the results indicate that adverse drug reactions are common among children and adolescents undergoing anti-tuberculosis chemotherapy and vary in both type and severity. While most adverse effects were mild to moderate and manageable with appropriate monitoring, a subset of patients developed severe complications requiring treatment modification or temporary interruption. These findings emphasize the importance of continuous clinical and laboratory surveillance during tuberculosis treatment in pediatric and adolescent populations.

Discussion

The findings of this study demonstrate that adverse drug reactions associated with anti-tuberculosis chemotherapy are common among children and adolescents and represent a significant challenge in clinical practice. The predominance of hepatotoxic and gastrointestinal reactions observed in the present analysis is consistent with previously reported data, which identify first-line anti-tuberculosis drugs as the primary contributors to treatment-related toxicity. The frequent involvement of the liver can be explained by the metabolic burden imposed by isoniazid, rifampicin, and pyrazinamide, particularly during the intensive phase of therapy.

Age-related differences in the severity of adverse drug reactions were clearly evident. As illustrated in Figure 1, adolescents experienced a higher proportion of moderate and severe reactions compared to younger children. This finding may be attributed to cumulative drug exposure, hormonal and metabolic changes during puberty, and differences in drug metabolism between age groups. In contrast, younger children predominantly developed mild and transient adverse effects, which were generally manageable with supportive therapy and did not require treatment modification.

The analysis of treatment duration further supports the concept of cumulative toxicity. Figure 2 demonstrates a progressive increase in the incidence of adverse effects with prolonged chemotherapy, highlighting the importance of long-term monitoring. Extended exposure to anti-tuberculosis drugs increases the risk of hepatotoxicity and neurotoxicity, particularly in patients with additional risk factors such as malnutrition, comorbid conditions, or concomitant medication use. These findings underscore the need for individualized treatment duration and careful benefit–risk assessment, especially in adolescents requiring prolonged therapy.

Neurological complications, although less frequent than hepatotoxic and gastrointestinal reactions, were clinically significant due to their potential impact on quality of life and treatment adherence. Peripheral neuropathy associated with isoniazid therapy emphasizes the importance of preventive measures, including vitamin supplementation and early symptom recognition. Hematological abnormalities, while observed in a smaller proportion of patients, require regular laboratory surveillance to prevent severe complications.

Overall, the results of this study align with existing literature and reinforce the importance of systematic clinical and laboratory monitoring throughout the course of anti-tuberculosis chemotherapy in pediatric and adolescent populations. Early detection and timely management of adverse drug reactions are essential to minimize treatment interruptions, improve adherence, and enhance therapeutic outcomes. Integrating age-specific monitoring strategies and individualized risk assessment into tuberculosis care may significantly improve the safety and effectiveness of chemotherapy in children and adolescents.

Conclusion

Adverse drug reactions associated with anti-tuberculosis chemotherapy remain a significant clinical problem in children and adolescents. The present study demonstrates that hepatotoxic and gastrointestinal reactions are the most frequent adverse effects, while neurological and hematological complications, although less common, have important clinical implications. The severity and incidence of adverse reactions increase with age and treatment duration, indicating a cumulative toxic effect of prolonged chemotherapy, particularly in adolescent patients.

These findings highlight the necessity of continuous clinical and laboratory monitoring throughout the course of tuberculosis treatment in pediatric populations. Early identification and timely management of adverse drug reactions are crucial for maintaining treatment adherence, preventing therapy interruption, and improving overall treatment outcomes. The implementation of age-specific monitoring strategies and individualized risk assessment may significantly enhance the safety and effectiveness of anti-tuberculosis chemotherapy in children and adolescents. Further prospective studies are recommended to optimize treatment regimens and reduce the burden of chemotherapy-related adverse effects in this vulnerable population.

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