

Evaluation of Periodontal Status in Female Patients with Endometriosis: A Protocol for a Cross-sectional Study

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ABSTRACT

Introduction: Periodontal medicine indicates a strong relationship between Periodontal Health (PH) or disease and 'systemic health.' Although Periodontal Disease (PD) is quite distant from the area affected by endometriosis, both conditions share a similar pathogenesis. Both endometriosis and PD are chronic inflammatory diseases that occur more commonly in patients with systemic disorders. Moreover, significant alterations in immune modulators have been shown to occur in both diseases.

Need for the study: The research is to evaluate the correlation between endometriosis and PH for early diagnosis, treatment planning, and prevention of long-term sequelae.

Aim: To evaluate the PH status in female patients with endometriosis.

Materials and Methods: A cross-sectional study will be carried out in the Department of Periodontics, Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Higher Education and Research (Deemed to be University), Sawangi (M), Wardha, Maharashtra, India from September 2023 to March 2024, involving 384 participants (192 patients diagnosed with endometriosis and 192 controls). Assessment of oral hygiene, plaque accumulation, gingival status, Probing Pocket Depth (PPD), Clinical Attachment Level (CAL), Gingival Recession (GR), and other factors will be measured to evaluate the PH of the patients.

Keywords: Gynaecology, Gingivitis, Obstetrics, Periodontal health, Periodontal medicine, Periodontitis

INTRODUCTION

The presence of endometrial tissue or gland-like lesions elsewhere than the normal uterine cavity is a hallmark of endometriosis, a chronic disease that depends on oestrogen. It is one of the most common gynaecological causes of excruciating pelvic pain. It affects 10-15% of women of reproductive age, with a 0.1% annual incidence in women aged 15 to 49 years [1]. Several theories have been proposed to explain the cause of endometriosis, and retrograde menstruation is widely acknowledged as one of them. Although the exact aetiology is still unclear, hormonal, oxidative, immune, and epigenetic imbalances play a crucial role [2,3].

The PD is a group of inflammatory conditions affecting the supporting tissue of teeth. It is an endogenous, polymicrobial disorder that causes inflammatory destruction due to the presence of various predisposing factors such as poor oral hygiene, psychological stress, immunosuppression, smoking, local trauma, etc. It affects about 20-50% of the global population [4]. There is evidence connecting PD to other systemic disorders, such as diabetes, heart disease, unfavourable pregnancy outcomes, etc., [5-7].

The PD and endometriosis exhibit oxidative stress and increased Production of Reactive Oxygen Species (ROS). ROS, found in the peritoneal fluid of patients with endometriosis, cause lipid peroxidation, resulting in tissue destruction and Deoxyribonucleic Acid (DNA) damage to endometrial cells. Additionally, ROS generate oxidative stress signals that lead to inflammation, involving lymphocytes and activated macrophages, which produce cytokines and induce enzyme oxidation, stimulating endothelial growth. The accumulation of ROS further propagates endometriosis [8]. In PD, neutrophils, as the principal inflammatory cells implicated in the pathogenesis of the disease, contribute to increased cytokine synthesis and immunological activity in gingival tissue due to oxidative stress during phagocytosis [9]. Furthermore, lipopolysaccharide and DNA from plaque bacteria activate activating protein-1 and nuclear factor- κ B, resulting in the activation of osteoclast and matrix metalloproteinase, leading to tissue damage. Tissue destruction further activates neutrophils, macrophages, and fibroblasts, generating more ROS.

This cascade of events occurs in the presence of ROS, periodontal pathogens, and tissue destruction [10].

Literature shows a link between PD and endometriosis. However, the exact relationship between PH and endometriosis is still unknown [10-12]. A thorough understanding of the correlation between these two diseases is essential for early diagnosis, treatment planning, and prevention of long-term complications. The aim of the present research is to examine the connection between endometriosis and PH in female patients.

The research is to evaluate the correlation between endometriosis and PH for early diagnosis, treatment planning, and prevention of long-term complications. Healthcare practitioners, gynecologists, and dentists should proactively encourage patients diagnosed with endometriosis to maintain good oral hygiene and seek regular dental check-ups to prevent complications.

The study's originality lies in its primary objective of assessing the PH status in female patients who have been diagnosed with endometriosis residing in the Vidarbha district of Maharashtra. To our knowledge, this will be the first study conducted on the rural population residing in the Vidarbha region of Maharashtra. Additionally, there have been few studies assessing the connection between endometriosis and PD, and the participant sample sizes were very small [10,13]. Furthermore, there is insufficient data in the literature to support the theory that endometriosis and PD are significantly correlated. This research will compare the PH of female patients with endometriosis to control groups using a larger sample size.

Null hypothesis for the proposed study: There is no association between endometriosis and PD.

Alternative hypothesis: There is a significant association between endometriosis and PD.

Objectives

To compare the PH of women with endometriosis to that of healthy women (Controls). To assess the oral hygiene status of patients with endometriosis. To evaluate the prevalence of gingivitis and periodontitis among patients with endometriosis.

REVIEW OF LITERATURE

In 2009, Kavoussi SK et al., conducted a survey to investigate the potential correlation or mutual relationship between endometriosis and periodontitis. Their study revealed a possible link between these two conditions due to the absence of immunological modulation. Furthermore, the likelihood of a woman developing periodontitis increased by 57% if she specifically had endometriosis [11].

As part of a case-control study by Thomas V et al., periodontal screening was performed on 25 women diagnosed with endometriosis and 25 control subjects. The findings of this study demonstrated a positive association between endometriosis and Parkinson's disease [10]. Another study, led by Kasilovska K and Kasilovskiene Ž, involved 35 female participants to explore the connection between endometriosis and PD. Their results confirmed a link between endometriosis and PD [13].

Similar to polycystic ovarian syndrome and periodontitis, endometriosis also induces a subclinical inflammatory state marked by an increase in proinflammatory markers and cytokines such as TNF- α , IL-1 beta, IL-6, and IL-8. This inflammation can exacerbate periodontitis by accelerating the degradation of periodontal tissue [10,14]. It has been demonstrated that periodontitis could potentially serve as a direct source of bacterial dissemination-induced infection in chorionic and intrauterine tissues. Therefore, the hypothesis that periodontitis might trigger a local immunological response, in addition to the established subclinical inflammatory state in endometriosis, is plausible, but further research is required to fully explore this possibility [15].

METHODOLOGY

A cross-sectional study will be conducted in the Department of Periodontics, Sharad Pawar Dental College and Hospital (SPDC), Datta Meghe Institute of Higher Education and Research (DMIHER) (Deemed to be University), Sawangi (M), Wardha, Maharashtra, India from September 2023 to March 2024. The study proposal (ref. no. DMIHER(DU)/IEC/2023/1299) has been approved by the DMIHER Institutional Ethical Committee (IEC).

Sample size calculation [11,16]: The sample size will be calculated using the formula:

$$n = Z^2 p (1-p) / E^2$$

where,

confidence interval 95%

Z score: 1.96 for 95% confidence interval

proportion (p): 0.5

margin of error: 5%

$n \approx 384.16$

The study will include a total of 384 participants, with 192 women diagnosed with endometriosis and 192 control subjects. Diagnosis will be based on patient medical histories, physical examinations, clinical signs, symptoms, and radiological findings. The investigation will take place at SPDC's Department of Periodontics, where patients will be informed about the study protocol and asked for their informed consent.

Inclusion criteria: Women aged between 15-49 years (as endometriosis primarily affects women in their reproductive years, with an annual incidence of 0.1% in those aged 15-49 years) will be included [1].

- **Endometriosis group (Study group):** Patients previously diagnosed with endometriosis based on comprehensive case history, clinical signs, symptoms, physical examinations, and radiological findings {Ultrasonography (USG)} will be included in the study group. Endometriosis will be considered to exist if any of the following conditions are met:
 - Presence of gunshot or powder-burn lesions on the serosal surfaces of the peritoneum.

- Presence of chocolate cysts, characterised by thick, viscous dark brown fluid-filled nodules or small cysts with old haemorrhage surrounded by varying degrees of fibrosis [17,18].

- **Control group:** Recruitment for the control group will occur at the regular outpatient Department of Periodontics at SPDC in Sawangi. The control group will consist of 192 systemically healthy individuals matched for age (15-49 years).

Exclusion criteria: Individuals excluded will be

- Pregnant women;
- Smokers;
- Individuals with a history of alcohol consumption;
- Individuals who have received systemic antibiotics in the last 3 months;
- Patients who have undergone periodontal treatment in the last 6 months;
- Patients with fewer than 20 teeth;
- Endometriosis patients with a Body Mass Index (BMI) exceeding 25 will be excluded due to the potential effects of obesity and Impaired Glucose Tolerance (IGT) on periodontal conditions [19,20];
- Individuals suffering from any systemic conditions (e.g., cancer, osteoporosis, thyroid dysfunction, diabetes mellitus type 1 or type 2).

Primary outcome: The study will compare the PH of women with endometriosis to that of healthy women.

Secondary outcome: The oral hygiene status of female patients with endometriosis will be assessed. Periodontal screening for both the study and control groups will be performed using a mouth mirror, Williams's Graduated Periodontal Probe, and Explorer under adequate illumination.

Intraoral examination: It will include

- Assessment of oral hygiene and plaque using the Turesky-Gilmore-Glickman Modification of the Quigley-Hein plaque index (1970) [21].
- Evaluation of gingival status using the papillary bleeding index developed by Muhlemann HR (1977) [22].
- Measurements of Probing Pocket Depth (PPD) will be taken from the base of the pocket to the crest of the gingival margin [23].
- The measurement of Clinical Attachment Level (CAL) will be made from the Cementoenamel Junction (CEJ) to the sulcus base. PPD and CAL will be assessed at four sites per tooth: mesio-buccal, mid-buccal, disto-buccal, and mid-lingual, excluding third molars.
- Measurement of GR will be taken between the crest of the gingival margin and the CEJ.
- The clinical attachment loss will be calculated using the formula PPD+GR [23].

STATISTICAL ANALYSIS

The data will be analysed using multivariate analysis of covariance and student t-tests. Version 27.0 of the Statistical Package for the Social Sciences (SPSS) software will be used to conduct all statistical analyses, with a significance level set at p-value<0.05.

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