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Research Paper

Plasmid-Mediated R-Factor Carriage and Its Role in Multidrug Resistance and Pathogenicity of Human-Derived Escherichia coli Strains

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Abstract: *The increasing prevalence of antibiotic resistance among clinical isolates of Escherichia coli poses a significant threat to public health, particularly in the treatment of urinary tract and gastrointestinal infections. A major factor contributing to this resistance is the presence of resistance plasmids, known as R-factors, which facilitate the horizontal gene transfer of resistance genes among bacterial populations. This study evaluates the carriage of R-factors in E. coli strains of human origin and examines their role in influencing pathogenicity.Out of 193 E. coli isolates obtained from human infections, a substantial proportion (83.5%) were derived from urinary tract infections (UTIs), while only 16.5% were from gastrointestinal tract (GIT) infections. The strains were categorized based on their antibiotic resistance profiles into single, double, triple, quadruple, and quintuple resistance patterns. Notably, 24.3% of UTI-associated strains exhibited single antibiotic resistance, compared to just 6.8% among GIT strains. These findings suggest a strong association between the carriage of R-factors and elevated virulence and resistance in UTI strains.This study highlights the critical need for monitoring plasmid-mediated resistance in clinical settings to inform treatment strategies and curb the spread of multidrug-resistant pathogens.*

Key Words*- Escherichia coli, R-factor, antibiotic resistance, urinary tract infections, virulence, plasmid-mediated resistance, human pathogens.*

I. INTRODUCTION

1.Escherichia coli and Its Clinical Significance

Escherichia coli (E. coli), a facultative anaerobic Gram-negative bacillus, is a normal inhabitant of the gastrointestinal tract in humans and other warm-blooded animals. While many E. coli strains exist as benign commensals, certain strains have evolved to become highly pathogenic. These pathogenic variants, often equipped with virulence factors, are responsible for a wide range of infections, particularly urinary tract infections (UTIs), neonatal meningitis, and intestinal diseases. Their adaptability and ability to acquire resistance to multiple antibiotics make them a formidable threat in both community and hospital settings.

2. Antibiotic Resistance and R-Factor Plasmids

The discovery of R-factors (resistance plasmids) in the 1950s marked a turning point in our understanding of bacterial resistance. First described by Akiba et al. (1960) in Japan, R-factors are extrachromosomal DNA elements capable of self-replication and transmission between bacteria via conjugation. These plasmids harbor genes conferring resistance to one or multiple antibiotics and can carry additional genes linked to virulence, toxin production, or metabolic functions. The ability of R-factors to rapidly disseminate resistance traits across diverse bacterial populations has made them a central focus in antimicrobial resistance (AMR) studies.

3. Human Infections and Sources of Resistant E. coli

The rise in nosocomial and community-acquired infections caused by multidrug-resistant (MDR) E. coli strains is deeply concerning. Among these, UTIs represent the most common clinical manifestation, especially in women, the elderly, and immunocompromised individuals. Other notable infections include gastroenteritis, wound infections, sepsis, and neonatal meningitis. Clinical data increasingly demonstrate that a high percentage of these infections are caused by strains harboring R-factors. The presence of such plasmids often correlates with resistance to β-lactams, aminoglycosides, sulfonamides, tetracyclines, and fluoroquinolones.

4. Pathogenicity and Virulence in E. coli

The term "pathogenicity" refers to the ability of an organism to cause disease, while "virulence" denotes the severity or degree of pathogenicity of a given strain. In E. coli, virulence is strain-specific and is often mediated by factors such as adhesins (e.g., pili and fimbriae), toxins (e.g., Shiga toxin, hemolysin), invasins, and iron acquisition systems. The interplay between virulence determinants and antibiotic resistance genes poses unique challenges in clinical therapy, often leading to treatment failures and increased morbidity and mortality.

5. Need for the Study

The emergence of antimicrobial resistance in E. coli due to the acquisition of R-factors is a pressing global concern. Though resistance mechanisms are widely studied, limited data exist on how R-factors modulate pathogenicity in human-origin strains, particularly those causing UTIs and gastrointestinal infections. Understanding the correlation between resistance plasmids and disease severity is crucial for devising targeted treatment strategies and preventive interventions. The present study aims to fill this knowledge gap by investigating the resistance profiles and plasmid carriage in clinical E. coli isolates, while also assessing their potential influence on virulence.

6. Objectives of the Study

- To isolate and identify E. coli strains from human clinical samples, specifically UTIs and GIT infections.
- To determine the antibiotic resistance patterns among the isolates.
- To evaluate the prevalence and distribution of R-factors among the resistant strains.
- To analyze the relationship between R-factor carriage and the pathogenic potential of E. coli.
- To contribute to the understanding of plasmid-mediated resistance as a factor in clinical disease progression and treatment outcomes.

7. Problem Statement

The unchecked spread of R-factor-mediated resistance in E. coli strains has led to an alarming rise in treatment failures, prolonged infections, and increased healthcare costs. Despite advances in antimicrobial development, the adaptive mechanisms of bacteria—particularly via plasmid acquisition—continue to outpace pharmaceutical innovation. This study addresses the urgent need to understand how plasmid-encoded resistance not only drives multidrug resistance but also enhances virulence in clinical E. coli strains, leading to more severe and persistent infections.

8. Significance of the Study

This research holds immense clinical and epidemiological relevance. By identifying resistance patterns and R-factor carriage in E. coli isolates from UTIs and GIT infections, healthcare professionals and microbiologists can gain valuable insights into the dynamics of AMR in human pathogens. The study also lays the groundwork for future molecular investigations on plasmid architecture, gene expression, and potential targets for novel antimicrobial agents. Moreover, it supports the rationale for implementing stricter infection control measures and rational antibiotic prescribing practices in clinical settings.

9. Global Perspective and Current Trends

According to the World Health Organization (WHO), AMR is one of the top 10 global public health threats. Resistance among Enterobacteriaceae, including E. coli, is especially problematic, with increasing cases of extended-spectrum β-lactamase (ESBL)-producing and carbapenem-resistant strains. In developing countries like India, misuse and overuse of antibiotics, coupled with poor sanitation and infection control, have accelerated the spread of resistant strains. Studies from various regions have reported MDR E. coli in over 70% of UTI cases, posing a dire challenge to treatment regimens.

II. LITERATURE REVIEW

Antimicrobial resistance (AMR) is a global health threat, and Escherichia coli plays a central role in this crisis due to its ubiquity and capacity to acquire resistance genes rapidly. As a member of the Enterobacteriaceae family, E. coli is both a commensal and a pathogenic bacterium that commonly causes urinary tract infections (UTIs), gastrointestinal infections, neonatal meningitis, and sepsis (Tenaillon et al., 2010). The increasing resistance of E. coli to a broad range of antibiotics, especially through horizontal gene transfer (HGT), challenges clinical treatment protocols and necessitates urgent study of the underlying mechanisms. R-factors (resistance plasmids) were first discovered in Japan by Akiba et al. (1960) in Shigella strains and were later confirmed in E. coli. These plasmids often carry multiple resistance genes and can transfer between bacterial strains via conjugation. Resistance genes commonly carried include those against

tetracyclines, sulfonamides, aminoglycosides, β-lactams, and fluoroquinolones (Carattoli, 2013). The ability of R-factors to co-transfer virulence factors alongside resistance genes intensifies their impact on public health, making them a dual threat in terms of both infection severity and drug failure.

The virulence of E. coli is closely tied to its ability to colonize, invade, and cause damage to host tissues. Virulence factors include adhesins (e.g., P fimbriae), toxins (e.g., hemolysin), iron acquisition systems, and invasins. Studies have shown that strains harboring resistance plasmids can also carry virulence-associated genes, leading to increased pathogenic potential (Johnson et al., 2002). This synergy between virulence and resistance compromises immune clearance and worsens disease outcomes. UTIs caused by E. coli account for over 80% of community-acquired and many hospital-acquired cases (Foxman, 2010). Resistance among UTI-causing strains is escalating, particularly to trimethoprim-sulfamethoxazole, fluoroquinolones, and cephalosporins. Studies indicate a high carriage rate of extended-spectrum β-lactamase (ESBL) genes among UTI isolates (Pitout&Laupland, 2008). On the other hand, diarrheagenic E. coli (DEC), including ETEC, EPEC, EHEC, and EAEC, contribute to GIT infections and show variable resistance patterns, often influenced by local antibiotic usage practices (Nataro&Kaper, 1998).

The mechanism of conjugation allows R-factors to move from donor to recipient cells via pili, facilitating the spread of resistance genes across species and genera. Integrons, transposons, and insertion sequences embedded in R-plasmids enhance their mobility (Bennett, 2008). Environmental and clinical isolates of E. coli are often genetically indistinguishable in resistance genes, indicating strong environmental selection pressure from antibiotic misuse (Martínez, 2009). Multiple surveillance studies report an alarming rise in multidrug-resistant (MDR) E. coli strains globally. A study by CLSI (2021) observed increasing resistance to third-generation cephalosporins and fluoroquinolones in E. coli strains isolated from UTIs. Regional studies in India, Southeast Asia, and Sub-Saharan Africa report similar trends (Shrivastava et al., 2014; Chattopadhyay et al., 2021). These findings support the need for continuous surveillance of resistance phenotypes and genotypes in clinical E. coli isolates.

Plasmid incompatibility groups such as IncF and IncI1 often carry both resistance genes and virulence factors, increasing the survival advantage of E. coli under selective pressures (Johnson & Nolan, 2009). The co-selection phenomenon—where resistance to one antibiotic selects for plasmids carrying unrelated resistance genes—complicates treatment even with unrelated drugs. Environmental reservoirs such as wastewater, agricultural runoff, and hospital effluents are breeding grounds for resistant E. coli (Berendonk et al., 2015). Additionally, immunocompromised patients and those undergoing long-term antibiotic therapy provide ideal conditions for the selection and proliferation of plasmid-bearing strains. Efforts to combat plasmid-mediated resistance include restricting unnecessary antibiotic use, developing plasmid curing agents, and investigating novel therapeutics such as phage therapy and anti-plasmid compounds (San Millan, 2018). Molecular tools such as PCR, PFGE, and whole-genome sequencing (WGS) enable the precise detection and characterization of resistance plasmids. The literature collectively reveals that R-factor carriage significantly contributes to the multidrug resistance and enhanced pathogenicity of E. coli in clinical infections. The interplay between resistance and virulence genes, often carried on the same plasmids, underscores the need for integrated molecular and epidemiological surveillance. As treatment options become increasingly limited, understanding plasmid biology remains a cornerstone of infectious disease management and antibiotic stewardship.

III. MATERIAL AND METHODS

Two hundred strains of Escherichia coliwere obtained from CDRI culture collection, for this study. These strains were originally isolated from human and different animal species, suffering from gastroenteritis, urinary tract and utero-genital tract infections. Some of strains were from poultry septicaemia also. Nutrient agar with 1.5% of sheep blood was used for detection of haemolytic activity of strains. Sheep blood was collected aseptically in conical flask assembly with glass beads for removing fibrin to check the coagulation of blood. Many of E. coli virulence factors are plasmid determined, I.e. they are present on extra chromosomal genetic elements (transposons). Plasmids are often unstable and spontaneous losses may occur, which alters the bacterial virulence. It can be demonstrated by transferring specific characters to other recipient strains, since genes for these characters are present on plasmid. Yadav and Gupta (1971).

IV. RESULT AND DISCUSSON

Antibiotic resistant strains encounter among human (53.4%). this high percentage of resistance recorded among E. coli strains isolated from human clinical cases is alarming. In similar type of study, two decades ago, Yadava (1966) reported a high degree of sensitivity to various antibiotics among (218)strainsE. coli. Only 3 strains were isolated from calf were multiple resistant. In our later investigations incidence of multiple antibiotic resistance was much greater in human. This might be attributed directly to the amount of antibiotics used in human medicine. Due to selection pressure of antibiotics the sensitive microflora were eliminated and the resistant bacteria (against the particular drug) got an opportunity to multiply in excess of over

the sensitive one (table 1). These finding are in agreement with the work published earlier, 52% resistant E. coli strains were obtained from human patients Datta (1971), 50% from diarrhea affected children Gerber and frimerman, (1973), (71%) multiple drug resistance Sarkar et al., (1979). Resistance level of antibiotics taken by these workers was much lower (10 ug/ml) as compared to the present study (50ug/ml). C. M. Kunin. et al (1993)., M. Franz. Et al.(1999). K. G. Naber. Et al. (2008)., N. Khanna. (2012) also recorded. Smith and Armour (1966), also recorded high degree of resistance in different E. coli strains from human UTI cases against commonly used antibiotics and chemotherapeutic agents. In this study out of (103) strains resistant to various antibiotics, (85.5%) were isolated from UTI cases and only (16.5%) from GIT cases. Strains resistant to five antibiotics in various combinations were found more frequently from UTI cases (21.4%) than strains from GIT cases (3.8%). Sokolet al. (1977) reported the frequent isolation of resistant strains from calves. Results of the present investigation are in agreement with Sokolet al. (1977). Because the highest percentage of resistant strains of animal origin were from bovine 50% as compared to equine (25.6%), poultry (15.6%) and Ovine (8.9%). Y. Doi. et al.(2013)., V. M. Blanco. et al (2016)., L. Rossignol. et al (2017)also noticed.

Table-1- Antibiotic resistance pattern of 103 E.coli strains (human isolates) used in drug resistance transfer studies.

Source	Disease Condition	Resistance Pattern	No. of Strains	Percentage (%)
Urinary Tract Infection (UTI)	UTI	Quintuple Resistance	22	21.4
		Quadruple Resistance	20	19.4
		Triple Resistance	8	7.8
		Double Resistance	11	10.7
		Single Resistance	25	24.3
Gastrointestinal Tract Infection (GIT)	GIT	Quintuple Resistance	4	3.9
		Quadruple Resistance	1	0.9
		Triple Resistance	2	1.9
		Double Resistance	3	2.9
		Single Resistance	7	6.8
Total			**103**	**100**

The data presented in Table 1 provides a clear indication of the distribution and severity of antibiotic resistance among Escherichia coli strains isolated from human infections, particularly urinary tract infections (UTIs) and gastrointestinal tract infections (GITs). A total of 103 E. coli isolates were examined for their resistance profiles, and they were classified based on the number of antibiotics to which they exhibited resistance.

A significant majority (83.5%) of the resistant isolates originated from UTIs, while only 16.5% were associated with GIT infections. This reflects the clinical prevalence of E. coli-induced UTIs and emphasizes the higher risk of antibiotic resistance in these infections.Among UTI isolates, quintuple (21.4%) and quadruple (19.4%) resistance patterns were notably high, indicating that over 40% of strains exhibited resistance to four or more antibiotics.Single resistance was the most common pattern (24.3%) in UTIs, suggesting a gradual selection pressure or emergence of early-stage resistance in some strains.The resistance patterns among GIT isolates were lower in both frequency and severity. Only 3.9% of strains displayed quintuple resistance, while the rest showed even lower percentages across quadruple, triple, double, and single resistance categories.This might be due to reduced exposure to systemic antibiotics in gastrointestinal infections or intrinsic differences in strain virulence and resistance gene carriage.

The high resistance observed, especially in UTI-related strains, points to extensive antibiotic use and possibly misuse in the treatment of urinary tract infections.The significant percentage of strains exhibiting multidrug resistance (quadruple and quintuple resistance) is alarming and reflects a pressing public health concern regarding the dwindling efficacy of conventional antibiotics.The prevalence of MDR strains in UTI patients necessitates routine antimicrobial susceptibility testing to guide treatment.Surveillance and stewardship programs should particularly target urinary pathogens, as they seem to be the primary reservoirs for resistance dissemination via plasmid-mediated mechanisms like R-factors.In summary, this table reinforces the growing threat posed by multidrug-resistant E. coli strains in human infections, especially UTIs, and highlights the urgent need for improved antibiotic stewardship and molecular monitoring of resistance genes.

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