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Economic Impact of Identifying Non-Pathogenic Urinary Isolates in Hospitalized Patients: A Longitudinal Study Using Stepwise Diagnostic Stewardship Model

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ABSTRACT

Background: Urinary tract infections (UTIs) are among the most common reasons for antibiotic prescriptions in hospitalized patients. However, distinguishing pathogenic from non-pathogenic urinary isolates remains challenging. The inappropriate treatment of colonizers and contaminants can result in unnecessary antimicrobial use, contributing to resistance, adverse events, and increased healthcare costs.

Objective: This study aims to evaluate the economic impact of identifying non-pathogenic urinary isolates using a stepwise diagnostic model in hospitalized patients.

Methods: In this longitudinal observational study conducted over 24 months at a tertiary care hospital, adult inpatients with positive urine cultures were assessed. A stepwise model integrating clinical, laboratory, and microbiological parameters was applied to classify isolates as pathogenic or non-pathogenic. Outcomes including antibiotic usage (duration and cost), 30-day mortality, and hospital stay length were compared between patients with pathogenic and non-pathogenic isolates.

Results: Among 275 isolates, 249 (90.54%) were identified as pathogenic and 26 (9.45%) as non-pathogenic. Median antibiotic duration showed no significant difference (7 days (IQR: 5–7) for both groups). However, median antibiotic cost was significantly higher in the pathogenic group (Rs. 2440 vs Rs. 640; $p < 0.001$), with a large effect size ($r = 0.48$). The median hospitalization duration was similar between groups (12 days (interquartile range [IQR]: 7–19) vs 10 days (IQR: 5.25–17.75); $p = 0.336$). The 30-day mortality was 2.0% in the pathogenic group; no deaths were reported in the non-pathogenic group.

Conclusion: Recognizing non-pathogenic isolates can reduce inappropriate antibiotic use and associated costs without adversely affecting patient outcomes. Implementation of such a diagnostic approach can strengthen antimicrobial stewardship programs and improve healthcare efficiency.

KEYWORDS: Urine culture interpretation; Antimicrobial stewardship; Colonization vs infection; Antibiotic overuse; Healthcare cost

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BACKGROUND

Urinary tract infections (UTIs) are among the most common causes of hospitalization due to bacterial infections globally and are particularly significant in vulnerable populations, such as the elderly, catheterized patients, and those with chronic comorbidities[1]. While urine culture remains the gold standard for diagnosis, the detection of organisms in urine does not always imply infection. A substantial proportion of positive urine cultures represents colonization or contamination rather than true infection [2,3].

The diagnostic dilemma arises in differentiating pathogenic organisms from commensals or contaminants, or even colonisers, particularly when clinical correlation is ambiguous. In many cases, empirical or culture-guided antibiotics are initiated without sufficient evaluation of the organism's clinical relevance, often resulting in overtreatment[4]. This contributes to antimicrobial resistance (AMR), adverse drug effects, increased length of hospital stay, and inflated healthcare costs [5,6].

Recent literature has emphasized the economic burden of inappropriate antimicrobial use in UTIs. Shafrin et al. demonstrated that antibiotic-non-susceptible urinary pathogens result in significantly higher medical costs and extended hospitalizations[7]. Similarly, Rozenkiewicz et al. reported that community-onset UTIs caused by extended-spectrum beta-lactamase (ESBL) producing *Klebsiella pneumoniae* led to prolonged hospitalization and increased direct medical expenditures[8]. Misclassification of non-pathogenic isolates as uropathogens thus not only misguides treatment but also poses substantial financial strain on healthcare systems[9].

In resource-constrained settings like India, where antimicrobial stewardship programs (ASPs) are still evolving and diagnostic laboratory capacities vary widely, the potential for overtreatment is even greater[10,11]. Several reports from tertiary Indian centers have highlighted the clinical and economic burden of unnecessary antibiotic prescriptions based on asymptomatic bacteriuria or misclassified cultures[12,13].

Although algorithms to classify urinary isolates into probable pathogens or non-pathogens exist, they are underutilized in real-world inpatient settings. Most studies have focused on the clinical impact of such algorithms, but few have evaluated their economic implications, particularly in terms of antibiotic duration, costs, or outcomes like mortality [14,15].

In this context, the present longitudinal study was conducted in a tertiary-care teaching hospital in India to determine the economic impact of identifying non-pathogenic urinary isolates. By categorizing isolates using a structured model and comparing antibiotic use, cost, and outcomes, this study aims to provide actionable evidence for better resource utilization and diagnostic stewardship in hospitalized patients.

METHODOLOGY

Study Design and Setting

This prospective longitudinal study was conducted at the All India Institute of Medical Sciences (AIIMS), Rishikesh, over a 24-month period between January 2022 and December 2023. Ethical approval was obtained from the Institutional Ethics Committee (Ref: AIIMS/IEC/2021/594).

Participants

All hospitalized adult patients (≥18 years) with positive urine cultures during the study period were eligible. Patients were included if microbiological report was accepted as clinically significant by both microbiologists and treating clinicians. If the microbiologist's report said the contaminant/coloniser couldn't be ruled out, then it was excluded. Similarly, if a clinician couldn't use antimicrobials as per culture/sensitivity reports, then it was excluded. Patients with incomplete records or discharged within 24 hours of admission were excluded.

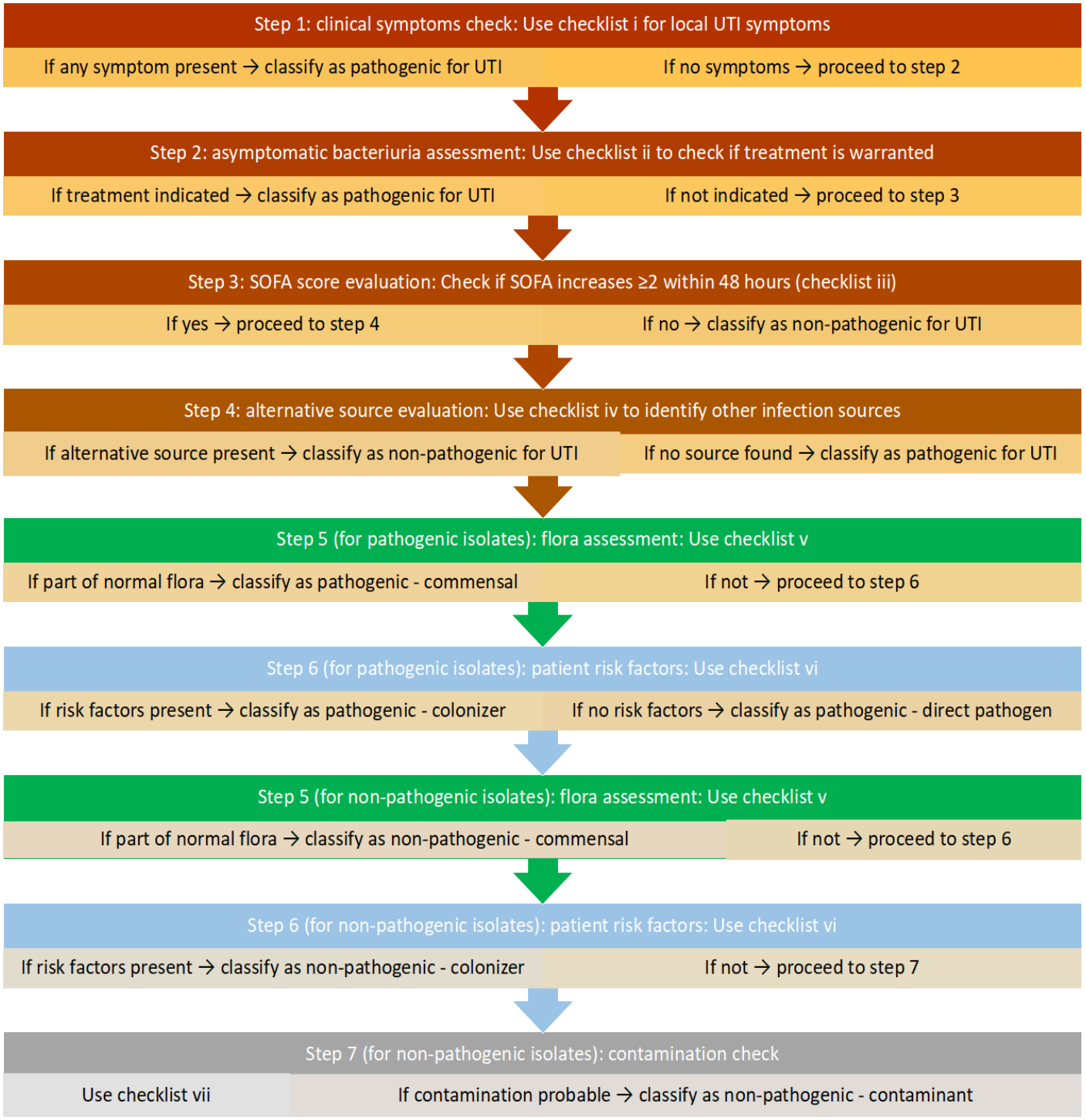
Classification of Isolates

A structured stepwise algorithm was employed to classify each urine isolate into one of the following categories:

- **Pathogenic (colonizer/commensal/direct)**: Clinically significant.
- **Non-pathogenic (commensal/contaminant)**: Not clinically significant.

This classification was based on evaluation by investigator team comprised of internist, microbiologist, and infectious disease specialist.

Stepwise algorithm (Box 1):



Data Collection

Data were prospectively collected using REDCap software and included:

- Demographics, comorbidities
- Clinical symptoms, urinalysis, culture results
- Antibiotic regimens: start date, duration, class
- Hospital stay duration, 30-day mortality
- Cost estimates: defined by hospital pharmacy price lists.

Outcomes

The primary outcome was economic impact, measured as:

- Antibiotic cost (Rs.)
- Duration of antibiotic therapy (days)

Secondary outcomes included:

- Hospital stay (days)
- 30-day mortality

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Various checklists **(Box 2)**:

CHECK LIST I

Any local symptoms/signs of UTI?

1. Is there increase in frequency to pass urine?
2. Is there urgency to pass urine?
3. Is there dysuria?
4. Is there pus in urine?
5. Is there blood in urine?
6. Is there flank pain/heaviness?
7. Any other local symptoms/signs of UTI ?

CHECK LIST II

Asymptomatic bacteriuria needed to be treated?

1. Is patient pregnant female?
2. Is patient undergoing urologic procedure ?
3. Is patient in first 3 months after renal transplantation?

CHECK LIST III

SOFA score

VARIABLE	0	1	2	3	4	SCORE
PaO2/FiO2 (mmhg)	>400	<=400	<=300	<=200	<=100	
Platelet (1000/uL)	>150	<=150	<=100	<=50	<=20	
Bilirubin (mg/dL)	<1.2	1.2-1.9	2-5.9	6-11.9	>12	
CVS	MAP >70	MAP< 70	Dop<= 5	Dop>5 or Epi <=0.1	Epi>0.1	
GCS	15	13-14	10-12	6-9	<6	
Creatinine (mg/dL)	<1.2	1.2-1.9	2-3.4	3.5-4.9	>5	

CHECK LIST IV

Any possible source other than UTI responsible for increase in SOFA ?

1. Any clinical feautures other than that of UTI?
2. Any lab parameters suggesting alternative foci?
3. Any imaging evidence suggesting foci other than UTI?

CHECK LIST V

Is microorganism part of normal flora for Urine?

1. E.coli
2. Candida
3. Klebsiella
4. Proteus
5. Alpha hemolytic streptococci
6. S. epidermidis
7. E. faecalis
8. Corynebacteria
9. Any other commensals as suggested by microbiologist?

CHECK LIST VI

Any patient characteristics contributing to growth of microorganism ?

1. Old age > 60 years
2. Type 2 Diabetes Mellitus
3. Indwelling catheter
4. Acquired immuno deficiency syndrome
5. Any Malignancy
6. Other foreign body in urinary tract?
7. Loss of VUR reflex on voiding cystourethrogram?
8. Any other characteristics contributing to growth of microorganism?

CHECK LIST VII

Any possibility of contamination?

A: SAMPLE COLLECTION
1. Was the site cleaned?
2. Was it clean catch and mid-stream?
3. Was it via Suprapubic method ?

B. TRANSPORT:
1. Was the lead tight condition maintained?
2. Was the temperature maintained?
3. Was the sterility maintained?

C. LAB HANDLING
1.How long was it stored before processing?
2.Was the temperature maintained?
3.Was aseptic condition maintained?

STATISTICAL ANALYSIS

Descriptive and inferential analyses were performed using SPSS v25. Continuous variables were expressed as mean ± SD and compared using t-tests or Mann–Whitney U as appropriate. Categorical variables were analyzed using Chi-square or Fisher's exact test. A p-value <0.05 was considered statistically significant.

RESULTS

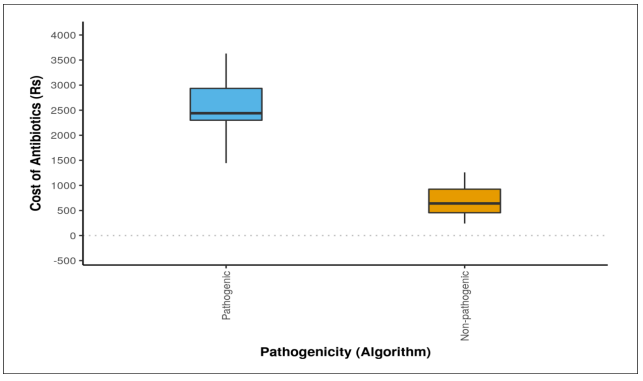
Baseline Characteristics

Among the 275 urinary isolates analyzed using the stepwise algorithm-based model, 249 (90.54%) were classified as pathogenic and 26 (9.45%) as non-pathogenic. Pathogenic isolates included pathogenic-commensals (n = 170, 61.81%), pathogenic-colonizers (n = 39, 14.18%), and direct pathogens (n = 40, 14.54%). Non-pathogenic isolates comprised non-pathogenic commensals (n = 19, 6.90%), colonizers (n = 5, 1.81%), and contaminants (n = 2, 0.72%). The baseline demographic analysis revealed that male patients had a higher median age than female patients.

Primary outcomes

Median antibiotic treatment duration was 7 days (IQR: 5–7) for both groups (Table 1). However, a significant difference was observed in the cost of antibiotic treatment. The median antibiotic cost for the pathogenic group was Rs. 2,440 (IQR: 2,300–2,935), substantially higher than Rs. 640 (IQR: 455–925) in the non-pathogenic group. This difference was statistically significant (W = 5411.0, p < 0.001) and was associated with a large effect size (Point-Biserial Correlation = 0.48) (Fig 1). No adverse outcomes were associated with withholding or limiting antibiotics in patients classified as having non-pathogenic isolates.

Figure 1: Box-and-Whisker plot showing association between Pathogenicity (Algorithm) and Cost of Antibiotics (Rs).



Note: *The middle horizontal line represents the median Cost of Antibiotics (Rs), the upper and lower bounds of the box represent the 75th and the 25th centile of Cost of Antibiotics (Rs) respectively, and the upper and lower extent of the whiskers represent the Tukey limits for Cost of Antibiotics (Rs) in each of the groups.*

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Secondary outcomes

The median duration of hospitalization for patients with pathogenic isolates was 12 days (interquartile range [IQR]: 7–19), compared to 10 days (IQR: 5.25–17.75) for those with non-pathogenic isolates. This difference was not statistically significant (Wilcoxon-Mann-Whitney U Test: W = 3608.0, p = 0.336) (Fig 2). The majority of isolates were linked to discharge outcomes, with only five deaths (2.0%) recorded within 30 days among the pathogenic group (Table 2). No mortality was observed among patients with non-pathogenic isolates.

Figure 2: The density plot depicting the distribution of Duration of Antibiotics (Days) in the 2 different groups of the variable Pathogenicity (Algorithm).

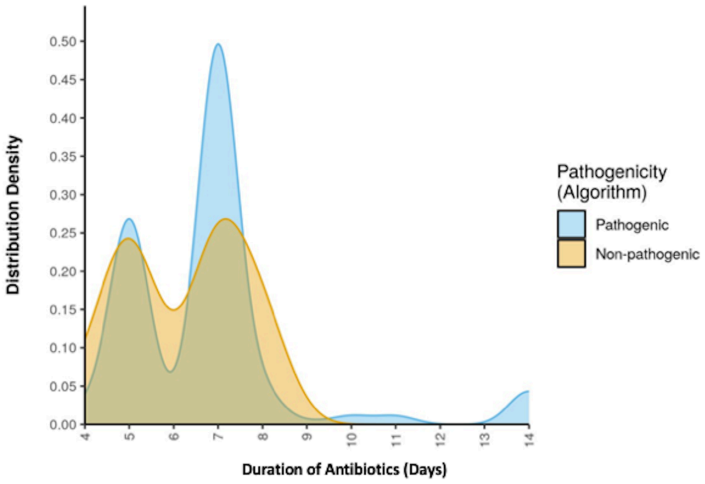

Table 1: Table for Association between Duration of Antibiotics (Days) and Parameters

Parameters	Duration of antibiotics (days)	p value
Age (years)	Correlation coefficient (rho) = -0.03	0.577
Age		0.750
18-30 years	7.11 ± 2.45	
31-40 years	6.53 ± 1.62	
41-50 years	6.69 ± 1.89	
51-60 years	6.70 ± 2.04	
61-70 years	6.87 ± 1.95	
71-80 years	6.38 ± 1.43	
81-90 years	6.83 ± 0.98	
>90 years	5.00 ± 0	
Gender		0.754
Male	6.68 ± 1.85	
Female	6.87 ± 2.17	
Localized symptoms of UTI		0.804
Yes	6.75 ± 1.92	
No	6.76 ± 2.25	
Symptom: increased urination		0.036
Yes	6.43 ± 1.62	
No	6.93 ± 2.12	
Symptom: urination urgency		0.215
Yes	6.33 ± 1.28	
No	6.84 ± 2.07	
Symptom: dysuria		0.085
Yes	6.87 ± 1.93	
No	6.59 ± 2.03	
Symptom: pyuria		0.522
Yes	6.57 ± 1.93	
No	6.77 ± 1.98	
Symptom: hematuria		0.720
Yes	6.29 ± 1.25	
No	6.76 ± 1.99	
Symptom: flank pain		0.443
Yes	6.48 ± 1.75	
No	6.79 ± 2.00	
Factor for asymptomatic bacteriuria: pregnancy		0.679
Yes	9.50 ± 6.36	
No	6.73 ± 1.93	
Factor for asymptomatic bacteriuria: urological procedure		0.478
Yes	6.67 ± 2.57	
No	6.76 ± 1.95	
Factor for asymptomatic bacteriuria: post renal transplant		-
Yes	-	
No	6.75 ± 1.97	
Factor for asymptomatic bacteriuria: none		0.959
Yes	6.62 ± 1.79	
No	6.77 ± 2.00	
SOFA score change >1		0.546
Yes	6.82 ± 2.26	
No	6.74 ± 1.84	
Pathogenicity (microbiologist) (pathogenic)	6.75 ± 1.97	-
Pathogenicity (algorithm)		0.398
Pathogenic	6.81 ± 2.02	
Non-pathogenic	6.23 ± 1.34	
Nature of organism		0.728
Commensal	6.61 ± 1.73	
Colonizer	7.09 ± 2.60	
Direct	7.05 ± 2.23	
Contaminant	6.50 ± 2.12	

Type of pathogenic organism		0.222
Pathogenic-commensal	6.62 ± 1.77	
Pathogenic-colonizer	7.36 ± 2.65	
Pathogenic-direct	7.05 ± 2.23	
Type of non-pathogenic organism		0.086
Non-pathogenic commensal	6.53 ± 1.31	
Non-pathogenic colonizer	5.00 ± 0.00	
Non-pathogenic contaminant	6.50 ± 2.12	
Patient outcome		0.187
Discharged	6.73 ± 1.97	
Death	6.40 ± 0.97	
Duration of hospitalization (days)	Correlation coefficient (rho) = -0.06	0.318
Cost of antibiotics (Rs)	Correlation coefficient (rho) = 0.09	0.119
Thirty day mortality		0.617
Yes	7.38 ± 2.83	
No	6.73 ± 1.94	

Table 2: Table for association between thirty day mortality and parameters

Parameters	Thirty day mortality		p value
	Yes (n = 8)	No (n = 267)	
Age (years)	36.00 ± 20.10	48.01 ± 16.48	0.051
Age			0.113
18-60 years	6 (75.0%)	202 (75.6%)	
>60 years	2 (25.0%)	65 (24.4%)	
Gender			0.478
Male	4 (50.0%)	168 (62.9%)	
Female	4 (50.0%)	99 (37.1%)	
Localized symptoms of UTI (yes)	6 (75.0%)	223 (83.5%)	0.625
Symptom: increased urination (yes)	3 (37.5%)	95 (35.6%)	1.000
Symptom: urination urgency (yes)	1 (12.5%)	45 (16.9%)	1.000
Symptom: dysuria (yes)	4 (50.0%)	154 (57.7%)	0.726
Symptom: pyuria (yes)	1 (12.5%)	22 (8.2%)	0.507
Symptom: hematuria (yes)	0 (0.0%)	7 (2.6%)	1.000
Symptom: flank pain (yes)	1 (12.5%)	32 (12.0%)	1.000
Factor for asymptomatic bacteriuria: pregnancy (yes)	1 (12.5%)	1 (0.4%)	0.057
Factor for asymptomatic bacteriuria: urological procedure (yes)	0 (0.0%)	12 (4.5%)	1.000
Factor for asymptomatic bacteriuria: post renal transplant (yes)	0 (0.0%)	0 (0.0%)	1.000
Factor for asymptomatic bacteriuria: none (yes)	1 (12.5%)	31 (11.6%)	1.000
SOFA score change >1 (yes)	6 (75.0%)	62 (24.4%)	0.005
Pathogenicity (microbiologist) (pathogenic)	8 (100.0%)	267 (100.0%)	1.000
Pathogenicity (algorithm)			1.000
Pathogenic	8 (100.0%)	241 (90.3%)	
Non-pathogenic	0 (0.0%)	26 (9.7%)	
Nature of organism			0.496
Commensal	6 (75.0%)	183 (68.5%)	
Colonizer	2 (25.0%)	42 (15.7%)	
Direct	0 (0.0%)	40 (15.0%)	
Contaminant	0 (0.0%)	2 (0.7%)	
Type of pathogenic organism			0.402
Pathogenic-commensal	6 (75.0%)	164 (68.0%)	
Pathogenic-colonizer	2 (25.0%)	37 (15.4%)	
Pathogenic-direct	0 (0.0%)	40 (16.6%)	
Type of non-pathogenic organism			1.000
Non-pathogenic commensal	0 (nan%)	19 (73.1%)	
Non-pathogenic colonizer	0 (nan%)	5 (19.2%)	
Non-pathogenic contaminant	0 (nan%)	2 (7.7%)	
Duration of hospitalization (days)	27.75 ± 29.56	13.52 ± 10.09	0.017
Duration of antibiotics (days)	7.38 ± 2.83	6.73 ± 1.94	0.617
Cost of antibiotics (Rs)	2202.50 ± 710.63	2290.05 ± 894.69	0.501

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DISCUSSION

This study demonstrates the tangible economic and clinical implications of correctly identifying non-pathogenic urinary isolates in hospitalized patients. While the mean duration of antibiotic therapy did not differ significantly between groups (7 days), trends suggest that those with non-pathogenic isolates received un-necessary therapy and incurred antibiotic costs. Patients with isolates categorized as non-pathogenic colonizers or contaminants had notably received antimicrobial expenditures. These findings mirror earlier studies where unnecessary antibiotic therapy was associated with increased cost and no improvement in clinical outcomes[7,8].

Shrestha et al. found that suboptimal or inappropriate UTI treatment increased hospital resource utilization without reducing mortality or complications[9]. Similarly, in our study, none of the patients with non-pathogenic isolates experienced 30-day mortality, reinforcing that conservative management is clinically safe. Although not statistically significant, patients with non-pathogenic isolates had hospital stays on average (10 days), aligning with prior observations that diagnostic accuracy can help de-escalate therapy and facilitate earlier discharge [15,16]. The absence of mortality in the non-pathogenic group in our study echoes similar findings in large UTI cohorts where overdiagnosis led to unnecessary hospitalization but not improved survival[17].

These findings align with earlier reports highlighting overtreatment of asymptomatic bacteriuria and colonizers in hospitalized settings, especially when urinary isolates are misinterpreted in the absence of robust clinical correlation[3]. Our use of a clinical-microbiological algorithm provides a replicable model for real-world antimicrobial stewardship. The large effect size (r = 0.48) for cost savings describes how modest diagnostic reclassification efforts can yield measurable resource benefits. One observation in this study needs to be discussed regarding the cost difference between the pathogenic and non-pathogenic groups despite the same median duration of hospital stay and antibiotic duration. This is mostly due to random effect or by chance, as statistically it was not significant; a future large study may clarify this.

These results emphasize the role of clinical decision-making and diagnostic stewardship in ASPs. Integrating structured algorithms into clinical workflows can enable clinicians to distinguish true infection from colonization, minimizing inappropriate treatment[18]. Our findings support previous recommendations to expand laboratory-clinician collaboration in diagnostic interpretation and real-time stewardship feedback[19].

Moreover, the absence of mortality in the non-pathogenic group reinforces the safety of withholding or de-escalating antibiotics in such cases. The model emphasizes a shift from microbiological positivity to clinically contextualized pathogen identification—resonating with stewardship principles outlined in recent IDSA guidance[20].

The implications are particularly relevant in low- and middle-income countries (LMICs), where limited healthcare budgets and high antibiotic resistance prevalence necessitate careful antibiotic allocation[10,12].The study presents a scalable, low-resource strategy—based on clinical judgment supported by structured isolate categorization—that can be implemented even in the absence of sophisticated molecular diagnostics.

Strengths of this study include its prospective design, structured isolate classification by multiple experts, and direct measurement of cost data. However, limitations include the single-centre setting, lack of long-term follow-up beyond 30 days, and absence of formal cost-effectiveness modelling. Furthermore, a small number of non-pathogenic isolates is a limitation too, calling for larger multicentric studies.

CONCLUSIONS

This study demonstrates a measurable economic and clinical impact of misidentifying non-pathogenic urinary isolates as pathogens. In this study, all non-pathogenic urinary isolates (9.45% of total cases) were initially misclassified as pathogenic by both microbiologists and treating clinicians, leading to a median antibiotic cost of ₹640 (IQR: ₹455–925), a median antibiotic duration of 7 days, and a median hospital stay of 10 days (IQR: 5.25–17.75), despite their non-pathogenic nature. Had the stepwise model been applied during real-time decision-making, unnecessary antimicrobial use and associated costs could have been avoided without compromising patient outcomes, as no mortality was observed in this group. These findings confirm the need for both microbiologists and treating clinicians to adopt structured, stepwise interpretation models to optimize antimicrobial use and reduce unnecessary treatment costs in hospitalized patients.

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CONFLICT OF INTERESTS STATEMENT

The authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

BY, PKP: Conceptualization; Data collection; Analysis; Writing the draft; critically review; Approve

JP, RK, BJO, SS, VKP, AND YAB: Analysis; critically review; Approve

DECLARATION FOR THE USE OF GENERATIVE ARTIFICIAL INTELLIGENCE (AI) IN SCIENTIFIC WRITING:

AI tool was used in preparing this manuscript to grammatically correct the draft.

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