



Prevalence of Extended Spectrum Beta Lactamase Producing *Escherichia Coli* in Urinary Tract Infections in Nepal: A Systematic Review and Meta Analysis

Bindu Ghimire¹, Sakar Adhikari², *Santosh Singh³, Mahesh Giri⁴, Prem Bogati⁵, Sudarshan Dhungana⁶, Pradeep Kumar Shah⁷

Department of Microbiology, Tri-Chandra Multiple Campus, Ghantaghar, Kathmandu, Nepal

*Corresponding E-mail: santoshsingh02058@gmail.com

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Abstract

Extended Spectrum Beta Lactamase producing *E. coli* (ESBL Ec) has been reported from urinary tract infection cases in tertiary care hospitals of Nepal. Despite its significance as antimicrobial resistance indicator, comprehensive national data is lacking for implementation of effective national action plans. The main aim is to determine the pooled prevalence and temporal trends of ESBL Ec in Nepal. Studies from January 2006 to January 2026 were included following PRISMA guidelines; risk of bias was assessed using AXIS tool, and random-effects model was applied to estimate pooled prevalence and heterogeneity. Funnel plot asymmetry was evaluated using Egger's weighted regression, temporal trends were analyzed by meta-regression, and meta-analyses were performed using CMA software (version 4). The pooled prevalence of ESBL Ec was 31.3% (95% CI: 26.436.1; $p < 0.001$) with significant heterogeneity ($I^2 = 94.35\%$, $p < 0.001$). Egger's regression test indicated statistically significant small-study effects ($\beta_0 = 5.84$, $p < 0.0001$) in conjunction with funnel plot asymmetry. ESBL *E. coli* prevalence increased significantly in 2023 (coefficient = 0.723, $p < 0.0001$) and 2025 (coefficient = 0.569, $p < 0.0001$) corroborated by an upward trend in the bubble plot (2019–2025). Reserve antibiotics, colistin and tigecycline, have been used to treat ESBL Ec since 2017. The findings indicate a rising prevalence of ESBL Ec in urinary tract infections in Nepal over recent years. The reliance on reserve-category antibiotics in tertiary care centers further highlights the necessity for robust nationwide antimicrobial resistance surveillance within all provinces of Nepal.

Keywords: ESBL *E. coli*, meta-analysis, prevalence

Introduction

Escherichia coli have been identified as a in ecosystem (Ramos et al., 2020). It is commonest pathogenic entity prevalent known to adapt in between two habitats

viz. intestinal tract warm-blooded animals and environment. The survival outside the biological host depends upon favorable niche (Alteri & Mobley, 2012). The assorted genetic reposition within *E. coli* has enabled it to function both as commensal and pathogenic moiety. Abrupt gene selection, presence of mobile genetic elements and with horizontal gene transfer mechanism in this species has led to development of various antibiotic resistance genotypes (Hall et al., 2021). The exposure of bacteria to selective pressure in and outside the living host and successive mechanism of horizontal gene transfer within and among gram negative organisms has enhanced risk for burden of anti-microbial resistant *E. coli* (Tao et al., 2022).

The ESBL Ec has been categorized as an indicator organism for AMR surveillance (Appling et al., 2023). Recognizing the high risk burden of antimicrobial resistant *E. coli*, World Health Organization (WHO) has categorized Extended Spectrum Beta Lactamase Producing *E. coli* (ESBL Ec) as critical priority pathogen (Olaitan et al., 2025). Valid microbiological reporting is utmost for repeated monitoring, effective surveillance to tackle high prevalence AMR *E. coli* (Lim et al., 2021). AMR surveillance started in Nepal in 1999. National Public Health Laboratory and Epidemiology and Disease control division are functioning

as National Coordination Laboratory and National Focal point for surveillance program coordinating with 42 (21 hospitals and 21 OPDs) sites in each province. ESBL Ec was listed in surveillance in 2002 and 0-60% third generation cephalosporin (3GC) resistance has been reported for *E. coli* (Gautam et al., 2023).

Despite the implementation of Nepal's National Action Plan on Antimicrobial Resistance (NAP-AMR) 2024–2028 and increasing reports of ESBL Ec from human, animal, and environmental sources (Acharya et al., 2024), comprehensive pooled estimate of the prevalence of ESBL Ec causing human infections in Nepal is lacking. Furthermore, evidence on temporal trends in ESBL Ec prevalence and consolidated resistance patterns to commonly used antimicrobial classes in clinical settings remains limited and fragmented, constraining effective AMR surveillance, antimicrobial stewardship programs, and evidence-based infection control policies. Hence, this study was conducted to estimate the pooled prevalence of ESBL Ec, an indicator organism for AMR surveillance, isolated from human urinary tract infections in Nepal, and to assess the temporal trends in reported ESBL Ec cases from 2006 onward.

Methodology

This systematic review was conducted using data reported from tertiary care

hospitals in Nepal. Laboratory-based studies that reported the identification of ESBL Ec in patients suspected of urinary tract infections (UTIs) at tertiary care hospitals in Nepal were systematically reviewed. All available data from January 2006 to January 2026 were included in the study. Comprehensive Meta-Analysis software VERSION 4 was used to perform the meta-analysis. The pooled prevalence of ESBL Ec was calculated where the data selection for the meta-analysis followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). This review is registered under PROSPERO CRD42021286959.

Study area: Urine samples from tertiary care hospitals in seven major districts of Nepal were used in this study to look into reported cases of urinary tract infections caused on by ESBL Ec. Bagmati Province, which includes Kathmandu (20 hospitals), Lalitpur (1 hospitals), Bhaktapur (1 hospital), and Chitwan (2 hospital), generated the highest amount of published reports. The study also included one hospital from Dhanusha district in Madhesh Province, four hospitals from Sunsari district in Koshi Province, and one hospital from Kaski district in Gandaki Province that reported ESBL Ec cases. The geographic locations of the tertiary care hospitals reporting ESBL Ec prevalence are illustrated on the map of Nepal (**Figure 1**).

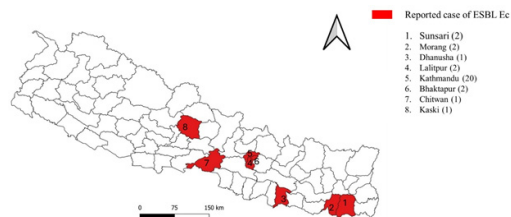


Figure 1: Map showing location of tertiary care hospital reporting ESBL *E. coli* in urine samples

Literature search strategy: All available data and records retrieved from electronic sources were included in the study. Articles were searched in PubMed, EMBASE, the Cochrane Library, Google Scholar, and Scopus databases. Cross-references from the selected articles were also screened to identify any additional relevant studies. The search terms “*Escherichia coli* in Nepal”, “Extended spectrum beta lactamase *E. coli*, Nepal”, “Urinary tract infection Nepal”, and “Prevalence of *E. coli*, Nepal” were used. The detailed search term and filters are provided in supplementary File 1 (SF1).

Inclusion criteria: It includes microbiological studies of *E. coli* conducted in tertiary care hospitals in Nepal; studies reporting both the total number of *E. coli* isolates and the number of ESBL-producing *E. coli* isolates from urine samples collected from outpatients and inpatients of all age groups; studies in which confirmatory testing for ESBL production was performed using the combination disk diffusion technique; and full-text articles available in the English language.

Exclusion criteria: The studies conducted outside tertiary-care hospitals, those that did not report the total *E. coli* and ESBL Ec isolates, and studies available only as abstracts were eliminated to ensure methodological consistency and precise prevalence estimation. Studies in which confirmatory testing was performed using non-standard techniques, or those reporting ESBL Ec isolates from patients with specific conditions such as children, the elderly, particular age groups, organ transplant recipients, or diabetic patients were also excluded. Due to their distinctive patterns of antimicrobial exposure, these populations might have a disproportionate impact on prevalence estimates and were less appropriate for baseline AMR surveillance. Additionally, retrospective studies and studies in which laboratory work was performed by individuals other than the authors were not considered to reduce selection bias and improve cross-study comparability.

Bias assessment: AXIS tool was used for bias assessment which encompasses twenty different components. The results for summary of the axis assessment are presented as supplementary File 2 (SF2).

Meta-analysis: The 30 studies selected for meta-analysis were entered into and analyzed by using the Comprehensive Meta analysis software V4.exe.lnk. A random-

effects model was applied because all the samples were urine samples, and similar procedures were used for the analysis and reporting of ESBL. The Mantel–Haenszel inverse variance method was employed with 95% confidence interval (CI) and a forest plot was generated. The I^2 statistic was calculated to assess heterogeneity among the study variables, and Egger’s test was used to determine the bias intercept and calculate the t -value for potential publication bias. Meta regression analysis was performed with time as moderators and bubble plot was generated. Hospital antibiotic-use patterns and antimicrobial resistance data were extracted from the studies included in the meta-analysis.

Results

Overview of the search output and screening assessment

Based on searches by place, title, abstract, and keywords, a total of 224 articles were initially identified. These articles were further scrutinized according to the variables outlined in the PRISMA checklist. Bias assessment was performed independently using the AXIS tool. Ultimately, 30 full-text articles were selected for inclusion in the meta-analysis. The flowchart of article identification, screening and inclusion is presented in PRISMA flowchart (**Figure 2**). The characteristics of the included studies are given in **Table 1**.

Table 1: *Characteristics of included study for systematic review and Meta analysis*

S.N	District	Authors	Year	Place	Total <i>E. coli</i>	ESBL Ec
1	Kathmandu	Pokharel et al. (2006)	2006	Tribhuvan University Teaching Hospital	323	58
3	Kathmandu	Poudyal et al. (2011)	2011	Kathmandu Model Hospital	133	15
2	Kathmandu	Baral et al. (2012)	2012	National Public Health Laboratory	178	16
4	Kathmandu	Chander & Shrestha (2013)	2013	KMC and Teaching Hospital	444	60
5	Kathmandu	Pokhrel et al. (2014)	2014	KMC and Teaching Hospital	80	24
6	Kathmandu	Yadav et al. (2015)	2015	National Kidney Center	67	18
7	Morang	Chakraworty et al. (2015)	2015	Bijayapur Hospital	69	12
8	Kathmandu	Subedi et al. (2016)	2016	Kathmandu Institute of Science & Technology	77	52
9	Kathmandu	Bhandari et al. (2016)	2016	National Public Health Lab	88	34
10	Morang	Dahal & Bhandari (2016)	2016	Bijayapur Hospital	63	11
11	Kathmandu	Nuepane et al. (2016)	2017	Chauni Hospital	208	69
12	Kathmandu	Shakya et al. (2017)	2017	Alka Hospital	365	33
13	Kathmandu	Rai et al. (2017)	2017	Alka Hospital	391	33
14	Bhaktpur	Khatrri et al. (2017)	2017	Korea Nepal Friendship Hospital	96	31
15	Dhanusha	Yadav & Prakash (2017)	2017	Janaki Medical College and Teaching Hospital	123	43
16	Kathmandu	Nepal et al. (2017)	2017	Om Hospital	116	38
17	Kathmandu	Wagle et al. (2018)	2018	Norvic Intenational Hospital	242	54
18	Kathmandu	Guragai et al. (2019)	2019	Everest Hospital	48	15
19	Kathmandu	Shrestha et al. (2019)	2019	ManMohan Memorial Medical college and Teaching Hospital	159	81
20	Sunsari	Shah et al. (2019)	2019	BP Koirala Institute of Health Science	105	49
21	Kathmandu	Pandit et al. (2020)	2020	Grande Hospital	154	62
22	Kathmandu	Chaudary et al. (2020)	2020	BP Koirala Institute of Health Science	1098	194
23	Kathmandu	Thapa Shrestha et al. (2020)	2020	Kathmandu Model Hospital	507	133
24	Chitwan	Gurung et al. (2021)	2021	Bharatpur Medical	37	14
25	Kathmandu	Koirala et al. (2021)	2021	Bir Hospital	171	74
26	Kathmandu	Khanal et al. (2022)	2022	Nepal Medical College Teaching Hospital	360	58
27	Kathmandu	Chaudary et al. (2023)	2023	Nepalese Army Institute of Health Sciences	215	194
28	Kathmandu	Sah et al. (2024)	2024	Grandae International Hospital	165	48
29	Kathmandu	Shrestha et al. (2024)	2024	ManMohan Memorial Medical college and Teaching Hospital	45	35
30	Kaski	Poudel et al. (2025)	2025	Manipal Teaching Hospital	135	101

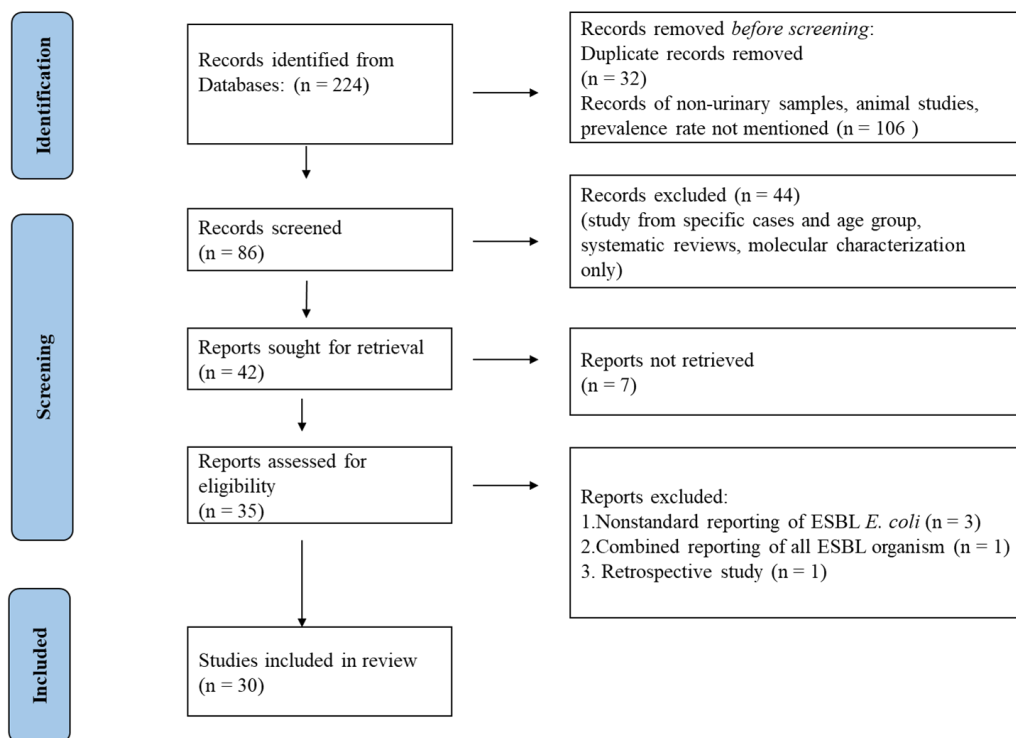


Figure 2: PRISMA framework showing the included study for systematic review

Temporal trend in ESBL *E. coli* (2006-2025)

The fitted line of regression in the bubble plot showed temporal trend of ESBL Ec in urine samples derived from meta regression analysis which demonstrated increasing prevalence in recent years (**Figure 3**). The early year bubble (2011-2019) clustered around smaller effect size showing minimal changes in prevalence rate. Meta regression analysis showed significant rise in ESBL Ec prevalence in 2023 ($\beta=0.7228$, $p<0.001$) and 2025 ($\beta=0.5686$, $p<0.001$) which was shown as later bubble (2019-2025) appearing higher on Y axis. The detail

of meta regression analysis is given as supplementary File 3 (SF3).

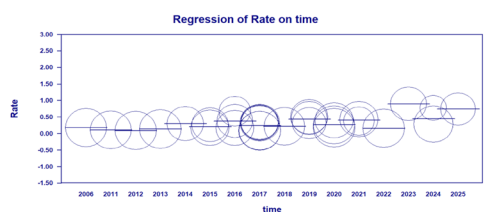


Figure 3: Timeline trend for prevalence of ESBL *E. coli* in Nepal

Heterogeneity and publication bias

The funnel plot was drawn to find the heterogeneity in the selected study. Although the symmetry of the funnel plot

showed no heterogeneity with almost equal distribution, the data were widely scattered (**Figure 4**). By applying the Duval and Tweedie's Trim and fill model to both the right and left side of the funnel plot, none of the studies were found to be missing in our study. Further I^2 value was calculated as 94.2%, $p < 0.001$ suggestive of heterogeneous study variables (**Figure 4**).

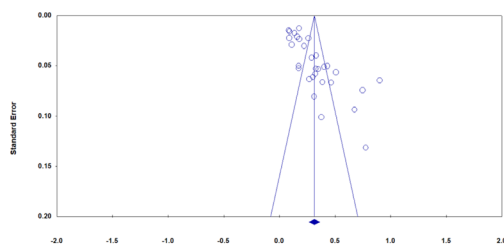


Figure 4: Funnel plot showing Logit event rate

Meta Analysis and prevalence rate calculation

Using the random-effects model, the pooled event rate was calculated to be 0.313, with a 95% confidence interval of 0.264 to 0.361, hence calculated pooled prevalence is approximately 31.3%. The pooled Z-value of 12.619 with a p-value of < 0.001 indicates that this estimate is highly statistically significant (**Figure 5**).

Initial use of antibiotics for Antibiotic Susceptibility Testing

Since the first reported case of ESBL in 2006 various antibiotics have been prescribed for the AST testing in the hospital setting.

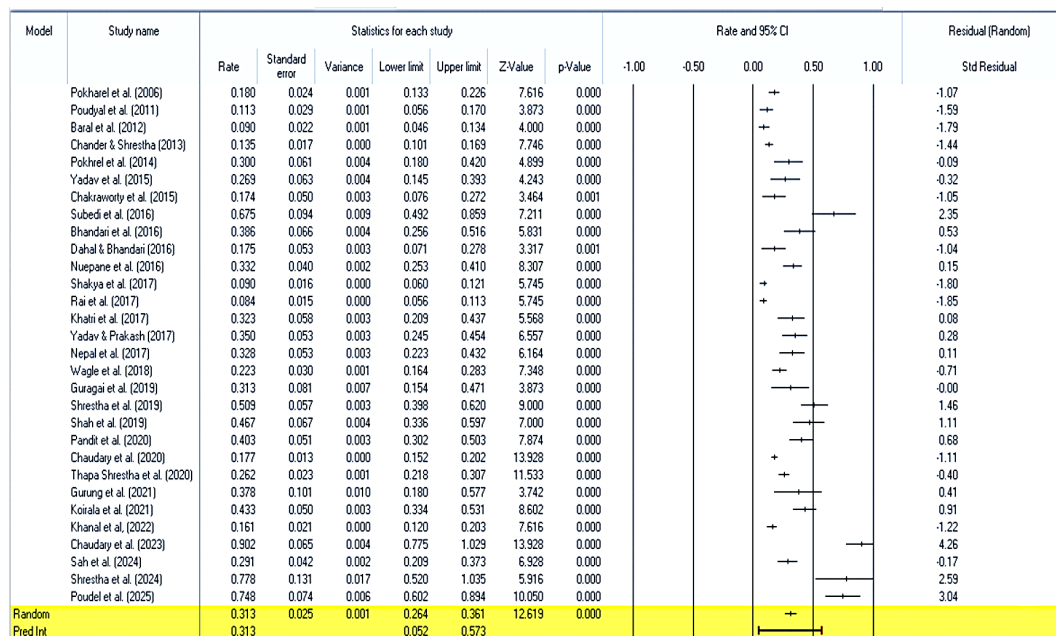


Figure 5: Forest plot and meta-analysis with pooled prevalence rate

Most of the access and watch groups of antibiotics are used in practice and since 2017 the reserve group of antibiotics Colistin and Tigecycline are also used.

The thirteen different classes of antibiotics are recently used in treatment of *E. coli* associated Urinary Tract Infection in Nepal (Table 2).

Table 2: Antibiotics used in treatment of urinary tract infection from 2006-2025

Antibiotic Class	AWARe Category	2006	2007	2013	2014	2015	2016	2017
Penicillin	Access	Ampicillin	Amoxycillin					
Beta lactam/ beta lactamase inhibitor	Access							Amoxi-clav
	Not Recommended Reserve					Cefoperazone/ Sulbactam Piperacillin/ tazobactam		
Cephalosporin First-generation	Access			Cephalexin	Cefazolin			
Second generation	Watch					Cefoxitin		
Third generation	Watch		Ceftazidime	Cefotaxime		Ceftriaxone	Cefixime	
Fourth generation	Reserve				Cefepime			
Fluoroquinolones	Access		Ciprofloxacin, Norfloxacin					
	Watch		Ofloxacin		Levofloxacin			
Sulfonamide- trimethoprim- combinations	Access		Cotrimoxazole					
Aminoglycosides	Access		Gentamicin	Amikacin		Tobramycin		
	Watch						Fosfomycin	
Nitrofurantoin	Access		Nitrofurantoin					
Macrolides	Watch					Erythromycin		
Amphenicols	Access			Chloramphenicol				
Carbapenem	Reserve				Meropenem		Imipenem	
Polymyxin	Reserve							Colistin
Glycylcyclines	Reserve							Tigecycline

Discussion

Antimicrobial resistance (AMR) is a critical global issue, addressed by international organizations and researchers worldwide. Its impact extends beyond infected patients; the carriage and transmission of resistant bacteria among healthy populations and through the environment have caused severe outbreaks of multidrug-resistant

(MDR) infections. A particularly serious threat is posed by ESBL-producing Enterobacteriaceae (Ho et al., 2025).

The major after effect of the antimicrobial resistance will be seen in the Low and middle income countries affecting 26.2M people (Ye et al., 2025). Among these

countries, the Federal Republic of Nepal faces challenges during the transitional phase of health sector development (Wasti et al., 2023), particularly in drafting and implementing rules and regulations to govern antimicrobial resistance (AMR) (Thapa et al., 2018). The burden of increased resistance towards the antimicrobial drug will challenge for punitive treatment which will be hard to render by citizens of Nepal (Acharya & Wilson, 2019).

The first case of multidrug-resistant *E. coli* in Nepal was reported by Tanakawa et al. in 1978. The first documented case of ESBL Ec, with a prevalence of 5.6%, was reported by Pokharel et al. in 2006. Since then, several large studies have been conducted in tertiary care hospitals to detect and monitor ESBL Ec. As ESBL Ec is considered an important indicator of antimicrobial resistance, it is essential to understand its prevalence and distribution across different countries.

In this study, the meta regression analysis using year as moderator value showed a higher prevalence of ESBL Ec from 2019 to 2025 rather than consistent linear temporal trend. The increased prevalence of urinary tract infections in Nepal caused by ESBL Ec increased due to a complex interaction between biological, clinical, and policy-level factors (Husna et al., 2023). Strong selection pressure for resistant strains has resulted from the widespread use and abuse of broad-spectrum antibiotics, often

without adequate culture and sensitivity testing (Rijal et al., 2021). These resistant organisms have been able to survive and spread due to inadequate antimicrobial stewardship and inadequate infection control procedures in many healthcare settings (Acharya & Wilson, 2019).

The highest number of cases, 66.6% (n = 20), was reported from Bagmati Province, compared to Province 1 and Province 2 and 4. No published data are available from the other three provinces of Nepal. Bagmati Province has the largest population in the country (20.8%) (Mishra et al., 2023) and hosts the highest number of tertiary care hospitals (57) (Ojha et al., 2025). The majority of the research included in this meta-analysis was carried out in tertiary care facilities that offer services to a significant urban population in Nepal's metropolitan and sub-metropolitan regions. As sentinel sites for the national antimicrobial resistance (AMR) surveillance program, these hospitals serve as important referral centers and provide a population-based approach for AMR surveillance in urban environments (Malla et al., 2014). However, because the included studies are largely restricted to urban tertiary care facilities, the generalizability of these findings at the provincial or national level may be limited (Maharjan et al., 2023).

A symmetry curve was plotted to assess the parametric distribution of the data. Using Duval and Tweedie's Trim and Fill method

on both sides of the funnel plot, no missing studies were identified in our analysis. Given the high heterogeneity ($I^2 = 94.2\%$, $p < 0.001$), a random-effects model was applied to calculate the pooled prevalence. The substantial I^2 value indicates considerable variability among the studies, which can be attributed to differences in geographical location, sample size, methodological approaches, and study periods. Variations in hospital settings, seasonal factors, diagnostic capacity among tertiary-care centers, and changes in antibiotic prescription and utilization patterns over time could all account for the significant heterogeneity reported (Azzam et al., 2024). Also, the axis assessment summarized the included studies of moderate quality, with an average score of 12 out of 20 (60%). Differences in their design, sampling, and reporting were likely contributed to the variation in results which is reflected in the I^2 statistic.

This meta-analysis estimated an event rate pooled prevalence of 31.3%, similar to 33% reported for South Asia by Islam et al. (2023). The growing number of ESBL-producing *E. coli* cases in Nepal is likely the result of everyday community spread, constant movement of people across the open border with India, infections picked up inside hospitals, and the continued misuse of antibiotics (Parajuli et al., 2024; Acharya et al., 2025).

In this study Colistin and Tigecycline, the reserve group of antibiotics are in use since

2017. For more than fifteen years, antibiotics from the Access and Watch groups have been routinely used in clinical practice to treat *E. coli* infections. Recently, the use of Reserve group antibiotics has accelerated, with these agents increasingly being selected as frontline treatments. The gradual selection of multidrug-resistant and ESBL *Ec* strains has likely been facilitated by the extensive use of Access and Watch group antibiotics over the past decade and a half (Ibrahim et al., 2023). Of particular concern is the increasing reliance on reserve-group antibiotics as primary treatment options. These agents are intended to be used only as last-line therapies, and their inappropriate early use risks accelerating the emergence of resistance, ultimately diminishing the effectiveness of the few remaining drugs available for severe or hard-to-treat infections (Sharland et al., 2018).

Nepal's AMR surveillance, initiated in 1999, includes ESBL-producing *E. coli* since 2002 and currently operates through 42 surveillance sites nationwide (Khadka & Giri, 2021). However, due to limited personnel capacity and underdeveloped diagnostic infrastructure, AMR reporting at the NPHL remains inconsistent, resulting in many ESBL *Ec* cases going unreported (Upadhaya et al., 2023). At the policy level, Nepal has recently strengthened its response to antimicrobial resistance through implementation of the National Action Plan on AMR (2024–2028), which emphasizes

integrated surveillance, stewardship programs, and rational antimicrobial use across human, animal, and environmental sectors (GoN, 2024). The country also participates in WHO's Tricycle surveillance project to monitor ESBL Ec and is working to improve diagnostic stewardship and clinician-laboratory collaboration to guide appropriate antibiotic use (Acharya et al., 2025). These efforts aim to curb inappropriate prescribing and enhance data-driven practices, although challenges in enforcement and widespread implementation remain (Gunasekara et al., 2025).

This is the first systematic review to calculate the pooled prevalence rate of ESBL Ec associated with UTI from Nepal reported from 2006 to 2025. However, the study had some limitations regarding the availability of the authentic prevalence data from across all the tertiary care hospitals within different provinces of Nepal. Provincial level data are largely unavailable, making it challenging to determine national burden of ESBL Ec based on the different spatial distribution. This gap in comprehensive reporting highlights the urgent need to strengthen the national surveillance framework by enhancing laboratory capacity, increasing trained human resources, and implementing standardized systems for data collection and reporting in order to more accurately monitor and address the growing threat of antimicrobial resistance in all district hospitals of Nepal.

Conclusions

This systematic review and meta-analysis indicate a significant pooled prevalence of ESBL Ec (31.3%) in urine samples from 20 hospitals in Bagmati Province, signifying a considerable public health risk. The considerable heterogeneity ($I^2 = 94.35\%$) and asymmetry in the funnel plot indicate variability in study populations, laboratory methodologies, and potential publication bias, necessitating careful interpretation of the overall estimate. Meta-regression shows a significant upward trend in ESBL prevalence from 2023 to 2025, demonstrating the rapid escalation of antimicrobial resistance Nepal. The ongoing dependency on reserve antibiotics (colistin and tigecycline) since 2017 indicates the depletion of first-line treatment alternatives and the urgent need for antimicrobial stewardship.

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Author's Contribution

Concept and design: BGT, SA, PKS; Development of data screening form: BGT, PB, PKS; study searching: MG, SA,SD, PB,SS; Data screening: BGT, SS, SA; Preparing bias assessment form: BGT, PB, MG, PKS; Data analysis and interpretation: BGT, PKS; Manuscript preparation, revision and correction: BGT

Conflict of Interest

The authors declare no conflict of interest.

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