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| Journal Name: | **[Archives of Current Research International](https://journalacri.com/index.php/ACRI)** |
| Manuscript Number: | **Ms\_ACRI\_133181** |
| Title of the Manuscript: | **The influence of periodontitis and dexamethasone on the development and morphology of mouse ovarian follicles** |
| Type of the Article |  |

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| **PART 1: Comments** | | |
|  | **Reviewer’s comment**  **Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.** | **Author’s Feedback** *(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*  The Authors hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript. |
| **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.** | This study provided new insights into the potential systemic effects of periodontitis and dexamethasone administration on reproductive health. It shows that periodontitis influenced ovarian follicle degeneration, particularly in the secondary and tertiary stages, which highlights the broader implications of chronic inflammation beyond the oral cavity. The findings of this in vivo study may have implications for clinical and therapeutic strategies in animals and humans. | Thank you for the comments. |
| **Is the title of the article suitable?**  **(If not please suggest an alternative title)** | Yes, the title of the article is suitable. | Thank you for the comments. |
| **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.** | Yes, the abstract is comprehensive, clear and structured. However, there are a few suggestions that may be worth considering. The abstract stated the effects of periodontitis and dexamethasone on ovarian follicles and oestrous cycle, but the authors did not provide specific number or statistical results. Suggestion: It would be better to add a *p*-value to support scientific claims. | Thank you for the comments. The P value was added. |
| **Is the manuscript scientifically, correct? Please write here.** | 1. Introduction  * Although this study was conducted in a mouse model, the implications of this study for humans are understated. Please add a few sentences about the potential clinical relevance. * The authors did not sufficiently highlight the gaps in previous studies and how this study can fill those gaps. Please explain more explicitly what previous studies have not answered and what needs to be conducted in this study. This will make this study stronger with the novelty and gap research clearly presented.  1. Materials and methods  * The authors did not explain why the dexamethasone dose of 0.5 mg/kg was chosen. Is this a standard dose based on previous studies? Please add references or justification based on previous studies for the dexamethasone dose used. * Did the researcher who analysed the data conduct a blind assessment? Please explain this.  1. Results  * Some results were simply stated as “significant,” but not always accompanied by a *p*-value or effect size. Please add more detailed *p*-values ​​and effect sizes to clarify the results of the study.  1. Discussion  * The explanation of how cytokines from periodontitis cause follicular degeneration is lacking in detail. Please add references or further discussion regarding inflammatory pathways that contribute to ovarian follicular degeneration. * The authors have not explained what implications these results have for future research or clinical applications. Please add a few sentences about how this study could form the basis for further studies in humans. * There is no section that explicitly addresses the limitations of the study. Please acknowledge the limitations of this study and suggest further research. | 1. Introduction   * According to the World Health Organization, severe periodontal diseases are estimated to affect more than 1 billion cases worldwide (World Health Organization, 2024). A systematic review investigating the association between infertility and periodontal disease found a higher prevalence of periodontal disease in infertility patients compared to controls (Márquez-Arrico et al., 2024) and in another systematic review, it was concluded that patients with Polycystic Ovary Syndrome (PCOS) appear to be more susceptible to developing periodontal diseases than women without the pathology (Márquez-Arrico et al., 2020). These studies highlighted the social importance of periodontal diseases, such as periodontitis, and their potential effects on the female reproductive system, of which the ovarian follicle is a fundamental part. * Despite the potential importance of this theme, to our knowledge, there is no study investigating the relationship between the ovarian follicle activity, periodontal disease and dexamethasone in mice.   2. Material and methods   * The dose was selected based on a previous study (Cavagni et al., 2005) which showed that a dose of 0.5 mg/kg dexamethasone in Wistar rats had an effect on bone resorption associated with experimental periodontitis. * During the analyses, the researchers did not know which groups were being analysed. Therefore, a blind evaluation was carried out for the assessment of the estrous cycle, the measurement of alveolar bone loss, the histopathological analysis of the mandibles and the histological analysis of the ovaries.   3. Results   * The P value was added and the number of animals in each analysis   4. Discussion   * Periodontitis can cause an increase in oxidative stress in Wistar rats with experimental periodontitis (Mester et al., 2018), the reactive oxygen species, related to this oxidative stress, can increase the production of cytokines (Higashi, 2022). Wang et al. (2023) demonstrated that injections of tumor necrosis factor alpha (TNF-α) and interleukin 1beta (IL-1β) into the gums of mice caused both increased local periodontal destruction and increased gene expression of IL-1 and TNF-α in the hippocampus of these animals, suggesting that periodontitis could have systemic implications through this pathway of inflammation. Similarly, the production of these cytokines by the host with periodontitis (Krejci and Bissada, 2002) may mean an increase in follicular effects linked to TNF-α and IL-1β, such as apoptosis in granulosa cells (Sasson et al., 2002) and effects in the nuclear and/or cytoplasmic oocyte maturation process (Silva et al., 2020). * The degeneration observed in ovarian follicles may provide a physiological explanation for the clinical correlation between patients with periodontitis and other diseases, such as PCOS (Machado et al., 2020; Márquez-Arrico et al., 2020). This study establishes a basis for future studies that address the more precise analysis of inflammation markers with an emphasis on ovarian follicles analysis in models of experimental periodontitis. This study provides new perspectives on the interactions between inflammatory diseases, immunosuppressive drugs and reproductive health. It opens doors to a deeper understanding of the mechanisms of ovarian function and fertility, as well as guidance on the clinical management of patients with inflammatory conditions such as periodontitis. * In future studies, other markers of inflammatory cytokines such as IL-6, IL-1, IL-11, TNGα and TGFβ can be evaluated. Additionally, different period of dexamethasone administration can be analyzed, since the dosage and time of use directly influence the side effects of this drug. |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.** | Yes, the references sufficient and recent. |  |
| **Is the language/English quality of the article suitable for scholarly communications?** | Yes, the language quality is suitable for scholarly communication. |  |
| **Optional/General** comments |  |  |

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| **PART 2:** | | |
|  | **Reviewer’s comment** | **Author’s comment** *(if agreed with the reviewer, correct the manuscript and highlight that part in the manuscript. 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 detail)* |  |