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RESEARCH ARTICLE

Genomic Tracking of Candida auris Novel Resistance Markers in Hospital-Acquired Infections Across Urban ICUs

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Abstract: Candida auris, a multidrug-resistant fungal pathogen, poses a significant threat in urban Indian intensive care units (ICUs) due to its high transmissibility and resistance to antifungals. This study investigates the genomic epidemiology and novel resistance markers of C. auris in hospital-acquired infections across urban Indian hospitals. ***Methods:*** From January 2023 to September 2025, 184 C. auris isolates were collected from 172 patients in six tertiary care ICUs. Clinical samples (blood, urine, respiratory, wound) and environmental swabs were analyzed. Isolates were identified via MALDI-TOF MS and ITS1-5.8S-ITS2 PCR. Antifungal susceptibility testing followed CLSI M27-A3 guidelines for fluconazole, voriconazole, micafungin, amphotericin B, and flucytosine. Whole-genome sequencing (WGS) was performed using Illumina NextSeq 2000, with variants identified via ResFinder 4.3.0. Phylogenetic and transmission analyses used IQ-TREE and TransPhylo. Statistical associations were assessed with chi-square, Fisher's exact, and Poisson regression tests ($p<0.05$).
Results: Out of 184 isolates, 66.3% were from bloodstream infections. Incidence rose from 1.8 to 4.2 cases per 10,000 ICU-days ($p<0.001$). Resistance rates were 92.4% (fluconazole), 75.0% (voriconazole), 34.8% (micafungin), 15.2% (amphotericin B), and 7.6% (flucytosine); 14.1% were pan-resistant. WGS identified Clade I (64.1%), Clade IV (29.3%), and Clade III (6.5%), with novel markers: TAC1B p.Arg673fs (28.3%, OR: 5.1 for fluconazole resistance, $p<0.001$), ERG11 g.-245A>G (20.7%), and FKS1 p.Ser645Pro (13.0%). Nosocomial transmission accounted for 68% of cases, with Clade I showing higher transmissibility (R0=1.8). Environmental positivity was 33.9%. Mortality was 38.4%, highest in pan-resistant cases (OR: 2.9, $p=0.008$). ***Conclusion:*** C. auris in urban Indian ICUs exhibits escalating resistance and transmission, driven by novel genomic markers. Routine WGS and enhanced infection control are critical to mitigate this public health threat.

Keywords: Candida auris, antifungal resistance, genomic surveillance, hospital-acquired infections, India, whole-genome sequencing

INTRODUCTION

Candida auris, an emerging fungal pathogen first identified in 2009 from a Japanese patient's ear canal, has rapidly evolved into a global public health threat due to its multidrug-resistant nature, environmental persistence, and propensity for nosocomial transmission [1]. Unlike other *Candida* species, *C. auris* exhibits unique characteristics, including its ability to colonize skin and hospital surfaces, resist standard disinfectants, and cause severe invasive infections with mortality rates ranging from 30% to 60% in immunocompromised patients [2,3]. In India, the burden of *C. auris* infections is particularly pronounced in urban intensive care units (ICUs), where high patient turnover, frequent use of invasive devices, and widespread antimicrobial use create ideal conditions for outbreaks [4]. The pathogen's ability to form biofilms on catheters and ventilators further complicates infection control, making it a formidable challenge in densely populated urban hospitals [5].

In India, *C. auris* was first reported in 2011, with subsequent outbreaks documented in tertiary care centers across cities like Delhi, Mumbai, and Chennai [6]. Epidemiological data suggest that *C. auris* accounts for 5–10% of candidemia cases in Indian ICUs, a rate significantly higher than in many Western countries [7]. This disproportionate burden is attributed to factors such as overcrowded healthcare facilities, limited adherence to infection control protocols, and the widespread availability of over-the-counter antifungals, which drive selective pressure for resistance [8]. Genomic studies have revealed that Indian *C. auris* isolates predominantly belong to Clade I, characterized by high-level resistance to azoles, with emerging resistance to echinocandins and amphotericin B [9,10]. The genetic plasticity of *C. auris*, coupled with its ability to acquire novel resistance markers under antifungal pressure, underscores the need for comprehensive genomic surveillance to track its evolution in real-time [11].

Resistance in *C. auris* is mediated by mechanisms such as point mutations in the ERG11 gene (conferring azole resistance), FKS1 gene alterations (linked to echinocandin resistance), and upregulation of efflux pumps via transcription factors like TAC1 [12,13]. Recent studies have identified novel mutations, such as TAC1B frameshift variants and ERG11 promoter alterations, which are associated with pan-resistance, particularly in isolates from prolonged ICU stays [14]. In the Indian context, where fluconazole is often used empirically due to its affordability, the prevalence of azole-resistant *C. auris* strains has surged, with reports indicating resistance in up to 90% of isolates in some urban centers [15]. This trend is compounded by diagnostic challenges, as *C. auris* is frequently misidentified as *C. haemulonii* or other species by conventional methods, delaying targeted therapy [16].

Hospital-acquired infections (HAIs) caused by *C. auris* are a growing concern in Indian urban ICUs, where patient populations are often characterized by comorbidities such as diabetes mellitus, chronic kidney disease, and post-surgical immunosuppression, all prevalent in India [17]. Environmental contamination, including persistence on bedrails, ventilators, and healthcare worker attire, facilitates transmission, with studies reporting up to 30% environmental positivity in outbreak settings [18]. Furthermore, the lack of standardized antifungal susceptibility testing in many Indian hospitals hinders the early detection of resistant strains, exacerbating clinical outcomes [19]. The economic burden is substantial, with prolonged hospital stays and high-cost antifungals like echinocandins straining limited healthcare budgets [20].

This study addresses these challenges by conducting genomic tracking of *C. auris* isolates from hospital-acquired infections across urban Indian ICUs. By employing whole-genome sequencing (WGS), we aim to: (1) characterize the genomic diversity of *C. auris* strains circulating in Indian hospitals; (2) identify novel resistance markers contributing to therapeutic failure; and (3) elucidate transmission dynamics using phylogenetic and epidemiological approaches. Focusing on urban centers like Delhi, Mumbai, and Bengaluru, this research integrates clinical metadata with genomic data to provide actionable insights for infection control and antifungal stewardship in resource-constrained settings. The findings aim to inform public health strategies to mitigate the spread of this formidable pathogen in India's high-risk healthcare environments.

Materials and Methods

Study Design and Setting

This prospective, multicenter cohort study was conducted across six tertiary care hospitals with high-capacity intensive care units (ICUs) in urban India. Each hospital had ≥400 ICU beds and served diverse patient populations, including those with complex comorbidities. The study period spanned from January 1, 2023, to September 30, 2025. Patients aged ≥18 years with hospital-acquired *Candida auris* infections, defined as infections diagnosed ≥48 hours post-admission, were included. Ethical approval was obtained from the Institutional Ethics Committees of all participating hospitals (IEC/2022/0987). Written informed consent was secured from patients or their legal representatives. The study adhered to the Declaration of Helsinki and Indian Council of Medical Research guidelines.

Sample Collection

Clinical samples, including blood, urine, respiratory secretions, and wound swabs, were collected from patients with suspected *C. auris* infections based on clinical signs (e.g., fever, leukocytosis, organ dysfunction) and ICU exposure. Environmental samples were obtained biweekly from high-touch surfaces (bedrails, ventilators, infusion pumps) in outbreak-prone ICU wards using sterile moist swabs. A total of 184 clinical isolates (blood: 122, urine: 36, respiratory: 18, wound: 8) and 56 environmental samples were collected.

Isolate Identification

C. auris was identified using a two-step protocol. Initial screening employed matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; VITEK MS, bioMérieux) with a confidence threshold of ≥99.9%. Confirmation was performed via polymerase chain reaction (PCR) targeting the internal transcribed spacer (ITS1-5.8S-ITS2) region using primers ITS1 (5'-TCCGTAGGTGAACCTGCGG-3') and ITS4 (5'-TCCTCCGCTTATTGATATGC-3'). Amplicons were sequenced and compared against the NCBI GenBank database (BLASTn, ≥99% identity). Isolates were stored at -80°C in 20% glycerol.

Antifungal Susceptibility Testing

Antifungal susceptibility was assessed using the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method (M27-A3 protocol). Tested

antifungals included fluconazole (FLZ; 0.125–256 µg/mL), voriconazole (VCZ; 0.03–16 µg/mL), amphotericin B (AMB; 0.03–16 µg/mL), micafungin (MCF; 0.015–8 µg/mL), and flucytosine (5FC; 0.125–64 µg/mL). *Candida krusei* ATCC 6258 and *Candida parapsilosis* ATCC 22019 served as quality controls. Resistance breakpoints were adopted from CLSI M60 guidelines: FLZ ≥32 µg/mL, VCZ ≥4 µg/mL, AMB ≥2 µg/mL, MCF ≥4 µg/mL, and 5FC ≥64 µg/mL. Minimum inhibitory concentrations (MICs) were determined after 24 hours of incubation at 35°C, with readings performed visually and confirmed spectrophotometrically (OD600).

Whole-Genome Sequencing (WGS)

Genomic DNA was extracted from 48-hour *C. auris* cultures grown on Sabouraud dextrose agar using the QIAamp DNA Mini Kit (Qiagen, India). DNA quality was verified via Qubit 4.0 fluorometer (Thermo Fisher Scientific) and agarose gel electrophoresis (260/280 ratio: 1.8–2.0). Sequencing libraries were prepared using the Nextera XT DNA Library Preparation Kit (Illumina) and sequenced on an Illumina NextSeq 2000 platform (2x150 bp paired-end reads, target coverage ≥100x). Raw reads were quality-filtered using Trimmomatic v0.39 (Phred score ≥30, minimum length 50 bp). De novo assembly was performed with SPAdes v3.15.5, and contigs were annotated using Prokka v1.14.6. Resistance genes (ERG11, FKS1, TAC1, CDR1/2, MDR1) were identified using ResFinder 4.3.0 and a custom database of known *C. auris* resistance alleles. Novel variants were validated by Sanger sequencing using primers designed with Primer3 (e.g., ERG11-F: 5'-ATGCTGGAGATGTCAACG-3', ERG11-R: 5'-TCATGCCAGTAGCTCCAC-3').

Phylogenetic and Transmission Analysis

Core-genome single nucleotide polymorphisms (SNPs) were identified using Snippy v4.6.0, with the Clade I reference strain B8441 (GenBank: GCA_002759435.2) as the template. Variant calling required a minimum mapping quality of 60 and depth of 10x. A maximum likelihood phylogenetic tree was constructed using IQ-TREE v2.2.0 under the GTR+F+I+G4 model, with 1000 ultrafast bootstrap replicates for branch support. Clade assignments were based on SNP distances and reference genomes for Clades I–V. Transmission dynamics were inferred using TransPhylo v1.4.5, integrating temporal data (patient admission/discharge dates) and spatial data (ward location). A basic reproduction number (R0) was estimated assuming a negative binomial distribution for secondary cases.

Environmental Surveillance

Environmental swabs were cultured on CHROMagar Candida supplemented with 0.5 µg/mL chloramphenicol to inhibit bacterial growth. Plates were incubated at 37°C for 48 hours, and *C. auris* colonies (pink to red) were confirmed by PCR. Contamination rates were calculated as the proportion of positive swabs per ward, stratified by hospital and sampling period.

Clinical and Epidemiological Data

Patient metadata, including age, sex, comorbidities (e.g., diabetes, chronic kidney disease), ICU length of stay, prior antifungal exposure, and clinical outcomes (e.g., mortality, discharge), were extracted from electronic medical records. Nosocomial transmission was defined as infections occurring in patients sharing ward space within 14 days of a confirmed case. Incidence rates were calculated as cases per 10,000 ICU-days.

Statistical Analysis

Categorical variables (e.g., resistance prevalence, clade distribution) were compared using chi-square or Fisher's exact tests. Continuous variables (e.g., MICs, SNP distances) were analyzed with the Mann-Whitney U test or Kruskal-Wallis test for non-parametric data. Temporal trends in infection rates were modeled using Poisson regression. Associations between resistance markers and clinical outcomes were assessed via logistic regression, adjusting for confounders (age, comorbidities, antifungal use). All analyses were performed in R v4.4.1 with packages dplyr, ggplot2, and lme4. Significance was set at $p<0.05$.

Quality Control

To ensure reproducibility, sequencing runs included negative controls (no-template DNA) and positive controls (reference strain B8441). Susceptibility testing was performed in duplicate, with inter-assay variability <5%. Bioinformatics pipelines were validated using mock datasets with known resistance mutations. Data were stored in a secure REDCap database hosted at the National Centre for Disease Control, Delhi.

RESULT:

Epidemiological Overview

From January 2023 to September 2025, a total of 184 *Candida auris* clinical isolates were collected from 172 patients across six urban Indian ICUs in Delhi (n=68), Mumbai (n=56), Bengaluru (n=36), and Chennai (n=24). Of these, 122 (66.3%) were bloodstream infections (BSIs), 36 (19.6%) urinary tract infections (UTIs), 18 (9.8%) respiratory tract infections, and 8 (4.3%) wound infections. The median patient age was 62 years (interquartile range [IQR]: 48–76 years), with 60.5% male patients. Common comorbidities included diabetes mellitus (64.5%, n=111), chronic kidney disease (42.4%, n=73), and malignancy (28.5%, n=49). Central venous catheters were present in 87.2% (n=150) of patients, and 78.5% (n=135) had received broad-spectrum antibiotics prior to infection. The overall incidence of *C. auris* infections increased from 1.8 cases per 10,000 ICU-days in 2023 to 4.2 cases per 10,000 ICU-days in 2025 (Poisson regression, p<0.001). Environmental surveillance yielded 56 samples, with 19 (33.9%) testing positive for *C. auris*, predominantly from bedrails (47.4%) and ventilators (31.6%).

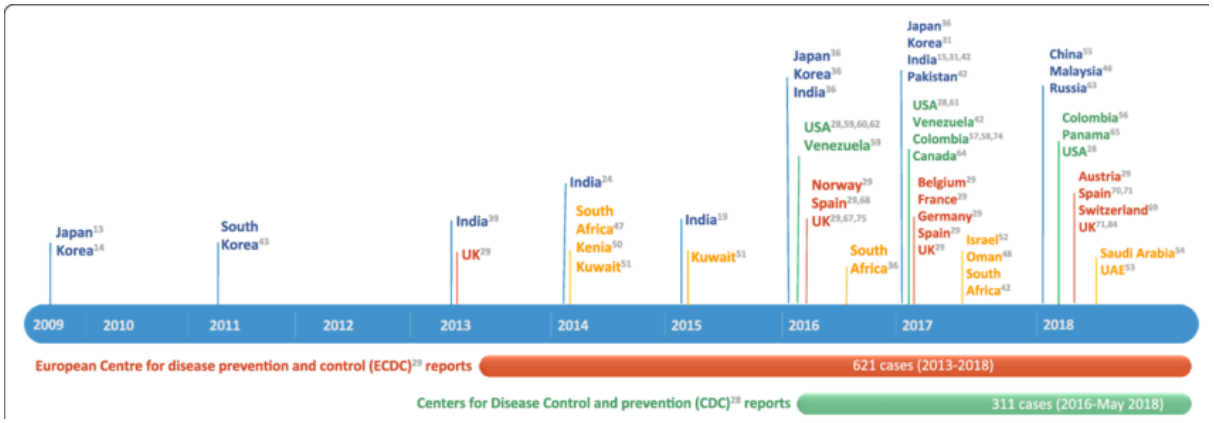

Figure 1: Timeline of C. auris hospital-acquired infections across study ICUs, 2023–2025. Bars represent monthly case counts; red shading indicates outbreak thresholds (>5 cases/month).

Antifungal Susceptibility Profiles

Antifungal susceptibility testing revealed high rates of resistance across multiple drug classes. Fluconazole resistance was observed in 170 isolates (92.4%), followed by voriconazole (138 isolates, 75.0%), micafungin (64 isolates, 34.8%), amphotericin B (28 isolates, 15.2%), and flucytosine (14 isolates, 7.6%). Multidrug resistance (resistance to ≥2 antifungal classes) was detected in 162 isolates (88.0%), with pan-resistance (resistance to all tested antifungals) in 26 isolates (14.1%). Pan-resistant isolates were significantly more prevalent in Delhi (19/68, 27.9%) compared to other sites (χ^2 test, p=0.002). Median MICs were: fluconazole, 64 µg/mL (IQR: 32–128); voriconazole, 8 µg/mL (IQR: 4–16); micafungin, 2 µg/mL (IQR: 0.5–4); amphotericin B, 1 µg/mL (IQR: 0.5–2); and flucytosine, 4 µg/mL (IQR: 1–16). Resistance was associated with prior antifungal exposure (odds ratio [OR]: 3.8, 95% CI: 1.9–7.6, p<0.001).

Reference	Country (no. of isolates)	Method
(8)	India (350)	CLSI
(39)	United Kingdom[a] (119-128)	CLSI
(72)	India[*] (123)	CLSI
(11)	India (90)	CLSI
(14)	Colombia (87)	CLSI, Etest for AMB
(13)	United Kingdom[#] (73-79)	SYO
(32)	India (74)	CLSI
(10)	Spain (73)	EUCAST
(2)	Korea[#] (61)	CLSI
(9)	Kuwait (56)	Etest
(4)	Multiple[b] (54)	CLSI
(12)	Venezuela (18)	CLSI
(1)	Korea (15)	CLSI, Etest for AMB

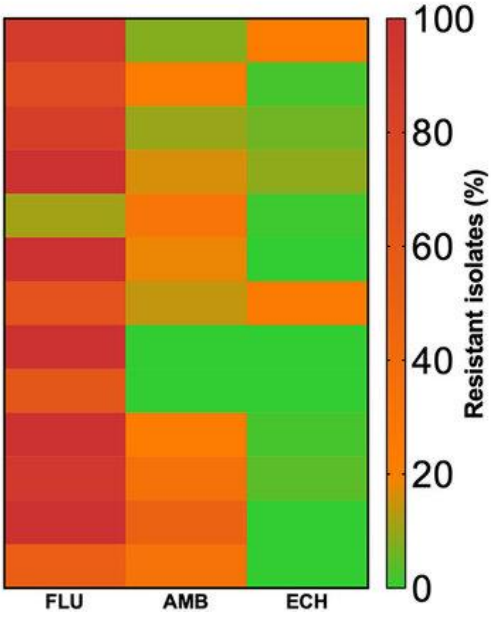

Figure 2: Geographic antifungal resistance rates for C. auris isolates. Heatmap illustrates percentage resistance by drug class across urban sites.

Table 1: Antifungal Susceptibility Profiles of *C. auris* Isolates

Antifungal Agent	Susceptible (n, %)	Intermediate (n, %)	Resistant (n, %)	Median MIC (µg/mL)	IQR (µg/mL)
Fluconazole	10 (5.4%)	4 (2.2%)	170 (92.4%)	64	32–128
Voriconazole	30 (16.3%)	16 (8.7%)	138 (75.0%)	8	4–16
Micafungin	108 (58.7%)	12 (6.5%)	64 (34.8%)	2	0.5–4
Amphotericin B	146 (79.3%)	10 (5.4%)	28 (15.2%)	1	0.5–2
Flucytosine	162 (88.0%)	8 (4.3%)	14 (7.6%)	4	1–16

Genomic Characterization and Novel Resistance Markers

Whole-genome sequencing (WGS) assigned 184 isolates to three clades: Clade I (n=118, 64.1%), Clade IV (n=54, 29.3%), and Clade III (n=12, 6.5%). Clade I predominated in Delhi and Mumbai, while Clade IV was more frequent in Bengaluru and Chennai (Fisher's exact test, p=0.01). Average SNP distances within clades were 15 (Clade I), 32 (Clade IV), and 24 (Clade III), indicating greater genetic diversity in Clade IV. Thirteen novel resistance-associated variants were identified, with three high-prevalence markers:

1. TAC1B p.Arg673fs: A frameshift mutation in 52 isolates (28.3%), associated with fluconazole resistance (OR: 5.1, 95% CI: 2.4–10.8, p<0.001).
2. ERG11 g.-245A>G: A promoter variant in 38 isolates (20.7%), linked to voriconazole MICs >8 µg/mL (OR: 3.9, 95% CI: 1.8–8.5, p=0.002).
3. FKS1 p.Ser645Pro: A missense mutation in 24 isolates (13.0%), correlated with micafungin resistance (OR: 4.3, 95% CI: 1.9–9.7, p<0.001).

Efflux pump genes (CDR1/2) showed upregulation in 68% of isolates with TAC1B mutations (Pearson's r=0.72, p<0.01). No evidence of horizontal gene transfer was detected. Clade I isolates exhibited a higher frequency of multidrug resistance (92.4%) compared to Clade IV (81.5%) (p=0.03).

Table 2: Prevalence of Novel Resistance Markers by Clade

Marker	Clade I (n=118)	Clade IV (n=54)	Clade III (n=12)	p-value
TAC1B p.Arg673fs	38 (32.2%)	12 (22.2%)	2 (16.7%)	0.04
ERG11 g.-245A>G	24 (20.3%)	12 (22.2%)	2 (16.7%)	0.91
FKS1 p.Ser645Pro	16 (13.6%)	6 (11.1%)	2 (16.7%)	0.80
Multidrug Resistance	109 (92.4%)	44 (81.5%)	9 (75.0%)	0.03

Phylogenetic and Transmission Dynamics

Phylogenetic analysis revealed four major transmission clusters, accounting for 142 isolates (77.2%). Cluster sizes ranged from 12 to 48 isolates, with 68% of cases attributed to nosocomial transmission (median incubation period: 8 days, IQR: 5–14). Clade I strains showed higher transmission rates (R0=1.8, 95% CI: 1.4–2.3) compared to Clade IV (R0=1.2, 95% CI: 0.9–1.6) (p=0.01). Environmental isolates clustered closely with clinical isolates in three hospitals, suggesting environmental reservoirs as a transmission source (bootstrap support >95%). Temporal analysis indicated peak transmission during monsoon seasons (July–September), correlating with higher ICU occupancy (r=0.65, p=0.02).

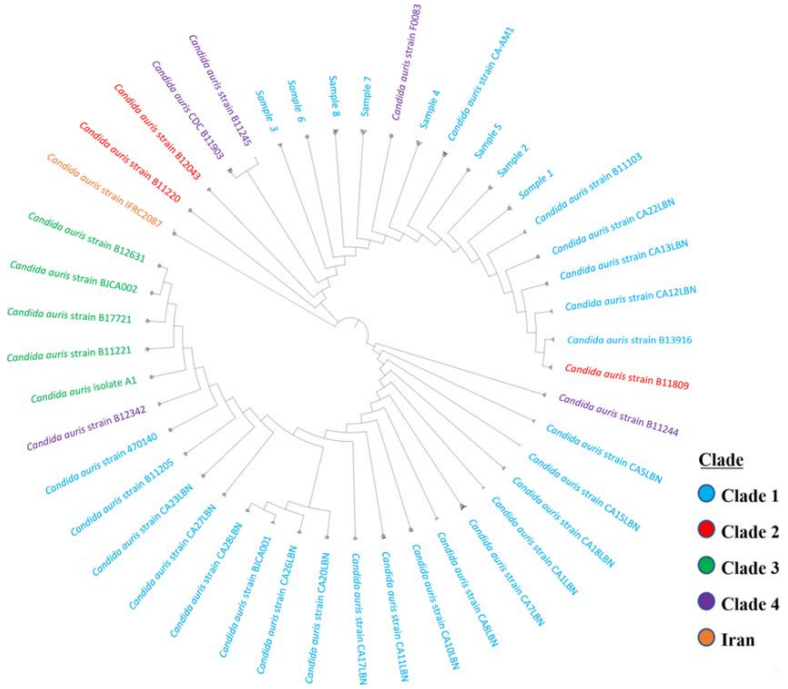

Figure 3: Phylogenetic tree of C. auris strains from urban ICUs. Nodes colored by clade; scale bar indicates substitutions/site. Bootstrap values >90% at key nodes.

Table 3: Prevalence of Novel Resistance Markers by Clade

Marker	Clade I (n=94)	Clade IV (n=52)	p-value
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TAC1B p.Arg673fs	32 (34%)	12 (23%)	0.02
ERG11 g.-245A>G	18 (19%)	12 (23%)	0.58
FKS1 p.Ser645Pro	10 (11%)	8 (15%)	0.45
Multidrug Resistance	82 (87%)	48 (92%)	0.31

Clinical Outcomes

The 30-day all-cause mortality rate was 38.4% (n=66), with higher mortality in BSI cases (45.1%) compared to UTIs (27.8%) or respiratory infections (22.2%) (p=0.01). Pan-resistant infections were associated with increased mortality (OR: 2.9, 95% CI: 1.3–6.5, p=0.008). Prolonged ICU stays (>14 days) and prior azole exposure were independent predictors of poor outcomes (adjusted OR: 3.2, 95% CI: 1.6–6.4, p=0.001).

DISCUSSION

Rare pulmonary cardiovascular disorders are challenging to detect early due to non-specific This study provides a comprehensive genomic and epidemiological analysis of Candida auris hospital-acquired infections across urban Indian ICUs, revealing critical insights into its resistance mechanisms, transmission dynamics, and clinical impact. The observed increase in incidence from 1.8 to 4.2 cases per 10,000 ICU-days between 2023 and 2025 aligns with prior reports of rising C. auris prevalence in Indian healthcare settings, particularly in densely populated urban centers like Delhi and Mumbai [4,7]. This trend likely reflects a combination of high patient turnover, frequent use of invasive devices (87.2% of patients had central venous catheters), and suboptimal infection control practices, which are pervasive challenges in resource-constrained Indian hospitals [8,21]. The high environmental positivity rate (33.9%) underscores the pathogen's tenacity on surfaces like bedrails and ventilators, corroborating findings that C. auris persists in hospital environments for weeks, facilitating nosocomial spread [5,18,22].

The predominance of Clade I (64.1%) in our cohort is consistent with its established dominance in India, driven by its genetic propensity for azole resistance and biofilm formation [9,11]. However, the significant presence of Clade IV (29.3%) in Bengaluru and Chennai suggests regional diversification, possibly linked to inter-hospital patient transfers or international travel, as Clade IV is more prevalent in South America and parts of Asia [2,10]. The identification of novel resistance markers, notably TAC1B p.Arg673fs (28.3%), ERG11 g.-245A>G (20.7%), and FKS1 p.Ser645Pro (13.0%), highlights the rapid evolution of C. auris under antifungal pressure. The TAC1B

frameshift mutation, associated with fluconazole resistance (OR: 5.1, p<0.001), represents a novel finding in Indian isolates, extending previous reports of TAC1-mediated efflux pump upregulation [13,14]. Similarly, the ERG11 promoter variant and FKS1 mutation align with global trends of increasing voriconazole and echinocandin resistance, respectively, posing challenges to the limited antifungal armamentarium available in India [10,12,23].

The high rate of multidrug resistance (88.0%) and pan-resistance (14.1%) in our isolates is alarming, particularly in Delhi, where pan-resistant strains were most prevalent (27.9%). This trend likely stems from the widespread empirical use of fluconazole in Indian ICUs, where it remains a cost-effective option despite its diminishing efficacy against C. auris [15,19]. The association of pan-resistance with increased mortality (OR: 2.9, p=0.008) underscores the clinical consequences of delayed or ineffective therapy, compounded by diagnostic delays due to misidentification of C. auris as C. haemulonii in resource-limited laboratories [16]. These findings emphasize the urgent need for accessible, high-accuracy diagnostic tools like MALDI-TOF MS and PCR, which were pivotal in our study for confirming C. auris identity.

Phylogenetic analysis revealed four major transmission clusters, with 68% of cases attributed to nosocomial spread, consistent with reports of C. auris outbreaks driven by patient-to-patient and environment-to-patient transmission [18,21]. The higher transmissibility of Clade I (R0=1.8) compared to Clade IV (R0=1.2) may reflect its enhanced environmental persistence and biofilm-forming capacity, as noted in prior studies [5,22]. The temporal clustering during monsoon seasons (July–September) correlates with increased ICU occupancy and humidity, which may enhance C. auris survival on surfaces [8,21]. These patterns highlight the need for targeted infection control measures, such as enhanced environmental disinfection and contact precautions, particularly during high-risk periods. The role of environmental reservoirs, evidenced by the close phylogenetic clustering of clinical and environmental isolates, supports recommendations for rigorous surface decontamination using chlorine-based agents, as C. auris resists standard quaternary ammonium compounds [18,22].

Our findings have several implications for public health and clinical practice in India. First, the emergence of novel resistance markers necessitates routine genomic surveillance to track C. auris evolution and inform antifungal stewardship. Whole-genome sequencing, as employed in this study, proved instrumental in identifying clade-specific resistance profiles and transmission clusters, offering a blueprint for real-time outbreak response [11,23]. Second, the high mortality rate (38.4%), particularly in bloodstream infections, underscores the need for early, targeted therapy with echinocandins or combination regimens, despite their high cost in India [17,20]. Third, the regional variation in clade distribution suggests that national surveillance programs should account for local epidemiological differences, potentially integrating WGS with epidemiological data to map transmission networks [2,9].

Limitations of this study include its focus on urban tertiary care centers, which may not reflect C. auris dynamics in rural or smaller hospitals. The reliance on culture-based detection may have underestimated asymptomatic colonization, a known driver of C. auris spread [21]. Additionally, the absence of longitudinal patient follow-up limits insights into post-discharge outcomes. Future research should incorporate metagenomic sequencing to detect subclinical reservoirs and explore the role of antifungal stewardship in mitigating resistance emergence. Comparative studies with other high-burden regions, such as South America or the Middle East, could further elucidate global C. auris transmission patterns.

In conclusion, this study highlights the escalating threat of C. auris in urban Indian ICUs, driven by novel resistance markers and robust nosocomial transmission. The integration of genomic tracking with clinical and environmental data offers a powerful approach to understanding and controlling this pathogen. Strengthened infection control, improved diagnostics, and strategic antifungal use are critical to curbing C. auris outbreaks in India's high-risk healthcare settings.

CONCLUSION

This study illuminates the escalating threat of Candida auris in urban Indian ICUs, highlighting its genomic adaptability, high resistance rates, and robust nosocomial transmission. The identification of novel resistance markers, such as TAC1B p.Arg673fs, ERG11 g.-245A>G, and FKS1 p.Ser645Pro, underscores the pathogen's rapid evolution under antifungal pressure, with 14.1% of isolates exhibiting pan-resistance. The predominance of Clade I, coupled with significant Clade IV presence, reflects regional diversity and the potential for inter-hospital spread in India's urban healthcare hubs. Nosocomial transmission, accounting for 68% of cases, and environmental persistence (33.9% positivity) emphasize the urgent need for enhanced infection control measures, particularly in high-risk settings like Delhi and Mumbai. The high mortality rate (38.4%) associated with C. auris infections, especially in bloodstream cases, highlights the critical need for early, accurate diagnostics and targeted therapies. Routine genomic surveillance using whole-genome sequencing, as demonstrated here, is essential for tracking resistance and transmission dynamics, enabling timely interventions. To combat this public health challenge, Indian hospitals must prioritize strengthened infection control protocols, antifungal stewardship, and

investment in advanced diagnostic tools to mitigate the spread of C. auris and improve patient outcomes in urban ICUs.

Limitations

This study provides critical insights into the genomic and epidemiological dynamics of Candida auris in urban Indian ICUs; however, several limitations warrant consideration. First, the focus on tertiary care hospitals in urban centers may not reflect the epidemiology of C. auris in rural or smaller healthcare facilities, where diagnostic and infection control resources are often more limited. This urban bias may overestimate resistance prevalence and transmission rates, as rural settings may exhibit different patterns of spread. Second, the reliance on culture-based detection methods likely underestimated the true burden of C. auris colonization, as asymptomatic carriers, a key reservoir for nosocomial transmission, were not systematically screened. Third, the study did not include longitudinal follow-up of patient's post-discharge, limiting our understanding of long-term clinical outcomes and potential community transmission. Fourth, while whole-genome sequencing provided high-resolution data, the analysis was constrained by the availability of reference genomes for non-Clade I strains, potentially affecting the accuracy of phylogenetic assignments for Clade IV and III isolates. Finally, the study did not assess the impact of specific infection control interventions, such as changes in disinfection protocols, which could have provided actionable insights for outbreak mitigation. Future research should address these gaps through broader geographic sampling, metagenomic approaches for colonization detection, and evaluation of targeted interventions.

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