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Laboratory Characteristics And Diagnostic Significance Of Antibiotic-Associated Diarrhea In Young Children

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Annotation

Objective. To determine the specific laboratory characteristics of AAD in early childhood and assess the diagnostic value of fecal calprotectin, C-reactive protein (CRP), and coprological parameters in differentiating disease forms.

Materials and Methods. A prospective single-center study was conducted between 2023 and 2025 at the Department of Propaedeutics of Childhood Diseases, Samarkand State Medical University, and the Samarkand Multidisciplinary Medical Children's Center. The cohort included 140 hospitalized children aged 1 month to 3 years with clinically confirmed AAD following antibiotic therapy. Laboratory investigations comprised measurement of fecal calprotectin, serum CRP (immunoturbidimetric method), leukocyte count, and detailed coprological analysis. Patients were divided into three subgroups:

1). Clostridioides difficile–associated AAD (CDI+);
2). Bacterial but C. difficile–negative AAD;
3). Noninfectious AAD.

Conclusion. Comprehensive laboratory evaluation—especially quantitative assessment of fecal calprotectin and CRP—serves as an effective, noninvasive diagnostic tool for differentiating infectious and noninfectious forms of AAD in early childhood. Integration of these parameters into routine diagnostic algorithms improves diagnostic accuracy, supports rational antibiotic use, and facilitates personalized therapeutic decision-making in pediatric practice.

Introduction

Antibiotic-associated diarrhea (AAD) represents one of the most frequent and clinically significant complications of antibacterial therapy in pediatric practice. The contribution of *Clostridioides difficile* (C. difficile) to the development of AAD has been extensively investigated in adults [2, 3]; however, data regarding its role in children remain limited. The interpretation of pediatric cases is further complicated by the high prevalence of asymptomatic carriage in neonates and infants [4, 5]. According to the World Health Organization (WHO), a steady global increase in antibiotic resistance has been observed, largely driven by the extensive and often unjustified use of antibiotics in children. In low- and middle-income countries, up to 70 % of antibiotic prescriptions occur at the primary (outpatient) care level, where systematic monitoring of adverse effects—including diarrhea—is challenging [6-7]. AAD not only worsens the course of the underlying disease but also imposes a considerable burden on healthcare systems through prolonged hospitalization, repeated readmissions, the need for infusion therapy, and additional pharmacological support. At the same time, limited access to modern laboratory diagnostics and the absence of validated clinical–laboratory severity scales contribute to the underdiagnosis and underestimation of AAD in early childhood. Therefore, comprehensive and evidence-based evaluation of this condition is urgently needed. In recent years, the relationship between antibiotic therapy and alterations of the intestinal microbiota has been actively studied, highlighting its crucial etiological role in pediatric AAD. Special attention has been directed toward the pathogenic mechanisms of *C. difficile* in severe cases and toward early diagnostic tools such as fecal calprotectin measurement and toxin detection [4]. Additionally, optimization of antibiotic selection and the potential inclusion of immunomodulatory agents—particularly lactoferrin—into complex therapeutic regimens are being discussed as promising strategies.

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Contemporary international literature underscores the importance of inflammation-based stratification and marker-guided diagnostic approaches. Nevertheless, despite active research efforts, several aspects of the pathogenesis, diagnosis, and management of AAD in early childhood remain insufficiently elucidated and require further systematic investigation.

Materials and Methods

The study was conducted between 2023 and 2025 at the Samarkand State Medical University and the Samarkand Regional Multidisciplinary Children's Medical Center. A total of 140 children aged 1 month to 3 years were included in the study.

Inclusion criteria:

- ✓ Systemic antibacterial therapy received within the preceding 2–8 weeks;
- ✓ Passage of loose or watery stools ≥3 times per day;
- ✓ Laboratory-confirmed diagnosis.

Diagnostic criteria and study groups:

1. **Microflora-associated AAD group:**
   - ✓ *Clostridioides difficile*–positive cases ($n = 62$);
   - ✓ Other bacterial pathogens (*Enterobacter spp.*, *Klebsiella spp.*, *Proteus spp.*, etc.) ($n = 23$).
2. **Functional–metabolic AAD group:** pathogenic microflora not detected ($n = 35$).
3. **Control group:** children who had received antibacterial therapy but did not develop diarrhea ($n = 20$).

Parameters studied:

Clinical and anamnestic data (age, sex, type of feeding, antibiotic type, duration of use, number of courses); complete blood count (leukocytosis, hemoglobin); C-reactive protein; coprological stool analysis; detection of *Clostridioides difficile* toxins by PCR; and fecal calprotectin determined by ELISA.

Statistical analysis:

Statistical processing was performed using the χ^2 test, odds ratio (OR), 95% confidence interval (CI), with $p < 0.05$ considered statistically significant.

Results

The majority of *Clostridioides difficile*–associated cases were observed among children aged 6–12 months (37.1%) and 1–3 years (40.3%) ($p < 0.05$).

In contrast, functional–metabolic forms of antibiotic-associated diarrhea were more frequently detected in infants younger than 3 months.

Table 1. Distribution of AAD cases by age groups and clinical subgroups

Age group	Clostridioides difficile, n=62%	Other flora, n=23%	Microflora-associated AAD group, n=85 %	Functional–metabolic AAD group, n=35%
1–3 months	5.0	9.0	10.0	37.0
3–6 months	9.0	31.0	18.0	23.0
6–12 months	23.0	40.0	39.0	26.0
1–3 years	14.0	26.0	28.0	14.0

Note: *The distribution of antibiotic-associated diarrhea (AAD) by age and etiology showed that Clostridioides difficile–associated and other infectious forms predominated in children aged 6–12 months and 1–3 years, whereas non-infectious (functional–metabolic) cases were more frequent among infants younger than 3 months.*

Clinical Symptoms. The most common clinical manifestations were abdominal distension (82.3%), decreased appetite (67.7%), and abdominal pain (53.2%). These symptoms were significantly more frequent in the microflora-associated group compared with the functional–metabolic group ($p < 0.05$).

Degree of Dehydration. Mild dehydration was more frequently observed in the functional–metabolic group (38.9%), whereas severe dehydration predominated in the microflora-associated group (22.6%).

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November 2025

Table 1. Frequency of clinical symptoms in children of early age with antibiotic-associated diarrhea (AAD) of different genesis

Symptom	Clostridioides difficile (Cl+) (n = 62)	Other bacterial flora (n = 23)	Functional–metabolic (n = 35)	χ^2	p-value
Abdominal pain	33 (53.2%)	7 (30.4%)	10 (28.6%)	7.071	0.029
Meteorism (abdominal distension)	51 (82.3%)	11 (30.4%)	13 (37.1%)	22.042	0.001***
Decreased appetite	42 (67.7%)	9 (39.1%)	8 (22.9%)	19.18	0.001**
Irritability	32 (51.6%)	6 (26.1%)	7 (20.0%)	11.12	0.004*
Dry skin	30 (48.4%)	8 (34.8%)	15 (42.8%)	1.294	0.524
Reduced tissue turgor	28 (45.2%)	10 (43.5%)	9 (25.7%)	2.02	0.365
Decreased diuresis	25 (40.3%)	8 (34.8%)	11 (31.4%)	0.992	0.609

Note: *Abdominal distension, loss of appetite, and irritability were significantly more common in the Clostridioides difficile–associated group compared with functional–metabolic AAD ($p < 0.05$).*

Coprological Findings. In the functional–metabolic group, signs of enzymatic insufficiency were recorded significantly more often, including the presence of fiber (57.1%; $p = 0.001$; OR = 4.06), starch (45.7%; $p = 0.001$; OR = 17.05), and undigested food residues (42.9%; $p = 0.001$). In contrast, leukocytes were detected in 100% of cases in the microflora-associated forms ($p < 0.001$).

Table 2. Comparative coprological findings in children with antibiotic-associated diarrhea (AAD) of different genesis

Indicator	Microflora-associated group (%)	Functional–metabolic group (%)	p-value	OR (95% CI)
Fiber	24.7	57.1	0.001	4.06 (1.77–9.33)
Starch	4.7	45.7	0.001	17.05 (5.12–56.85)
Undigested food residues	11.8	42.9	0.001	—
Leukocytes in stool	100	—	<0.001	—

Note: *Significant differences were observed between the microflora-associated and functional–metabolic groups ($p < 0.05$).*

Fecal Calprotectin. The mean fecal calprotectin levels were as follows: in the *Clostridioides difficile*–positive group — 393.6 ± 39.2 µg/g, in the group with other bacterial pathogens — 195.4 ± 24.5 µg/g, in the functional–metabolic group — 85.2 ± 11.7 µg/g, and in the control group — 31.6 ± 3.8 µg/g ($p \leq 0.001$).These results demonstrated a consistent gradient of inflammatory activity in the following order: Cl^+ > Other bacteria > Functional–metabolic

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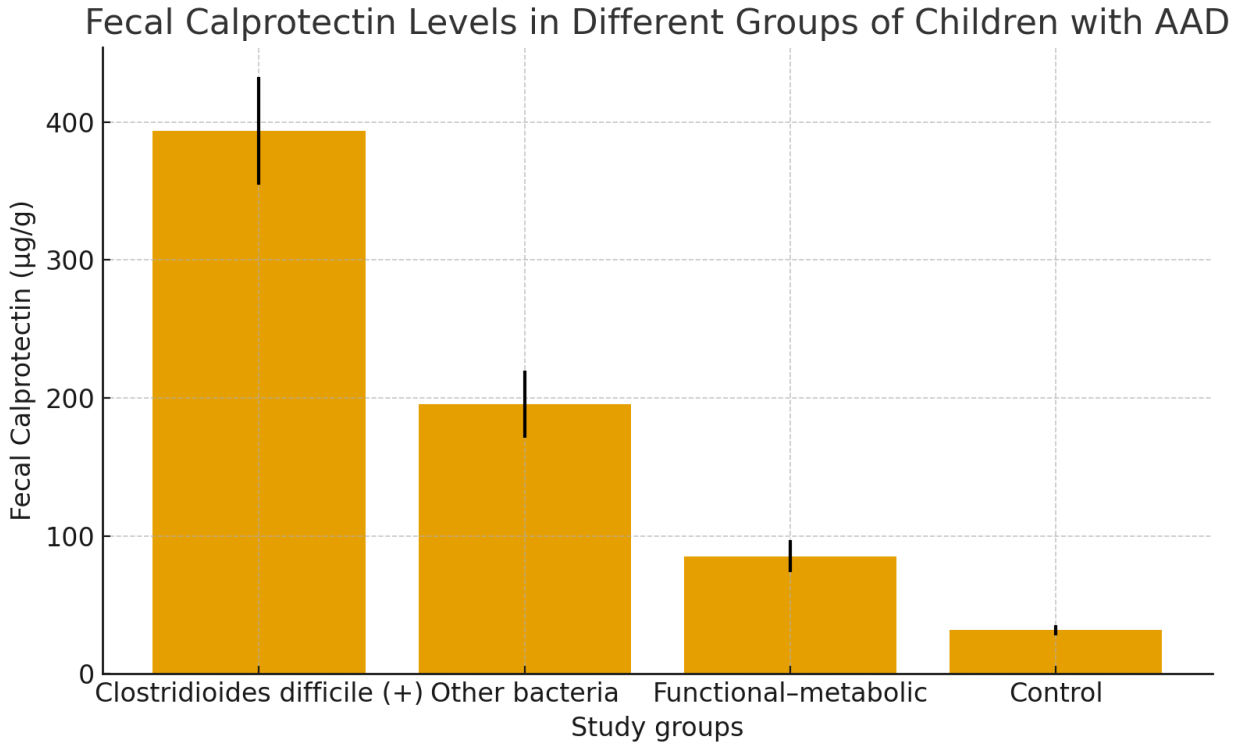

Discussion

The results emphasize the importance of making clinical decisions with consideration of the etiological differentiation of antibiotic-associated diarrhea (AAD). In the microflora-associated group, a pronounced neutrophilic inflammatory process was observed, as evidenced by elevated fecal calprotectin levels. In contrast, in functional–metabolic forms, signs of inflammation were not predominant. The severity of AAD does not directly depend on the severity of the underlying disease; therefore, the use of specific clinical severity scales and laboratory inflammatory markers is advisable for accurate assessment and management.

Conclusion.

1.Antibiotic-associated diarrhea (AAD) is one of the major complications of antibiotic therapy in early childhood, and its microflora-associated and functional–metabolic types differ in both clinical and laboratory characteristics.

2.Fecal calprotectin is a sensitive marker reflecting the degree of intestinal inflammation and plays a key role in differential diagnosis.

3.The use of a modified clinical–laboratory severity scale improves diagnostic accuracy and reduces the risk of complications.

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ISSN NO: 2770-2936
November 2025

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