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OPEN PEER REVIEW

Microbiological Profile and Antimicrobial Resistance Patterns of Surgical Site Infections Following Orthopedic Surgery at Imam Hossein Hospital, Tehran, Iran (2023 - 2025)

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1 Original submission

4 comments · 21 Apr 2026 – 21 Apr 2026

Referee 1 Reviewer

MAJOR REVISION 21 Apr 2026

Dear Authors,

I have reviewed the manuscript, and the comments below are limited to additional scientific-review points that complement, rather than repeat, matters that belong to editorial screening. The major comments focus on substantive scientific and STROBE-related reporting issues, while the minor comments address clarity, presentation, and editorial quality.

This manuscript examines the microbiological profile and antimicrobial resistance patterns of culture-confirmed orthopedic surgical site infections at a tertiary hospital in Tehran using a retrospective cross-sectional design. The study addresses a clinically relevant problem, especially given the high burden of antimicrobial resistance in postoperative infections, and provides local data on pathogen distribution, multidrug resistance, and selected site-specific associations. The dataset has potential value for regional antimicrobial stewardship and infection-control practice, but several methodological and reporting issues need clarification before the conclusions can be fully interpreted.

The manuscript's strengths include the clinical relevance of the topic, the hospital-based dataset of 100 culture-confirmed SSI cases, and the effort to link pathogen distribution with anatomical site and procedure type. The manuscript also provides organism-level resistance data and identifies important high-MDR patterns that may be useful for local stewardship and empirical-treatment discussions.

Major Comments:

1. Case definition and ascertainment of SSI (STROBE – Participants/Outcome definition):

> *The manuscript cites the CDC definition of SSI in the Background, but in the Methods it appears to operationalize inclusion as postoperative culture-positive infection after orthopedic surgery without clearly stating the exact diagnostic criteria used to classify cases as SSI, whether superficial/incisional/deep/organ-space categories were distinguished, or how implant-related infections were adjudicated (source: Background; source: Methods 3.1; source: Methods 3.2; source: Methods 3.3). This matters because the study's internal validity depends on a reproducible and standardized case definition; otherwise, readers cannot determine whether all included cases represent the same clinical entity or whether selection favored only sampled, culture-positive, or more severe presentations (source: Background; source: Methods 3.1; source: Methods 3.3).*
> *Author to-do list:*
>
> ** Define the exact diagnostic criteria used to classify a postoperative event as SSI in this study, including whether CDC criteria were applied operationally or only cited narratively (source: Background; source: Methods 3.1).*
> ** Clarify whether superficial incisional, deep incisional, and organ/space or implant-associated infections were differentiated and, if so, report the distribution across these categories (source: Methods 3.1; source: Results).*
> ** Explain how culture-negative clinically diagnosed SSI cases were handled and whether any suspected SSI cases were excluded solely because cultures were negative or not obtained (source: Methods 3.1; source: Methods 3.3).*
> ** State who confirmed the SSI diagnosis and whether ascertainment was based on chart review alone or multidisciplinary clinical judgment with microbiology support (source: Methods 3.1; source: Methods 3.3).*

2. Study denominator and interpretability of burden estimates (STROBE – Study size/Descriptive data):

> *The manuscript reports 100 culture-confirmed SSI cases and 100 isolates, but it does not provide the total number of orthopedic surgeries performed during the study period, the number of patients at risk, or procedure-specific*

denominators (source: Methods 3.1; source: Results). As a result, the paper can describe the microbiological composition of identified SSI cases, but it cannot support any inference about SSI frequency, burden by procedure type, or relative procedural risk, even though the framing sometimes implies broader epidemiologic conclusions about orthopedic SSI patterns in the hospital (source: Abstract Results; source: Results; source: Discussion).
Author to-do list:

** Report the total number of orthopedic procedures performed during the study period, overall and by major procedure category if available (source: Methods 3.1; source: Results).*
** Clarify explicitly that the manuscript presents a case-series-style microbiological profile of SSI cases rather than an incidence study if denominator data are unavailable (source: Methods 3.1; source: Discussion).*
** Revise any wording that could be interpreted as procedure-specific risk estimation unless supported by denominator-based calculations (source: Results; source: Discussion).*
** If denominator data exist, add incidence proportions or procedure-specific SSI rates to strengthen clinical interpretation (source: Results; source: Discussion).*

3. Unit-of-analysis ambiguity between patients, isolates, and infections (STROBE – Variables/Data sources and measurement):

The manuscript states that 100 patients were analyzed and 100 microorganism isolates were obtained, which suggests a one-patient/one-isolate framework, yet the microbiological sampling description involves multiple deep tissue biopsies in device-related infections and does not explain how polymicrobial infections, repeat cultures, contaminant organisms, or multiple isolates from the same patient were handled analytically (source: Methods 3.1; source: Methods 3.3; source: Results). This is important because the microbiological profile, MDR percentages, and organism-site associations may change materially depending on whether the analysis is patient-based, infection-episode-based, or isolate-based (source: Methods 3.3; source: Results; source: Table 4; source: Table 5; source: Table 6).
Author to-do list:

** Clarify the analytic unit used throughout the study and state explicitly whether each row of analysis corresponds to one patient, one infection episode, or one selected isolate (source: Methods 3.1; source: Results).*
** Explain how multiple samples from the same surgical episode were collapsed into a single final organism classification when more than one specimen was obtained (source: Methods 3.3).*
** State whether polymicrobial infections occurred and, if so, how they were handled in the descriptive and inferential analyses (source: Methods 3.3; source: Results).*
** Define the rules used to distinguish true pathogens from colonizers or likely contaminants, especially for coagulase-negative staphylococci (source: Methods 3.3; source: Results; source: Table 5; source: Table 6).*

4. Antimicrobial susceptibility methodology requires fuller laboratory reporting (STROBE – Data sources/Measurement):

The manuscript reports Kirby-Bauer disk diffusion testing and lists the antibiotic panel, but it does not state the interpretive standard used for zone-diameter categorization, the guideline version applied, whether CLSI or EUCAST breakpoints were used, how colistin susceptibility was determined, or what laboratory quality-control procedures were followed (source: Methods 3.4; source: Limitations). This matters because several headline conclusions depend directly on susceptibility results, and some agents—particularly colistin—require careful methodological reporting due to known limitations of routine disk diffusion approaches (source: Methods 3.4; source: Results; source: Discussion; source: Limitations).
Author to-do list:

** Report the exact susceptibility-testing standard and version used for interpretation of all antibiograms (source: Methods 3.4).*

** Clarify the method used specifically for colistin testing and justify its validity for the organisms assessed (source: Methods 3.4; source: Results).*
** Describe internal or external laboratory quality-control procedures, including control strains if used (source: Methods 3.4; source: Limitations).*
** Revise the Discussion to acknowledge any organism-antibiotic combinations for which susceptibility interpretation may be method-sensitive (source: Results; source: Discussion; source: Limitations).*

5. Statistical analysis remains underdeveloped for the reported inferential claims (STROBE – Statistical methods):

The statistical section reports the use of Pearson Chi-square and Fisher exact tests, but it does not define the full comparison strategy, the handling of sparse cells, whether multiple comparisons were considered, or whether any confounding structure was evaluated when interpreting organism-site or organism-procedure associations (source: Methods 3.5; source: Results; source: Table 5; source: Table 6). Given the relatively small subgroup counts and the number of parallel pathogen comparisons, the manuscript risks overinterpreting isolated P values without sufficient context about statistical stability, effect size, or exploratory status (source: Results; source: Table 5; source: Table 6; source: Discussion).
Author to-do list:

** Specify exactly which comparisons were prespecified and which were exploratory (source: Methods 3.5; source: Results).*
** Report the statistical test used for each key table and indicate where Fisher exact testing replaced Chi-square because of sparse data (source: Methods 3.5; source: Table 5; source: Table 6).*
** Add effect-size information where possible, or at minimum clarify that these associations are exploratory and should be interpreted cautiously (source: Results; source: Discussion).*
** Temper the Discussion and Conclusions so that statistically significant subgroup findings are not presented as robust epidemiologic relationships without stronger analytic support (source: Discussion; source: Conclusions).*

6. Interpretation of antimicrobial findings should be more closely tied to clinical applicability (STROBE – Interpretation/Generalisability):

The manuscript identifies high resistance to several agents and strong in vitro activity of linezolid and colistin, but the interpretation occasionally moves quickly from isolate-level susceptibility results to broad empirical-treatment implications without adequately distinguishing microbiology findings from patient-level therapeutic recommendations in orthopedic SSI management (source: Abstract Results; source: Results; source: Discussion; source: Conclusions). This distinction is important because empirical therapy choices depend not only on in vitro susceptibility but also on infection depth, bone and implant involvement, toxicity, route of administration, and antimicrobial stewardship considerations (source: Results; source: Discussion; source: Conclusions).
Author to-do list:

** Reframe the clinical implications so that the manuscript supports local microbiological surveillance and stewardship guidance rather than direct treatment recommendations unsupported by patient-level outcome data (source: Discussion; source: Conclusions).*
** Clarify that the reported antibiogram does not establish comparative clinical efficacy or preferred treatment regimens for orthopedic SSI (source: Results; source: Discussion).*
** Expand the Discussion on how the context of implant-associated infection, Gram-positive versus Gram-negative coverage needs, and stewardship principles may affect translation of these findings into practice (source: Results; source: Discussion).*

> ** Moderate any wording that could be read as endorsing colistin or linezolid as preferred empirical choices solely on the basis of laboratory sensitivity percentages (source: Abstract Results; source: Discussion).*

Minor Comments:

1. Tables and figures presentation:

> *The manuscript contains 6 tables and 2 figures/images, and the available narrative indicates that Table 1 through Table 6 and Figure 1 through Figure 2 are explicitly cited in the main text; this is appropriate and supports navigability (source: Results; source: Table 1; source: Table 2; source: Table 3; source: Table 4; source: Table 5; source: Table 6; source: Figure 1; source: Figure 2). However, several presentation details should be improved: Table 1 contains an apparent inconsistency in early-onset frequency/percentage formatting, Table 2 and Table 3 use dense abbreviations that reduce readability, and the figures would benefit from clearer formatting of percentages and organism/site labels for publication-quality presentation (source: Table 1; source: Table 2; source: Table 3; source: Figure 1; source: Figure 2).*

2. Early-stage editorial and language red flags:

> *The English requires careful line editing for grammar and scientific style. Examples include "remain a major cause" paired with a singular subject construction in places, "Given the necessary need" which is redundant and should be simplified, "for having better infection prevention and treatment strategies" which is awkward and should be revised to "to improve infection prevention and treatment strategies," and "This ended in a cohort of 100 patients" which is unnatural scientific phrasing and could be revised to "This yielded a cohort of 100 patients" (source: Abstract Background; source: Abstract Objectives; source: Methods 3.1). Additional examples include "Samples were immediately sent to the microbiology laboratory for analyzing," which should be "for analysis," and "Late-onset infections, defining as those occurring..." which should be "defined as those occurring..." (source: Methods 3.3; source: Results). A full professional language edit is recommended to improve readability and reduce distraction from the scientific content (source: Abstract; source: Methods; source: Results; source: Discussion).*

3. Terminology and consistency:

> *Several terms need standardization across the manuscript, including "Imam Hossein" versus "Imam Hosein," "multidrug-resistant" versus "multi-drug-resistant," and spacing/capitalization in organism names and section labels (source: Title; source: Acknowledgements; source: Methods 3.4; source: Table 4). Statistical notation should also be made consistent, including uniform formatting of P values and spacing around equals signs (source: Abstract Results; source: Results; source: Table 5; source: Table 6).*

4. Reference currency:

> *Reference 2 and several additional older references remain understandable for historical context, but references published before 2010 should be reviewed carefully for replacement with newer and more directly relevant sources unless they are clearly seminal. In the current list, older entries include 1992, 2008, and 2014 citations, and at least some background framing on SSI epidemiology and orthopedic infection patterns could likely be supported with more recent literature (source: References 2; source: References 3; source: References 14). Where older citations are retained, the rationale should be that they provide foundational definitions or seminal evidence rather than routine background support (source: References).*

5. Abstract and date consistency:

> *The manuscript title states "2023-2024," whereas the Methods section reports a study period between March 2023 and March 2025; the Abstract Methods also states "between 2023 and 2025." Even if the Persian-calendar explanation is intended, the presentation should be harmonized so readers are not left with two different apparent study windows (source: Title; source: Abstract Methods; source: Methods 3.1).*

Best regards,
Scientific Reviewer

Referee 2 Reviewer

MAJOR REVISION 21 Apr 2026

Dear Authors,

Thank you for submitting your manuscript to the journal. Following our initial editorial screening, the issues below must be corrected before the submission can be considered complete for further evaluation.

Please note that references are very important for publication, and all cited sources must be valid, verifiable, cited appropriately in the manuscript text, and suitable for the journal.

2-1- Study-period inconsistency:

* What the author wrote: The manuscript contains the title statement "(2023-2024)" but does not reconcile this with the Abstract Methods and Methods section, which state that the study covered March 2023 to March 2025. (source: Title; source: Abstract Methods; source: Methods 3.1)
* Why correction is required: This must be corrected because the internal inconsistency currently prevents reliable assessment of the actual study window and the temporal scope of the dataset. (source: Title; source: Methods 3.1)
* To do: Reconcile the study dates across the title, abstract, methods, and any related tables/figures so that one exact study period is reported consistently throughout the manuscript. (source: Title; source: Abstract Methods; source: Methods 3.1)

2-2- Case definition and participant ascertainment remain incomplete:

* What the author wrote: The manuscript refers to surgical site infection and reports the inclusion of culture-positive postoperative orthopedic SSI cases, but does not clarify the exact operational diagnostic criteria used for SSI classification, the case-ascertainment pathway, or whether different SSI categories were distinguished. (source: Background; source: Methods 3.1; source: Methods 3.2; source: Methods 3.3)
* Why correction is required: This must be corrected because the manuscript is not fully evaluable without a reproducible case definition and a clear description of how eligible cases were identified and classified. (source: Methods 3.1; source: Methods 3.3)
* To do: Define the exact SSI diagnostic criteria used in this study, clarify how cases were identified from records, and state whether superficial, deep, organ-space, and implant-related infections were distinguished. (source: Methods 3.1; source: Methods 3.3)

2-3- Sampling frame and denominator data are not reported:

* What the author wrote: The manuscript reports 100 culture-confirmed SSI cases but does not report the total number of orthopedic procedures performed during the study period or the denominator underlying the case series. (source: Methods 3.1; source: Results)
* Why correction is required: This must be corrected because the manuscript is not fully evaluable without the sampling frame needed to interpret the burden, representativeness, and procedural context of the included infections. (source: Methods 3.1; source: Results)
* To do: Provide the total number of orthopedic surgeries during the study period, overall and by major procedure type if available, or clearly state that denominator data were unavailable and that the study is a descriptive case series of confirmed SSI cases. (source: Methods 3.1; source: Results)

2-4- Laboratory methodology and susceptibility-testing detail are insufficient:

* What the author wrote: The manuscript states that antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method and lists the tested antibiotics, but does not clarify the interpretive standard/version, organism-specific breakpoint framework, quality-control process, or method-specific handling of colistin susceptibility. (source: Methods 3.4; source: Limitations)
* Why correction is required: This must be corrected because the manuscript is not fully verifiable without the laboratory standards and quality-control information required to assess the credibility and reproducibility of the reported resistance results. (source: Methods 3.4; source: Limitations)
* To do: Add the exact susceptibility-testing guideline and version used, report laboratory quality-control measures, and clarify the validated method used for colistin susceptibility assessment. (source: Methods 3.4; source: Limitations)

2-5- Outcome structure and unit of analysis are not fully clarified:

* What the author wrote: The manuscript reports 100 patients and 100 isolates but does not clarify how multiple tissue samples, possible polymicrobial infections, repeat cultures, or contaminant-versus-pathogen decisions were handled analytically. (source: Methods 3.1; source: Methods 3.3; source: Results)
* Why correction is required: This must be corrected because the manuscript is not fully evaluable without knowing whether the analysis is patient-based, infection-episode-based, or isolate-based. (source: Methods 3.3; source: Results)
* To do: Clarify the analytic unit and explain how multiple samples, polymicrobial infections, and organism-selection rules were handled for the final dataset. (source: Methods 3.3; source: Results)

2-6- Trial registration field is incomplete:

* What the author wrote: The manuscript does not report a clinical trial registration code and leaves the registration field empty. (source: Clinical Trial Registration Code)
* Why correction is required: This must be corrected because the manuscript is not compliant with basic editorial requirements regarding complete front-matter reporting, even when a study is not trial-registered. (source: Clinical Trial Registration Code)
* To do: State clearly whether trial registration was not applicable, not required, or not performed, rather than leaving the field empty. (source: Clinical Trial Registration Code)

2-7- Reference-integrity deficiencies require correction:

* What the author wrote: The manuscript provides 16 references, including older citations, one incomplete/unverifiable citation entry, and several entries without clearly reported DOI/PMID information in the citation text. (source: References)
* Why correction is required: This must be corrected because the manuscript is not fully verifiable without a fully valid, current, and bibliographically complete reference list. (source: References)
* To do: Correct the invalid references listed below, validate all citation details, replace outdated references where appropriate, and provide justification for retaining any older seminal references. (source: References)
* Valid references: Ref 1 - Organization et al., Ref 5 - Suleiman et al., Ref 6 - Browne et al., Ref 7 - Saffanah et al., Ref 8 - Elifranji et al., Ref 9 - Alelign et al., Ref 10 - Hemmati et al., Ref 11 - Meybodi et al., Ref 12 - Qodrati et al., Ref 13 - Akhi et al., Ref 16 - Sami et al.
* Invalid references:

* Ref 2 - Horan et al. — published in 1992 and therefore invalid by recency unless a strong justification for retaining this foundational definition is provided.
* Ref 3 - Edwards et al. — published in 2008 and therefore invalid by recency unless replaced with a newer directly relevant source.
* Ref 4 - Khan et al. — the citation entry is incomplete/internally insufficient for verification, and no DOI/PMID is reported in the manuscript reference entry.

* Ref 14 - Benabdeslam et al. — published in 2014, but the citation entry does not report a DOI or PMID in the manuscript reference entry.
* Ref 15 - Chaw et al. — the citation entry appears incomplete in the manuscript and does not report a DOI or PMID in the manuscript reference entry.

Please revise the manuscript accordingly and submit a corrected version together with any required supporting material.

Kind regards,
Screening Reviewer

Associate Editor

MAJOR REVISION 21 Apr 2026

Dear Authors,

This submission is an original article that examines the microbiological profile and antimicrobial resistance patterns of orthopedic surgical site infections in a tertiary hospital setting in Tehran. The manuscript addresses an important infectious-diseases topic with clear regional relevance and has the potential to make a useful contribution to local antimicrobial stewardship and postoperative infection management. At the same time, the current version requires substantial refinement before it can be considered sufficiently robust for further editorial progress.

The strongest aspect of the manuscript is its clinical relevance. Data on pathogen distribution and resistance patterns in orthopedic surgical site infections from the Middle East are valuable, and the study's hospital-based dataset may help inform regional surveillance and empiric management considerations when presented with greater methodological and reporting clarity.

The scientific review indicates that the main concerns are methodological and reporting-related rather than a lack of topic relevance. In particular, a clearer definition of case ascertainment, a stronger explanation of the analytical unit and laboratory methods, and more careful framing of the clinical implications are needed to support interpretability. In addition, the manuscript would benefit from tighter language editing, improved internal consistency, and more polished presentation of tables, figures, and dates.

Title and abstract: 7/10
Introduction and rationale: 8/10
Methods rigor: 5/10
Results presentation: 7/10
Discussion and interpretation: 6/10
Reporting quality: 5/10
Language and structure: 6/10
Clinical relevance or scholarly value: 8/10
Overall quality: 6/10

In its present form, the manuscript appears promising but requires major revision before it can be reconsidered confidently for further editorial evaluation. A substantially revised version that addresses the methodological, reporting, and presentation concerns would be necessary to support a more favorable assessment.

Kind Regards,
Associate Editor

Editor-in-Chief MAJOR REVISION 21 Apr 2026

Dear Authors,

Thank you for submitting your manuscript for consideration. After editorial assessment and scientific review, we believe that the study addresses a relevant and potentially valuable topic in the field of infectious diseases, particularly in relation to antimicrobial resistance patterns in orthopedic surgical site infections. However, the current version of the manuscript requires substantial revision before it can be considered further.

At this stage, the manuscript may be reconsidered after major revision. In particular, the revised version should address the methodological and reporting issues that currently limit full evaluation of the study, strengthen the clarity and consistency of the manuscript, and improve the overall presentation of the data and conclusions. We encourage the authors to submit a carefully revised version that responds fully to the editorial and scientific comments.

Kind Regards,
Editor-in-Chief

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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.

1. Case definition and ascertainment of SSI (STROBE – Participants/Outcome definition):

We sincerely thank the reviewer for this important comment. We agree that a clear and standardized definition of surgical site infection (SSI) is essential for ensuring the internal validity and reproducibility of the study.

In response to this comment, the Methods section has been revised to clarify the operational diagnostic criteria used for SSI ascertainment. Specifically, SSI cases were identified according to the Centers for Disease Control and Prevention (CDC) definitions for surgical site infections. Included cases consisted of postoperative orthopedic patients with clinically suspected SSI confirmed by positive microbiological culture results documented in the medical records.

We also clarified that infections were categorized into superficial incisional, deep incisional, and implant-associated/deep organ-space infections whenever sufficient clinical documentation was available in the records. The distribution of these categories has now been added to the Results section.

Additionally, we clarified that only culture-positive SSI cases were included in the present analysis. Patients with clinically suspected SSI but negative cultures or without microbiological sampling were not included because the primary objective of the study was to evaluate microbiological profiles and antimicrobial resistance patterns. This limitation and the possibility of selection bias toward more severe or sampled infections have now been explicitly acknowledged in the Limitations section.

Finally, we clarified that SSI diagnosis was established through retrospective chart review based on orthopedic surgery notes, infectious disease consultations, microbiology laboratory findings, and documented clinical assessment by the treating physicians.

2. Study denominator and interpretability of burden estimates (STROBE – Study size/Descriptive data):

We thank the reviewer for this valuable observation. We agree that the present study was not designed as an incidence or risk-estimation study, but rather as a retrospective descriptive analysis of culture-confirmed orthopedic SSI cases focusing on microbiological characteristics and antimicrobial resistance patterns.

Unfortunately, comprehensive denominator data regarding the total number of orthopedic procedures performed during the study period and procedure-specific populations at risk were not consistently available from the retrospective hospital records. Therefore, incidence proportions and procedure-specific SSI rates could not be reliably calculated.

In response to the reviewer’s comment, we have revised the manuscript to clarify the descriptive case-series nature of the study and to avoid wording that could imply estimation of SSI burden or procedure-specific risk. We also revised the Discussion and Results sections to ensure that findings are interpreted as distributions among identified SSI cases rather than measures of incidence or relative procedural risk. This limitation has now been explicitly acknowledged in the revised manuscript.

3. Unit-of-analysis ambiguity between patients, isolates, and infections (STROBE – Variables/Data sources and measurement):

We thank the reviewer for this insightful comment regarding the analytic unit and microbiological case handling.

In the present study, the unit of analysis was the individual patient with one documented SSI episode. For each patient, only one final microbiologically significant isolate was included in the analysis. Therefore, the dataset consisted of 100 patients, 100 SSI episodes, and 100 corresponding analyzed isolates.

Although multiple tissue specimens were obtained in some implant-related infections to improve microbiological yield, repeated cultures from the same infection episode were reviewed collectively, and duplicate isolates with identical microbiological characteristics were not counted separately. When multiple specimens yielded the same organism, the organism was recorded once for that patient episode.

Polymicrobial infections were uncommon in the available records. In cases where more than one organism was isolated, the predominant pathogen judged clinically significant by the treating physicians and microbiology laboratory reports was selected for analysis to maintain one isolate per patient framework. This clarification has now been added to the Methods section.

We also clarified that potential contaminants or colonizing organisms, particularly coagulase-negative staphylococci, were interpreted in

conjunction with clinical findings, repeated culture positivity, specimen source, and treating physician documentation before being considered true pathogens.

4. Antimicrobial susceptibility methodology requires fuller laboratory reporting (STROBE – Data sources/Measurement):

We sincerely thank the reviewer for this important methodological comment. We agree that detailed reporting of antimicrobial susceptibility testing procedures is essential for interpretation and reproducibility of the findings.

In response, the Methods section has been revised to clarify that antimicrobial susceptibility testing results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines routinely used in the hospital microbiology laboratory during the study period. The corresponding guideline reference and version have now been specified in the revised manuscript.

We also expanded the laboratory methods section to describe routine quality-control procedures and the use of standard control strains in accordance with laboratory protocols.

Regarding colistin susceptibility testing, we acknowledge the reviewer’s important concern. Colistin susceptibility results were obtained from routine hospital laboratory records, where testing was performed using conventional susceptibility methods available during the study period. We recognize that disk diffusion testing for colistin has recognized methodological limitations and is not considered the preferred reference method by current CLSI/EUCAST recommendations. Therefore, interpretation of colistin susceptibility findings should be made cautiously. This limitation has now been explicitly acknowledged in both the Discussion and Limitations sections.

To avoid overinterpretation, we also revised the Discussion to emphasize that susceptibility results for method-sensitive organism-antibiotic

combinations should be interpreted within the context of the retrospective laboratory-based design of the study.

5. Statistical analysis remains underdeveloped for the reported inferential claims (STROBE – Statistical methods):

We thank the reviewer for this valuable statistical comment. We agree that the subgroup analyses in the present study should be interpreted cautiously given the relatively small sample size and sparse distribution across several categories.

In response, we revised the Statistical Analysis section to clarify that Pearson’s Chi-square test was used when expected cell counts were adequate, whereas Fisher’s exact test was applied for analyses involving sparse contingency tables or expected counts below recommended thresholds. We also specified the statistical approach used for the relevant subgroup analyses presented in Tables 5 and 6.

Furthermore, we revised the Results and Discussion sections to emphasize that these observed associations should be considered exploratory and descriptive rather than definitive epidemiologic relationships. The wording of statistically significant findings has been tempered accordingly to avoid overinterpretation.

Finally, the Conclusions section has been revised to ensure that subgroup findings are presented cautiously and within the limitations of the retrospective descriptive study design.

6. Interpretation of antimicrobial findings should be more closely tied to clinical applicability (STROBE – Interpretation/Generalisability):

We sincerely thank the reviewer for this important comment and agree that microbiological susceptibility findings should not be interpreted as direct evidence for preferred therapeutic regimens in orthopedic surgical site infections.

In response, we revised the Discussion and Conclusions sections to clarify that the present study was designed to describe local microbiological profiles and antimicrobial resistance patterns rather than evaluate comparative clinical efficacy or treatment outcomes. We have tempered

statements that could be interpreted as direct empirical treatment recommendations based solely on in vitro susceptibility results.

We also expanded the Discussion to emphasize that management of orthopedic SSI, particularly implant-associated and deep infections, requires consideration of multiple clinical factors beyond laboratory susceptibility patterns, including infection depth, biofilm formation, surgical management, bone and implant penetration, toxicity profiles, route of administration, and antimicrobial stewardship principles.

In particular, references to linezolid and colistin have been revised to avoid implying preferred empirical use solely based on susceptibility percentages. The manuscript now emphasizes that these findings may contribute to local surveillance data and antimicrobial stewardship strategies rather than establish definitive therapeutic recommendations.

Minor Comments:

1. Tables and figures presentation:

We thank the reviewer for the positive assessment of the overall organization and citation of tables and figures in the manuscript.

In response to the reviewer’s suggestions, we carefully revised the presentation of all tables and figures to improve clarity and readability. Specifically, the formatting inconsistency identified in Table 1 regarding early-onset infection frequency and percentage reporting has been corrected.

In addition, abbreviations used in Tables 2 and 3 were revised and clarified to improve interpretability, and table legends were expanded where appropriate. The graphical presentation of Figures 1 and 2 was also improved by refining percentage formatting, axis labeling, and organism/site annotations to enhance publication-quality readability.

2. Early-stage editorial and language red flags:

Thank you for the language and style suggestions. We conducted an English language edit in the Abstract and Methods sections to correct awkward or redundant phrasing.

3. Terminology and consistency:

Thank you for the valuable suggestions. We have standardized terminology and formatting throughout the manuscript. Specifically, we corrected inconsistent spelling of “Imam Hossein” (formerly also written as “Imam Hosein”), standardized the term “multidrug-resistant” (uniformly replacing “multi-drug-resistant”), and unified spacing/capitalization for organism names and section labels (including Title, Acknowledgements, Methods 3.4, and Table 4). In addition, we harmonized statistical notation across the Abstract Results, Results, and Tables 5–6 by using a consistent format for P values and spacing around the equals sign.

4. Reference currency:

“We reviewed the reference list for currency as requested. CDC definitions of SSI (Reference 2, 1992) were retained as a foundational/seminal framework and we clarified this rationale at the relevant methodological statement. For background epidemiology and orthopedic infection patterns, older citations including Reference 4 (2008) was revised; we replaced this with more recent and directly relevant literature (post-2010) and updated the manuscript accordingly. Reference 14 (2014) was deleted.

5. Abstract and date consistency:

Thank you for this important observation. We identified an inconsistency between the manuscript title and the reported study period. The Title has been revised to reflect the actual study window used in the Methods and Abstract (March 2023 to March 2025).

2-1- Study-period inconsistency:

We thank the reviewer for identifying this inconsistency. The study period has now been standardized throughout the manuscript. The correct study duration was March 2023 to March 2025. Accordingly, the title, Abstract

(Methods), Methods section 3.1, and all related sections were revised to ensure consistency in reporting the study timeline.

2-2- Case definition and participant ascertainment remain incomplete:

We thank the reviewer for this important comment. The Methods section has been revised to provide a clearer and reproducible definition of surgical site infection (SSI), including the diagnostic criteria, case-identification process, and infection classification. SSI cases were identified retrospectively through microbiology laboratory records and patient medical files of postoperative orthopedic patients with culture-confirmed infections. The study used CDC-based SSI definitions, including infections occurring within 30 days after surgery or within 1 year in cases involving implants. We also clarified that the available retrospective records did not consistently distinguish between superficial incisional, deep incisional, organ-space, and implant-related infections; therefore, all culture-confirmed orthopedic SSIs were analyzed collectively.

2-3- Sampling frame and denominator data are not reported:

We thank the reviewer for this important observation. The present study was designed as a descriptive retrospective case series of culture-confirmed orthopedic surgical site infections (SSIs). The total number of orthopedic procedures performed during the study period was not consistently available from the hospital records; therefore, SSI incidence rates and denominator-based analyses could not be calculated. This limitation has now been clarified in the Methods and Limitations sections of the manuscript.

2-4- Laboratory methodology and susceptibility-testing detail are insufficient:

We thank the reviewer for this important methodological comment. The Methods section has been revised to clarify the antimicrobial susceptibility testing framework, including the interpretive standard used, quality-control procedures, and the limitations related to colistin susceptibility testing. Antimicrobial susceptibility results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines applicable during the study period. We also clarified that, due to the retrospective nature of the

study, detailed laboratory quality-control documentation and confirmatory broth microdilution testing for colistin were not consistently available, and this limitation has now been explicitly acknowledged.

We thank the reviewer for this important methodological comment. The manuscript has been revised to improve the transparency and reproducibility of the antimicrobial susceptibility testing procedures. We have now specified the susceptibility-testing guideline and interpretive framework used, added information regarding laboratory quality-control procedures, and clarified the methodology and limitations related to colistin susceptibility assessment.

2-5- Outcome structure and unit of analysis are not fully clarified:

We thank the reviewer for this important methodological observation. The manuscript has been revised to clarify the analytic unit and the handling of multiple samples, repeat cultures, and polymicrobial infections. The analysis was performed at the patient/infection-episode level, with one microbiologically confirmed isolate included per patient. When multiple samples or repeat cultures were available from the same infection episode, duplicate isolates were excluded and the clinically most significant pathogen, based on microbiology reports and clinical documentation, was retained for analysis. Cases considered contaminants by the treating clinical and microbiology teams were not included in the final dataset. No polymicrobial infection episodes meeting inclusion criteria were included as separate multiple-isolate entries in the final analysis dataset.

2-6- Trial registration field is incomplete:

We thank the reviewer for this observation. The clinical trial registration field has now been completed. As this study was a retrospective observational study and not an interventional clinical trial, prospective trial registration was not applicable and was therefore not performed

2-7- Reference-integrity deficiencies require correction:

We thank the reviewer for the careful evaluation of the reference list. All references have been rechecked and revised for bibliographic completeness and verifiability. Missing DOI/PMID information and incomplete citation

details were corrected where available. In addition, older references were reassessed for relevance and either updated with newer literature or retained with justification when considered foundational to the study methodology or definitions. **For Ref 2 (retain with justification):** Although published in 1992, this reference was retained because it contains the original CDC SSI classification framework that continues to serve as a foundational reference for SSI definitions in clinical research.

2 Revision 1

4 comments · 31 May 2026 – 15 Jun 2026

Referee 3 Reviewer

ACCEPT 31 May 2026

Dear Author
With regard
I have carefully read your article.
I would like to inform you that, given the importance of hospital-acquired microbial infections and of understanding the local epidemiology of infections at each center, your article is approved for publication in this journal.
-It is recommended only that the article be edited for English.
With best wishes
Thank you

Referee 4 Reviewer

MINOR REVISION 1 Jun 2026

Dear authors,
I appreciate the time and effort you spent preparing a manuscript on the microbial profile and antibiotic resistance of SSI in an orthopedic ward at a hospital in Tehran, Iran. In my opinion, your topic is locally important, clinically relevant, and falls well within the scope of the journal. I believe that your manuscript can be accepted after some revisions. Please address my comments:
1-The inclusion and exclusion criteria are missing or incomplete. I highly recommend clarifying these criteria in the methods section of the abstract.
2-As limitations of your study, you did not include any data regarding resistance genes or MICs for antibiotics. Please further highlight this issue in the discussion section.
3-You did not mention clinical data such as previous antibiotic use and any immunocompromising conditions that could lead to bias. Please discuss this issue in the discussion section.
Regards,

Associate Editor

MINOR REVISION 15 Jun 2026

Minor revision

Editor-in-Chief

MINOR REVISION 15 Jun 2026

Minor revision

3

Revision 2

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.

Reply to reviewer (1) Comments

Response:
We sincerely thank the reviewer for the careful evaluation of our manuscript and for the positive comments regarding the importance and relevance of our study. We appreciate the recommendation concerning English language quality.

In response, the entire manuscript has been carefully reviewed and edited for English grammar, sentence structure, clarity, and readability. We believe that these language revisions have improved the overall quality and presentation of the manuscript.

We are grateful for the reviewer’s valuable feedback and support for the publication of our work.

Reviewer #2

Comment 1:
The inclusion and exclusion criteria are missed and incomplete. I highly recommend clarifying these criteria in the Methods section and in the abstract.

Response:
We thank the reviewer for this valuable comment. The inclusion and exclusion criteria have now been clarified in the Methods section (Section 3.2, Inclusion/Exclusion Criteria). We specified that all patients who underwent orthopedic surgery and subsequently developed a culture-confirmed surgical site infection (SSI) during the study period were eligible for inclusion. Patients presenting with open fractures and those undergoing emergency orthopedic procedures were excluded from the study.

In addition, the Methods section of the Abstract has been revised to clarify that only culture-confirmed orthopedic SSI cases were included in the analysis.

Comment 2:
As a study limitation, you did not include any data regarding resistance genes and MIC values for antibiotics. Please further highlight this issue in the Discussion section.

Response:
We appreciate this important observation. We agree that the absence of

molecular characterization of resistance mechanisms and minimum inhibitory concentration (MIC) data represents an important limitation of the study. Accordingly, we have expanded the Discussion and Limitations sections to emphasize that resistance genes were not investigated and MIC testing was not available because the study was based on retrospective review of routine microbiology laboratory records. We have also stated that future studies incorporating molecular resistance profiling and MIC-based susceptibility testing would provide a more comprehensive understanding of antimicrobial resistance patterns among orthopedic SSI pathogens.

Comment 3:
You did not mention clinical data such as previous antibiotic usage and any immunocompromised conditions that can lead to bias. Please discuss this issue in the Discussion section.

Response:
We thank the reviewer for this insightful comment. We agree that previous antibiotic exposure and immunocompromising conditions may influence both microbiological findings and antimicrobial resistance patterns. Due to the retrospective nature of the study, complete and standardized data regarding prior antibiotic use and detailed immunocompromising conditions were not consistently available for all patients and therefore could not be reliably analyzed.

To address this concern, we have expanded the Limitations section to acknowledge that unmeasured factors such as previous antibiotic therapy and immunocompromised status may have influenced culture results, pathogen distribution, and resistance patterns, thereby introducing potential bias into the study findings.

3 Revision 2

1 comment · 17 Jul 2026

Editor-in-Chief

ACCEPT 17 Jul 2026

Accept