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REVIEWER'S REPORT

Manuscript No.: IJAR- 50059 Date: 27/01/2025

Title: "A Review on In vitro and In vivo Model Advancements for the Study of Escherichia coli-Induced Urinary Tract Infections"

Recommendation:

✓ Accept as it is .....
Accept after minor revision.....
Accept after major revision .....
Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality		✓		
Techn. Quality		✓		
Clarity		✓		
Significance		✓		

Reviewer Name: Dr. S. K. Nath **Date:** 28/01/2025

Reviewer's Comment for Publication.

The paper successfully underscores the importance of advanced experimental models in studying *E. coli*-induced UTIs and developing innovative treatments. It contributes significantly to understanding pathogenesis, antimicrobial resistance, and therapeutic strategies. However, integrating quantitative analyses, addressing limitations of advanced techniques, and offering a roadmap for clinical translation could enhance its impact.

Reviewer's Comment / Report

Strengths of the Paper:

1. **Relevance of the Topic:** The study focuses on urinary tract infections (UTIs), a critical public health issue with growing concerns over antimicrobial resistance, particularly in Uropathogenic *E. coli* (UPEC). The emphasis on advanced experimental models is timely and highly relevant.

2. **Comprehensive Overview:** The paper provides a detailed review of traditional and modern *in vitro* and *in vivo* models, including organoids, microfluidic systems, zebrafish models, and murine systems, showcasing advancements in studying UTI pathogenesis and therapeutic interventions.

3. **Insight into Antimicrobial Resistance (AMR):** The discussion highlights the challenges posed by multidrug-resistant (MDR) UPEC strains and their ability to form biofilms, which makes infections persistent and difficult to treat.

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4. **Application of Innovative Technologies:** The paper introduces cutting-edge techniques like 3D printing, organ-on-chip systems, and imaging technologies, demonstrating their utility in studying bacterial behavior, host-pathogen interactions, and antibiotic resistance.

5. **Focus on Therapeutic Advancements:** The exploration of novel treatments such as vaccines, phage therapy, and anti-virulence agents aligns with the need for alternatives to traditional antibiotics.

6. **Use of Advanced Analytical Tools:** Incorporating genomics, transcriptomics, and high-throughput screening methods enriches the understanding of molecular mechanisms and helps identify biomarkers for diagnostics and therapeutics.

Weaknesses and Areas for Improvement:

1. **Lack of Quantitative Data:** While the paper discusses experimental models, it does not provide quantitative comparisons or metrics to evaluate the efficacy of various models.

2. **Limited Clinical Integration:** There is little discussion on how the findings from these models translate into clinical practice or their potential for regulatory approval.

3. **Inadequate Coverage of Limitations:** While the paper mentions some constraints of traditional models, it does not delve deeply into the limitations of advanced systems like organoids or microfluidic chips.

4. **Geographical and Demographic Relevance:** The review lacks context regarding the global burden of UTIs and how advancements in experimental models could address region-specific challenges.

5. **Recommendations for Future Research:** Although the paper emphasizes innovation, it could benefit from explicit recommendations for further research and development, especially in tackling MDR UPEC.

Suggestions for Improvement:

1. **Quantitative Comparisons:** Include data on the performance, cost, and reliability of various models to help researchers and clinicians choose the most appropriate tools for their needs.

2. **Clinical Applicability:** Discuss strategies for bridging the gap between laboratory findings and clinical implementation, including pilot studies and regulatory challenges.

3. **Focus on Model Limitations:** Provide a balanced analysis by elaborating on the limitations of advanced models, such as cost, scalability, and reproducibility.

4. **Global Perspective:** Address how the advancements discussed in the paper can be adapted to low-resource settings where UTIs are prevalent.

5. **Future Directions:** Highlight emerging areas of research, such as personalized medicine or AI-based predictive models, to inspire further studies.

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