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| Journal Name: | [**Journal of Advances in Medicine and Medical Research**](https://journaljammr.com/index.php/JAMMR) |
| Manuscript Number: | **Ms\_JAMMR\_139711** |
| Title of the Manuscript: | **A Prospective Study on the Safety, Efficacy, and Cost-Effectiveness of Nitrofurantoin for Urinary Tract Infections in Pregnancy** |
| Type of the Article | **Original Research Article** |

**PART 1: Comments**

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|  | **Reviewer’s comment****Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.** | **Author’s Feedback** (It is mandatory that authors should write his/herfeedback here) |
| **Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | The manuscript titled "A Prospective Study on the Safety, Efficacy, and Cost-Effectiveness of Nitrofurantoin for Urinary Tract Infections in Pregnancy" presents important findings on the use of nitrofurantoin in a pregnant population. |  |
| **Is the title of the article suitable?****(If not please suggest an alternative title)** | **Yes** |  |
| **Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.** | **No** |  |
| **Is the manuscript scientifically, correct? Please write here.** | Yes, However, several aspects of the article's structure, coherence, and clarity could be improved to enhance the research's impact and readability. |  |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.** | Yes |  |

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| **Is the language/English quality of the article suitable for scholarly communications?** | Yes |  |
| **Optional/General** comments | 1. The manuscript could benefit from a reorganization of the results and discussionsections to better align with the stated objectives. Specifically, the cost-effectiveness analysis is buried within the discussion instead of being prominently featured in the results. The cost-effectiveness findings are introduced late in the discussion, which might lead readers to overlook this critical aspect of the study.2. Breaking down the discussion into several paragraphs with subheadings such as "Interpretation of Findings," "Study Limitations," and "Future Research Directions" would enhance readability and help the reader navigate through the authors' conclusions and recommendations.3. There is a logical gap in addressing how the study's findings compare with existing literature, especially regarding safety outcomes. The manuscript mentions a case of neonatal hemolytic anemia but does not contextualize this finding within the broader literature. A brief review of existing studies addressing the safety of nitrofurantoin, especially in late pregnancy, would provide a more comprehensive understanding of where this study's findings fit within the current body of knowledge.4. In conclusion, while the manuscript provides valuable insights into the use of nitrofurantoin for UTIs in pregnancy, improvements in flow, coherence, clarity, structure, and addressing logical gaps would enhance its contribution to the field.5. Limitations**:** The limitations section of the paper outlines several potential concernsregarding the generalizability and applicability of the study's findings. However, there are additional limitations and areas for improvement that could be addressed to enhance the robustness and relevance of the study.I) Single-Center Design: While the study acknowledges the limitation of being conducted at a single center, it might benefit from a more detailed discussion on how this affects the external validity of the findings. For example, the regional antimicrobial resistance patterns and prescribing habits might differ significantly from those in other parts of the world or even within the same country. An acknowledgment of how these factors might influence the applicability of the results to different populations would be valuable.Expanding on how the study's location and setting (e.g., urban vs. rural, tertiary care center vs. community hospital) might influence the observed outcomes would provide readers with a better understanding of the contexts in which the findings are most relevant.II. Sample Size and Power Calculation: The paper does not mention if a power calculation was conducted to determine the adequacy of the sample size for detecting differences not only in common outcomes but also in rare adverse events. Given the relatively small number of participants (180), the study might be underpowered to detect rare but clinically significant adverse outcomes associated with nitrofurantoin use during pregnancy. Including a power calculation based on expected outcome frequencies, especially for rare adverse events, would help justify the sample size and offer insights into the study's ability to detect significant differences.III. Lack of Control Group: The absence of a comparison group receiving an |  |

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alternative treatment or no treatment limits the ability to attribute observed outcomes directly to nitrofurantoin. Without a control group, it's challenging to differentiate between the effects of the medication and the natural course of UTIs in pregnancy or the impact of concurrent interventions. Future studies should consider incorporating a control group for comparison. If a randomized controlled trial is not feasible, a well- designed observational study with matched controls could offer valuable comparative insights.

IV. G6PD Screening: The paper mentions that G6PD deficiency was an exclusion criterion but also notes that the assessment of G6PD deficiency was not systematically performed for all participants. This oversight could mask potential adverse effects of nitrofurantoin in G6PD-deficient participants and affect the safety profile. Systematic screening for G6PD deficiency in future studies would enhance the safety assessment of nitrofurantoin in pregnancy. Additionally, discussing the potential impact of undiagnosed G6PD deficiency on the study's safety findings would provide a more nuanced understanding of the risks.

VI. Long-term Follow-up of Neonatal Outcomes: The study assesses neonatal outcomes at birth and up to 1 year for major congenital malformations but does not provide detailed long-term follow-up for other potential effects, such as neurodevelopmental outcomes or growth parameters. Including a plan for the results of longer-term follow-up of children exposed to nitrofurantoin in utero could offer valuable information on the drug's safety profile. This is particularly relevant for medications used during pregnancy, where delayed adverse effects may not be apparent at birth.

VII. Consideration of Antibiotic Resistance Development: While the paper discusses the low resistance rates to nitrofurantoin, it does not address whether the use of nitrofurantoin in the study population led to any changes in resistance patterns among uropathogens over time. Future research could benefit from including an analysis of antimicrobial susceptibility patterns before and after treatment to assess the impact of nitrofurantoin use on local resistance rates. This would provide important insights into the sustainability of nitrofurantoin as an effective treatment option for UTIs in pregnancy.

By addressing these additional limitations and incorporating the recommended improvements, the study could offer a more comprehensive understanding of the role of nitrofurantoin in managing UTIs during pregnancy, enhancing its relevance and applicability to a wider audience

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| **PART 2:**  |
|  | **Reviewer’s comment** | **Author’s Feedback** (It is mandatory that authors should write his/her feedback here) |
| **Are there ethical issues in this manuscript?**  | *(If yes, Kindly please write down the ethical issues here in details)* |  |

**Reviewer details:**

**Ranu Soni, MMCMSR, India**