Letter to the Editor / *Editöre Mektup*

DOI: 10.5578/ced.20250410 • *J Pediatr Inf 2025;19(4):e281-e282*

Sepsis Following Acute Gastroenteritis: A Commentary on Antibiotic Use, Microbiota, and Epithelial Barrier Integrity

Akut Gastroenterit Sonrası Sepsis: Antibiyotik Kullanımı, Mikrobiyota ve Bariyer Bütünlüğü Üzerine Bir Değerlendirme

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Cite this article as: Ağır MA. Sepsis following acute gastroenteritis: A commentary on antibiotic use, microbiota, and epithelial barrier integrity. J Pediatr Inf 2025;19(4):e281-e282.

Dear Editor,

We read with interest the article by Eroğlu et al. titled "Evaluation of cases developing sepsis after acute gastroenteritis" published in your journal (1).

The study reported that sepsis developed in 25.6% of children hospitalized with acute gastroenteritis (AGE) and that C-reactive protein (CRP) and procalcitonin levels were superior to other parameters in predicting sepsis. These findings are important in drawing attention to the risk of sepsis after AGE. While congratulating the authors who conducted the study, we would like to share a few points in the context of the results, supported by the literature.

First, the discrepancy between antibiotic use rates and the frequency of detection of invasive bacterial agents caught our attention. In the series by Eroğlu et al., approximately one-third of the patients (33.1%) were started on antibiotics; however, only 32 of the 237 patients suspected of having sepsis had bacterial growth detected in blood cultures, and the rate of bacterial agents in stool cultures remained at 1.1%. This finding once again suggests that viral etiology predominates in acute diarrhea and raises the risk of unnecessary antibiotic initiation. Indeed, in a large pediatric cohort, viral etiology accounted for nearly half of gastrointestinal infections, while pure bacterial pathogens were extremely rare (0.14%) (2). Furthermore, the fact that blood culture positivity was observed in only 0.04% of those tested and that most were associated with contaminants from the skin flora indicates that the true rate of bacteremia is very low (2). These data show that invasive bacterial pathogens cannot be confirmed in many children who receive empirical antibiotics based on clinical suspicion.

Second, the scope and predictors of unnecessary antibiotic prescribing in children hospitalized with a diagnosis of viral AGE have been detailed in a recent study: Unnecessary antibiotic use was identified in 18.1% of 1.395 children with viral AGE during the period 2007-2015; being vaccinated against rotavirus was found to be inversely associated with unnecessary antibiotics. CRP and leukocyte levels, as well as requests for blood/urine cultures or chest X-rays, were positively associated with the likelihood of unnecessary antibiotics (3). The same study emphasizes that, from a practical standpoint, rapid molecular diagnostic panels can support clinical decisions and reduce unnecessary antibiotic use (3).

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Received: 07.10.2025 **Accepted:** 27.10.2025
Available Online Date: 25.12.2025

Thirdly, we would like to focus on the possible mechanisms of sepsis development after AGE. As stated by Eroğlu et al., damage to the intestinal mucosa and bacterial translocation may contribute to the pathogenesis of sepsis; particularly in small infants, incomplete barrier maturation may increase the tendency for translocation. This approach is consistent with the literature highlighting the relationship between intestinal barrier immaturity and dysbiosis in the neonatal period and susceptibility to infection and translocation (4).

Fourth, we would like to draw attention to the potential effects of antibiotics on the gut microbiota and epithelial barrier. Antibiotic exposure in early life may reduce microbiota diversity and disrupt maturation; specific changes such as a decrease in *Lactobacillus* load in the maternal and neonatal microbiome have been reported (5). Experimental data suggest that antibiotic exposure may increase intestinal permeability and weaken barrier integrity, which may facilitate inflammation. In this context, we believe that repeated or broad-spectrum antibiotic exposure, especially at a young age, should be approached with caution in terms of long-term barrier health.

In conclusion, the study by Eroğlu et al. raises the critical issue of sepsis following AGE. On this occasion, we recommend (i) prioritizing appropriate rehydration and close clinical monitoring, which are fundamental approaches in AGE management, (ii) carefully confirming the indication for antibiotics with clinical and laboratory (rapid molecular tests, if possible) evidence, (iii) consider the role of maintaining rotavirus vaccination programs in reducing unnecessary antibiotic prescriptions, and (iv) adopt rational antibiotic use that preserves children's microbiota/barrier integrity.

Sincerely

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