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PICO ANALYSIS OF ANTIBIOTIC EFFICACY IN MULTIDRUG-RESISTANT SHIGELLOSIS (2015–2025): A COMPREHENSIVE DECADE STUDY

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ANNOTATSIYA / АННОТАЦИЯ / ABSTRACT

O'zbek tilida: Ushbu tadqiqotda 2015–2025 yillar oralig'idagi o'n yillik davrda shigellyoz qo'zg'atuvchilarining antibiotiklarga chidamlilik dinamikasi PICO modeli orqali tahlil qilindi. Tadqiqot davomida 284 ta namunaning PCR tahlili va 172 ta kultura natijalari o'rganildi. Natijalar shuni ko'rsatdiki, Azitromitsinga rezistentlik 71.4% ga yetgan. Maqolada multirezistent (MDR) va keng rezistent (XDR) shtammlarning tarqalish epidemiologiyasi va diagnostik qiyinchiliklar yoritilgan.

На русском языке: В данном исследовании с помощью модели PICO проанализирована динамика антибиотикорезистентности возбудителей шигеллеза за период 2015–2025 гг. Изучены результаты ПЦР 284 образцов и 172 культур. Результаты показали, что резистентность к азитромицину достигла 71,4%. В статье освещены эпидемиология мультирезистентных (MDR) и широкорезистентных (XDR) штаммов, а также диагностические трудности.

In English: This study utilizes the PICO framework to analyze the decade-long (2015–2025) dynamics of antibiotic resistance in *Shigella* species. Analyzing 284 PCR samples and 172 cultures, the research identified a critical 71.4% resistance rate to Azithromycin. The article discusses the epidemiology of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains, along with diagnostic challenges and genomic surveillance.

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Key words: *Shigella spp.*, PICO, AMR, Azithromycin, WHO BPPL 2024, XDR, ESBL, *ipaH* gene.

1. INTRODUCTION (KIRISH)

The global escalation of antimicrobial resistance (AMR) represents a primary threat to clinical medicine. Shigellosis, an acute diarrheal disease, contributes significantly to global morbidity, especially in resource-limited settings. According to the **WHO Bacterial Priority Pathogens List (BPPL) 2024**, fluoroquinolone-resistant *Shigella spp.* is ranked as a "High Priority" pathogen with a threat score of 70%.

The pathogen's exceptionally low infectious dose (less than 10 bacteria) facilitates rapid person-to-person spread, making outbreaks difficult to contain. This study focuses on the 2015–2025 decade, evaluating how traditional "gold standard" treatments are performing against evolving bacterial clades carrying mobile genetic elements.

2. LITERATURE REVIEW AND GLOBAL CONTEXT

Since the first WHO BPPL release in 2017, the resistance landscape has shifted. While 13 new antibiotics were approved, many pathogens now show resistance to even these newer agents. The 2024 update highlights that community-acquired infections, like those caused by *Shigella*, pose a disproportionate burden in low- and middle-income countries.

Recent surveillance indicates shigellosis is increasingly recognized not just as a foodborne illness but as a sexually transmitted infection (STI), particularly among men who have sex with men (MSM) in major urban centers. This epidemiological shift requires a re-evaluation of treatment protocols and public health strategies.

3. METHODOLOGY (METODOLOGIYA)

This retrospective study analyzed 284 fecal samples detected via *ipaH* PCR between 2015 and 2025.

PICO Model Structure:

- **P (Population):** Patients with laboratory-confirmed *Shigella spp.* presenting with dysenteric symptoms (bloody diarrhea, tenesmus).
- **I (Intervention):** Treatment with Azithromycin or Ceftriaxone.
- **C (Comparison):** Traditional use of Ciprofloxacin or Ampicillin.
- **O (Outcome):** Clinical recovery, duration of bacterial shedding, and prevention of complications like Hemolytic Uremic Syndrome (HUS).

Antibiotic susceptibility testing (AST) followed EUCAST methodologies using automated broth microdilution and gradient strip diffusion.

4. RESULTS AND STATISTICAL ANALYSIS

4.1. Pathogen Distribution Out of 284 PCR-positive samples, the culture recovery rate was 65.8%.

- **S. sonnei:** 61.9% (Prevalent in urban outbreaks).
- **S. flexneri:** 33.5%.
- **S. boydii:** 2.8%.

4.2. Resistance Profiles (The "71.4% Crisis") The study found alarming resistance rates among confirmed isolates:

- **Azithromycin (AZM): 71.4% resistance.** This is critical as AZM is the WHO-recommended first-line therapy for children.
- **Ampicillin (AMP):** 73.3% resistance.
- **Ciprofloxacin (CIP):** 31.8% resistance.
- **Ceftriaxone (3-GC): 18.8% resistance.** This remains the most effective option, though its usage is limited by parenteral requirements.

4.3. MDR, ESBL, and XDR Trends Multidrug-resistant (MDR) rates increased steadily, with ESBL-producing isolates accounting for 18.8% of the total. Most notably, the study identified **4 extensively drug-resistant (XDR)** isolates in 2023, which were resistant to all standard oral options.

5. DIAGNOSTIC CHALLENGES: THE "SILENT" PATHOGEN

A significant finding in this decade-long analysis is the unreliability of traditional diagnostic markers. Approximately **33% of confirmed culture-positive specimens had zero white cells** on stool microscopy. This suggests that clinicians cannot rely on fecal cell counts to rule out shigellosis, potentially leading to delayed treatment and further community spread.

6. DISCUSSION: GENETIC BASIS OF RESISTANCE

The failure of Azithromycin is primarily attributed to the dissemination of *macA-B* and *mphA* genes. Furthermore, the rise in ESBL rates (from 18.8%) is often linked to the *blaCTX-M* plasmid, which has caused prolonged outbreaks in major cities. The PICO analysis confirms that while Ciprofloxacin was the historical standard, its current 31.8% resistance rate makes it an unreliable choice for empirical monotherapy in many regions.

Here is the expanded and professional **Conclusion** section for your scientific article, written entirely in English and based on the provided sources:

7. CONCLUSION

The ten-year epidemiological analysis spanning from 2015 to 2025 demonstrates that *Shigella spp.* has effectively transitioned into a "super-pathogen" within the global antimicrobial resistance (AMR) crisis. The findings of this study lead to the following critical conclusions for public health and clinical practice:

Crisis of the "Gold Standard": The identification of a **71.4% resistance rate to Azithromycin**—the current WHO-recommended first-line therapy for pediatric shigellosis—represents a clinical emergency. This high level of resistance, driven by the dissemination of *macA-B* and *mphA* genes, indicates that empirical treatment protocols using macrolides are failing in the majority of cases and require immediate national and international revision.

Escalation of MDR and XDR Threats: The study highlights a steady increase in multidrug-resistant (MDR) and extensively drug-resistant (XDR) isolates. The emergence of **four XDR strains in 2023** alone signifies a dangerous shift toward untreatable shigellosis, where no oral antibiotic options remain viable. This trajectory justifies the **WHO BPPL 2024** classification of fluoroquinolone-resistant *Shigella* as a **"High Priority"** pathogen with a threat score of 70%.

Necessity for Diagnostic Shifts: A critical epidemiological finding is that **33% of confirmed culture-positive specimens exhibited zero white cells** on stool microscopy. This demonstrates that traditional fecal cell counts are unreliable diagnostic markers. To prevent delayed treatment and further community transmission, clinical protocols must shift toward molecular diagnostics, specifically **ipaH-targeted PCR**, as the primary screening tool.

Strategic Recommendations:

- **Ceftriaxone** currently remains the most effective tested option with an **18.8% resistance rate**; however, its parenteral requirement limits its use in community settings.
- There is an urgent need for the development of new oral therapeutic agents and enhanced genomic surveillance to track the spread of *blaCTX-M* plasmids associated with ESBL-producing outbreaks.

- Beyond pharmaceutical intervention, a sustainable reduction in the AMR burden for community-acquired infections like shigellosis must integrate **WASH (Water, Sanitation, and Hygiene)** infrastructure improvements and the accelerated development of effective vaccines.

In summary, the evolution of *Shigella* resistance over the last decade necessitates a more aggressive, data-driven approach to both treatment and epidemiological surveillance to mitigate the risk of large-scale, untreatable outbreaks.

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