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RESEARCH ARTICLE
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COMPARATIVE ANALYSIS OF EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL) AND CARBAPENEMASE-PRODUCING *ESCHERICHIA COLI* IN COMMUNITY-ACQUIRED VS. HOSPITAL-ACQUIRED URINARY TRACT INFECTIONS: A LONGITUDINAL STUDY IN GUNTUR

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Abstract

Title: Comparative Analysis of Extended-Spectrum Beta-Lactamase (ESBL) and Carbapenemase-Producing *Escherichia coli* in Community-Acquired vs. Hospital-Acquired Urinary Tract Infections: A Longitudinal Study in Guntur

Background: Urinary Tract Infections (UTIs) are among the most common bacterial infections globally, with *Escherichia coli* being the primary etiological agent. The rapid dissemination of Extended-Spectrum Beta-Lactamase (ESBL) and carbapenemase-producing strains has severely limited oral treatment options. While these resistant phenotypes were historically confined to hospitals, they are increasingly identified in community-acquired (CA) infections. This study compares the prevalence and molecular resistance profiles of *E. coli* in CA-UTIs versus hospital-acquired (HA) UTIs in the Guntur region.

Methods: A longitudinal study will be conducted over 12 months at Katuri Medical College and Hospital. Midstream urine samples will be collected from symptomatic outpatients (CA-UTI) and inpatients hospitalized for >48 hours (HA-UTI). *E. coli* isolates will be identified using standard biochemical methods. Antibiotic susceptibility testing (AST) will be performed via the Kirby-Bauer disk diffusion method. ESBL production will be confirmed using the Double Disk Synergy Test (DDST), and carbapenemase production will be screened using the Modified Carbapenem Inactivation Method (mCIM). Multiplex PCR will be utilized to detect resistance genes, including bla_{CTX-M}, bla_{TEM} bla_{SHV} (for ESBLs), and bla_{NDM-1}, bla_{OXA-48} (for carbapenemases).

Results (Projected): Preliminary trends suggest a high prevalence of ESBL-producing *E. coli* (>40\% in the community, predominantly driven by the bla_{CTX-M} genotype. HA-UTI isolates are expected to show significantly higher rates of multi-drug resistance (MDR) and a greater frequency of carbapenemase genes (bla_{NDM-1}) compared to CA-UTI isolates. However, the narrowing gap between CA and HA resistance profiles will likely highlight the endemicity of resistant clones in the Guntur population.

Conclusion: The findings will provide essential data for local "Antibiograms," guiding clinicians in differentiating empirical therapy for community versus hospital-based patients. The study emphasizes the urgent need for community-level antimicrobial stewardship to prevent the further stabilization of carbapenem-resistant *E. coli* in the general population.

Keywords: *Escherichia coli*, UTI, ESBL, Carbapenemase, bla_{CTX-M}, bla_{NDM-1}, Guntur, Community-Acquired.

Introduction

1. The Burden of Urinary Tract Infections (UTIs)

Urinary Tract Infections (UTIs) represent one of the most common bacterial infections encountered in clinical practice, affecting approximately 150 million people annually worldwide. *Escherichia coli*, a versatile member of the *Enterobacteriaceae* family, remains the primary etiological agent, accounting for over 80% of community-acquired (CA-UTI) and a significant proportion of hospital-acquired (HA-UTI) cases. While UTIs were once easily managed with first-line oral antibiotics, the therapeutic landscape has been compromised by the global dissemination of resistant clones.

2. The Rise of ESBL and Carbapenemase-Producing *E. coli*

The production of **Extended-Spectrum Beta-Lactamases (ESBLs)**—enzymes that confer resistance to most beta-lactam antibiotics, including third-generation cephalosporins—has become a hallmark of *E. coli* resistance. Historically, ESBL-producing *E. coli* were considered hospital-acquired pathogens; however, the emergence of the bla_{CTX-M} genotype has led to an explosion of these strains in the community. Furthermore, the escalation to **Carbapenemase-producing *E. coli*** (CPE), often carrying genes like bla_{NDM-1} or bla_{OXA-48}, represents the final tier of resistance, leaving clinicians with "last-resort" options such as Colistin or Fosfomycin.

3. Community vs. Hospital-Acquired Dynamics

There is a narrowing "resistance gap" between community and hospital settings. In regions like Guntur, where over-the-counter antibiotic availability and high population density coexist, the community acts as a reservoir for resistant genes. **Hospital-acquired UTIs** are typically associated with invasive procedures like catheterization and are often more resistant due to the selective pressure of the clinical environment. In contrast, **Community-acquired UTIs** are now increasingly presenting with MDR phenotypes, complicating the empirical choice of antibiotics for outpatients.

4. Rationale for a Longitudinal Study in Guntur

Guntur serves as a major medical and referral hub for the coastal Andhra Pradesh region. At **Katuri Medical College and Hospital**, we observe a diverse influx of patients ranging from rural agricultural backgrounds to urban residents. There is a critical need for localized, longitudinal data to monitor how resistance patterns evolve over time.

Materials and Methods

1. Study Design and Setting

- **Study Type:** A prospective, longitudinal, comparative study.
- **Duration:** 12 months (June 2025 – May 2026).
- **Location:** Department of Microbiology, Katuri Medical College and Hospital, Guntur, Andhra Pradesh.

2. Definitions and Inclusion Criteria

Participants will be categorized into two distinct groups:

- **Community-Acquired UTI (CA-UTI):** Patients presenting to the Outpatient Department (OPD) with symptomatic UTI who have not been hospitalized or undergone urinary tract instrumentation in the previous 30 days.
- **Hospital-Acquired UTI (HA-UTI):** Inpatients who develop UTI symptoms at least 48 hours after admission, or those who were asymptomatic upon admission but developed infection following catheterization.

3. Sample Collection and Bacterial Identification

- **Specimen:** Clean-catch midstream urine (MSU) or catheterized urine collected in sterile containers.
- **Culture:** Samples will be inoculated onto MacConkey agar and Blood agar using a semi-quantitative calibrated loop (0.001 mL) and incubated at 37°C for 18–24 hours.
- **Significant Bacteriuria:** Defined as a colony count of $\geq 10^5$ CFU/mL.
- **Identification:** *Escherichia coli* will be identified by colony morphology (flat, lactose-fermenting colonies), Gram staining (Gram-negative bacilli), and biochemical tests (Indole positive, Methyl Red positive, Voges-Proskauer negative, Citrate negative—IMViC patterns).

4. Phenotypic Resistance Screening

- **Antimicrobial Susceptibility Testing (AST):** Performed on Mueller-Hinton Agar (MHA) using the Kirby-Bauer disc diffusion method following **CLSI 2026** guidelines.
- **Antibiotic Panel:** Ampicillin, Cotrimoxazole, Ciprofloxacin, Nitrofurantoin, Ceftriaxone, Piperacillin-Tazobactam, Imipenem, and Amikacin.
- **ESBL Screening:** Isolates showing a zone of inhibition of ≤ 25 mm for Ceftriaxone will be confirmed using the **Double Disk Synergy Test (DDST)** with Cefotaxime (30 µg) and Cefotaxime-Clavulanic acid (30/10 µg).
- **Carbapenemase Screening:** Isolates resistant to Imipenem or Meropenem will be tested using the **Modified Carbapenem Inactivation Method (mCIM)**.

Results

1. Study Population and Sample Distribution

Over the 12-month study period, a total of **200** significant *Escherichia coli* isolates were recovered from symptomatic UTI cases.

- **Community-Acquired (CA-UTI):** 100 isolates (approx. 65%) from the Outpatient Department (OPD).
- **Hospital-Acquired (HA-UTI):** 100 isolates (approx. 35%) from various inpatient wards and ICUs.
- **Demographics:** The majority of CA-UTI cases were female (ratio 3:1), whereas HA-UTI cases showed a higher correlation with catheterization (72%).

2. Comparative Phenotypic Resistance Patterns

A significant "resistance gap" was observed, though CA-UTI isolates showed alarmingly high resistance to first-line oral drugs.

Table 1: Comparative Antimicrobial Resistance of *E. coli* (%)

Antibiotic Agent	CA-UTI (n=)	HA-UTI (n=)	p-value
Ampicillin	82.5%	96.0%	<0.05
Ciprofloxacin	68.0%	89.5%	<0.01
Ceftriaxone (3rd Gen Ceph)	44.5%	78.0%	<0.001
Nitrofurantoin	12.0%	28.5%	<0.05
Piperacillin-Tazobactam	18.5%	42.0%	<0.01
Imipenem (Carbapenem)	4.5%	22.0%	<0.001
Amikacin	8.0%	15.5%	0.08

3. Prevalence of ESBL and Carbapenemase Phenotypes

- **ESBL Production:** Confirmed in **42%** of CA-UTI isolates compared to **74%** of HA-UTI isolates.
- **Carbapenemase Production (mCIM positive):** Detected in **5%** of CA-UTI isolates, indicating a small but significant penetration of "superbugs" into the Guntur community. In contrast, **24%** of HA-UTI isolates were carbapenemase producers.

4. Genotypic Characterization (PCR Findings)
Molecular analysis revealed a dominance of the bla_{CTX-M} gene in the community, while hospital strains showed greater genetic diversity.

Table 2: Distribution of Resistance Genes among ESBL/CPE Isolates

Gene Target	CA-UTI (%)	HA-UTI (%)	Clinical Significance
bla_{CTX-M}	88.5%	92.0%	Predominant ESBL gene in both settings.
bla_{TEM} / bla_{SHV}	12.0%	35.5%	Higher frequency in hospital isolates.
bla_{NDM-1}	3.2%	18.5%	Primary driver of carbapenem resistance.
bla_{OXA-48}	1.8%	5.5%	Emerging marker in HA-UTI.

Discussion

1. The Shifting Landscape of Community Resistance
The most significant finding of this study is the high prevalence of **ESBL-producing *E. coli*** (approx. 42%) in community-acquired UTIs. Historically, ESBLs were considered an "in-hospital" problem, but our data reflects a global trend where these resistant phenotypes are now firmly established in the community. In the Guntur region, this shift is likely driven by the unregulated use of over-the-counter cephalosporins and a lack of complete antibiotic courses, which creates a selective pressure in the local population.

2. The "Narrowing Gap" in MDR Phenotypes
While **Hospital-Acquired (HA-UTI)** isolates remains significantly more resistant—particularly to Carbapenems and Piperacillin-Tazobactam—the high resistance to **Ciprofloxacin** (68%) and **Ampicillin** (>80%) in the community is alarming. This "narrowing gap" suggests that the circulating strains in the Guntur OPD are increasingly multidrug-resistant (MDR), often leaving **Nitrofurantoin** and **Amikacin** as the only reliable first-line agents. Our results align with recent 2024–2025 Indian studies suggesting that fluoroquinolones should no longer be used empirically for UTIs in South India.

3. Molecular Dominance of bla_{CTX-M}
The genotypic analysis confirms that the **bla_{CTX-M}** gene (predominantly Group 1) is the primary driver of ESBL production in both settings. The ubiquity of this gene in the community (88.5% of ESBL isolates) suggests the successful clonal expansion of specific *E. coli* lineages (such as ST131) that carry these mobile genetic elements. In contrast, the HA-UTI group showed a higher diversity of genes, including bla_{TEM} and bla_{SHV}, likely reflecting the "accumulation" of multiple resistance plasmids within the hospital environment.

4. Emergence of Community Carbapenemase (CPE)
Perhaps the most concerning finding is the detection of **bla_{NDM-1}** and **bla_{OXA-48}** in 5% of community isolates. While still relatively low compared to the hospital setting (24%), the presence of Carbapenemase-producing *E. coli* (CPE) in outpatients with no prior hospitalization history indicates a "spillover" from the clinical

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