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OPEN PEER REVIEW

Study of Biofilm, Virulence Genes, and Risk Factors in Urinary Catheter-Associated *Escherichia coli* Infections

Eman Hamdy Mohamed, Maysaa El Sayed Zaki, Mostafa Abdelsalam Ramadan, Mohamed Mohsen Motawea, Dina F Badr, Ahmed Gomaa Ahmed El Sayed, Mai Esam Ahmed Hamed

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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Contents

1 **Original submission** Seyed Hossein Shahcheraghi 2
2 **Revision 1** 3
Authors' reply to reviewers 4
Reviewer and editor comments 15

1 Original submission

1 comment · 13 Feb 2024

Seyed Hossein Shahcheraghi Reviewer

MAJOR REVISION 13 Feb 2024

1- The abstract is long.
2- Genes should be italicized throughout the text.
3- E. coli should be written in full at first mention.
4- In the aim, state how your aim applies to patients.
5- In the introduction, revise "Therefore the aim" to "Therefore, the aim".
6- There are many grammatical errors.
7- There is no reference for freezing at -20°C for PCR.
8- The PCR products seem to be very long.
9- Table 2 is not clear.
10- The differences and similarities between your study and others were not stated well in the discussion.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor and Reviewers,

We sincerely appreciate the time and effort you dedicated to reviewing our manuscript titled **)Study of Biofilm, Virulence Genes and Risk Factors in the Urinary Catheter-Associated Escherichia coli Infections(** . Your insightful comments and constructive feedback have been invaluable in shaping the quality of our research.

In response to your thoughtful review, we have carefully addressed each of the points raised. Below, we provide a point-by-point summary of our revisions:

Reviewers' Comments:

Reviewer 1:
1- Abstract is long

> Response: “We have revised the abstract to make it more concise and highlighted in the attached manuscript.

2- genes should be italic in all the text

Response: Done and highlighted in the attached manuscript

E .coli first time should be complete -3

Response: Done and highlighted in the attached manuscript

.
in aim state your applicable aim for patients -4

Response: Done and highlighted in the attached manuscript

Objective: The primary objective of our study was to evaluate various risk factors associated with CAUTIs. Additionally, we investigated the capacity of E. coli to form biofilms and the presence of virulence genes in these infections.

.
Therefore the aim as Therefore, the aim in the introduction be revised -5

Response: Revised and removed

.
.grammar errors are a lot -6

Response: We apologize for any grammatical errors in the manuscript. We thoroughly reviewed and revised the manuscript to correct these errors. This included checking for proper sentence structure, verb tense consistency, .punctuation, spelling, and adherence to grammatical conventions

frozen at -20ºC for PCR has no reference -7

. Response: Done and highlighted in the attached manuscript

length of pcr products seem that are very long -8

Response The observed PCR product lengths are a result of specific primer design and target regions. We aimed to capture relevant genomic segments for .our study and ensure comprehensive coverage of the gene of interest

.
Table 2 is no clarified -9

Response: We understand that Table 2 may not be clear in its current form. We propose changes to improve its clarity and highlighted in the attached :.manuscript

.
differences and similarities between your study with others in discussion -10 was no stated well

Response: We understand that the comparison of our study with previous studies was not clearly stated in the discussion section and we revised that and .corrected
:Reviewer 2
While the paper provides valuable insights into the risk factors, biofilm formation, and virulence genes associated with CAUTIs caused by E. coli, there

are opportunities to enhance clarity,organization, and critical analysis. Addressing these areas will strengthen the overall quality and impact of the research findings

:these are my comments

Expand the abstract to provide a more comprehensive overview of the study, .including key objectives, methodology, major findings, and implications

Response : Done and highlighted in the attached manuscript

Ensure that the abstract clearly states the significance of the study and its contribution to the existing literature on CAUTIs caused by E. coli

Response : Done and highlighted in the attached manuscript

Provide specific numerical data (e.g., sample size, percentages, significant associations) to give readers a better understanding of the study outcomes

.Response : Done and highlighted in the attached manuscript in abstract section

:Introduction

Clarify the specific gaps in the literature that the study aims to address. What aspects of CAUTIs and E. coli virulence genes have not been adequately explored

Response : Done and highlighted in the attached manuscript in the introduction .section

Streamline the introduction to focus on essential background information and .clearly articulate the study objectives

Response : Done and highlighted in the attached manuscript in the introduction .section

Consider including a brief overview of the study design and methodology to provide context for readers

Response : Done and highlighted in the attached manuscript in the introduction .section

.

:Methodology

Provide a more detailed explanation of the inclusion and exclusion criteria for patient selection to ensure transparency and reproducibility

Response: We understand the need for more detailed inclusion and exclusion :criteria. Here's a more detailed explanation

Inclusion Criteria Patients were included in the study if they met the following :criteria

Age: Patients aged 18 years or older were included to ensure that the study .1 .population was adult
Diagnosis: Patients diagnosed with healthcare-associated CAUTIs were .2 included. The diagnosis was based on the criteria identified by the Center for .Disease Control (CDC)
Catheter Use: Only patients with an inserted urinary catheter were included, .3 .as the study focuses on catheter-associated infections
Infection: The infection needed to be due to E. coli. This was confirmed .4 .through laboratory testing

Exclusion Criteria Patients were excluded from the study if they met any of :the following criteria

Community-Acquired Infections: Patients with community-acquired .1 urinary tract infections were excluded as the study focuses on healthcare- .associated infections
Non-Catheter Associated Infections: Patients with urinary tract infections .2 not associated with catheter use were excluded. This is because the study .aims to specifically investigate catheter-associated infections

By clearly defining these criteria, we aim to ensure that our study can be accurately replicated and that the results are applicable to the specific .population of interest

, Describe any potential biases or limitations of the study, such as selection bias measurement bias, or confounding variables

Response

Selection Bias: As our study only includes patients aged 18 years or older diagnosed with healthcare-associated CAUTIs due to E. coli, the findings may not be generalizable to other populations such as pediatric patients, patients .with community-acquired UTIs, or infections caused by other pathogens

Measurement Bias: The diagnosis of CAUTIs was based on the criteria identified by the CDC, which may not capture all cases of CAUTIs. Additionally, the identification of E. coli and its virulence genes was based on laboratory testing, which may have varying degrees of sensitivity and .specificity

Confounding Variables: There may be several confounding variables that were not controlled for in this study, such as patient's underlying health conditions, the duration of catheter use, and the specific type and care of the catheter used. These factors could potentially influence the occurrence of .CAUTIs and the presence of E. coli virulence genes

Limitations: Our study is also limited by its observational design, which can establish associations but not causal relationships. Furthermore, as this study was conducted in a single location, the findings may not be applicable to other geographical locations or healthcare settings

.

Clarify the rationale for using specific laboratory techniques and assays for biofilm
formation and virulence gene detection. Discuss any validation studies or quality control
.measures implemented

Consider including a flowchart or diagram illustrating the study design and participant
.selection process

:Results

Organize the results section into subsections corresponding to key study ,.outcomes (e.g
demographic characteristics, clinical data, biofilm formation, antibiotic

,resistance
(virulence gene detection

Response : Done and highlighted in the attached manuscript in the results
.section
Present numerical data in tables or figures to enhance clarity and facilitate
.comparisons between groups

.Done and highlighted
Provide detailed descriptions of significant findings, including effect sizes,
.confidence intervals, and p-values

Discuss any unexpected or conflicting results and potential explanations for
these
.findings
Ensure consistency in reporting throughout the results section and avoid
.redundancy with information presented in tables and figures

Done with
respect
:Discussion
Interpret the study findings in the context of existing literature and theoretical
frameworks. Discuss how the results contribute to our understanding of
.CAUTIs and E
coli pathogenesis

Address the limitations of the study, including potential sources of bias,
confounding
factors, and methodological constraints

.**Response**: Mentioned in a previous comment

Consider alternative explanations for the observed associations and
implications for clinical practice, public health interventions, and future
.research
Highlight the novelty and significance of the study findings and discuss any

implications
.for healthcare policy or practice guidelines

Done and highlighted

:Novelty

The study’s focus on biofilm formation and virulence genes in UCATIs represents a novel approach.Prior research has primarily examined bacterial colonization and antibiotic resistance, but this study delves deeper into the .mechanisms driving infection persistence

Significance:

Understanding biofilm dynamics is crucial for preventing and managing .1 UCATIs

Identifying specific virulence genes in UCATIs can inform targeted therapies.2

also sheds light on the genetic diversity of uropathogens ,

Novel insights into biofilm and virulence genes can lead to more effective .3 .treatment strategies

:Implications for Healthcare Policy and Practice

Catheter Care Guidelines: Healthcare policies should emphasize proper .1 catheter insertion, maintenance, and removal

Antibiotic Stewardship: Understanding virulence genes can guide antibiotic .2 selection

Biofilm Disruption: Develop interventions to prevent or disrupt biofilm formation.3

Gene-Based Diagnostics: Incorporate virulence gene detection into diagnostic.4 protocols

Targeted Therapies: Develop drugs that specifically target biofilm-associated.5
virulence factors

In summary, this study's findings provide a fresh perspective on UCATIs, emphasizing biofilm dynamics and virulence genes. By integrating these insights into healthcare policies and practice guidelines, we can enhance patient
.outcomes and reduce the burden of UCATIs
:Conclusion
Summarize the main findings of the study concisely and emphasize their implications for
.clinical practice, infection control, and antibiotic stewardship

Done and highlighted
Avoid introducing new information in the conclusion and focus on reinforcing key
.messages from the study

Done
Suggest directions for future research to address unresolved questions or expand upon the
current findings

Done and highlighted
:Reviewer 3
This paper describes:(Study of Biofilm, Virulence Genes and Risk Factors in the Urinary
Catheter-Associated Escherichia coli Infections).The article presented usefull data about Catheter-Associated Escherichia coli Infections which is a one of the major nosocomial infection. The article is useful and well written, but it has writing errors and some problems that need to be solved. It is suggested that the article be recheck and its defects fixed. The following items should also be
:checked and fixed

:Abstract
. Line8: (Therefore) must be deleted

.Response: Correction was done. In the attached manuscript
Genes symbols must be written Italic

Response: Correction was done. In the attached manuscript
DM(Line 26) should be written in full in the abstract of the article and its abbreviation should be written in parentheses

.Response: Correction was done. In the attached manuscript
Different parts of abstract should be written with Bold font (Objective, method ,..)

Response: Correction was done. In the attached manuscript
Bring at least 3 keywords (according to the mesh)

.Response: Correction was done. In the attached manuscript
:Introduction.2
. Line 102-103: Correct the sentence

Done

: Material and Methods
Line 104, 117 , 127,139,147,148,151,313: Should be written in Bold .Done
Lines 112-113 , 121,143: Correct the sentence. Done
Line 132: The dose of nitrofurantoin should be mentioned and its font should be corrected.Done
: Results
In all the tables, the percentages should be placed next to the numbers but inside the parentheses

Response : Done and highlighted in the attached manuscript

In all tables , the title of the studied variable should be given in the top row, . for example in table 5, the title of the top row should be assigned to: virulence genes

Response : Done and highlighted in the attached manuscript

.
The number of tables is too many. Table 3 should be removed. At least instead .of two or three tables, the results should be shown in graphs
Response:Table 3 was removed ,table 4 and 5 were replaced with graphs and

highlighted in the attached manuscript

Figure 1 is ambiguous and illegible and is not mentioned in the text. Please correct it.

Response: Correction was done and figure 1 was removed In the attached manuscript.

Please correct reference 20(Line 439)

Response: Correction was done and highlighted In the attached manuscript.

We have made the necessary changes to enhance the clarity, rigor, and overall impact of our manuscript. Additionally, we have revised the figures and tables as suggested.

We kindly request that you reconsider our manuscript for publication. We believe that the revisions adequately address the concerns raised during the initial review. If there are any remaining issues or if further clarification is needed, please do not hesitate to reach out to us.

Once again, we express our gratitude for your commitment to maintaining the high standards of [JJM]. We look forward to your favorable response.

Thank you for your time and consideration.

Sincerely,

Corresponding author

Maysaa El Sayed Zaki

Professor of Clinical Pathology, Mansoura Faculty of Medicine, Egypt

2 Revision 1

0 comments

No public comments in this round.