Exploring the Relationship Between Gingivitis and Pregnancy Outcomes: A Mini-review on the Molecular and Epidemiological

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ABSTRACT

Pregnancy is a unique and transformative period in a woman's life. While most studies focus on often on maternal health, it is crucial to recognize the intricate relationship between oral health and pregnancy outcomes. Gingivitis is a common gum disease characterized by inflammation of the gums. In the current review, we delve into the connection between gingivitis and pregnancy outcomes, shedding light on the epidemiological and molecular link that underlies this association.

Keywords: Gingivitis; Pregnancy Outcomes; Preterm Labor; Low Birth Weight (LBW); Preeclampsia; Narrative Review Article.

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Introduction

Pregnancy is a unique physiological process during which the maternal body undergoes numerous adaptations to support fetal development. Hormonal fluctuations during pregnancy can affect the oral cavity in various ways. For instance, increased blood flow to the gums may cause swelling and sensitivity, and increase patients' hesitancy toward oral hygiene. Also, the body's response to plaque may be altered, leading to an increased risk of gum disease. More importantly, pregnancy hormones can affect salivary flow, potentially causing dry mouth and an increased risk of both nonbacterial and bacterial inflammation.

Gingivitis is a common oral disease characterized by inflammation of the gums. It has garnered attention as a potential risk factor for adverse pregnancy outcomes. The link between gingivitis and pregnancy outcomes has been established through extensive research and observational studies (1-4). This article aims to delve into the connection between gingivitis and pregnancy outcomes, and explore related pathophysiology.

Identification of pregnancy outcomes related to gingivitis:

Multiple studies have consistently demonstrated an association between gingivitis and adverse pregnancy outcomes. These studies often involve large cohorts of pregnant women and assess their oral health status, particularly the presence of gingivitis, while monitoring subsequent pregnancy outcomes (1, 5). Here are some key pregnancy outcomes associated with gingivitis:

- Preterm Birth: Several studies have found a higher incidence of preterm birth among pregnant women with gingivitis than those with healthy gums. A meta-analysis combining multiple studies showed a significant association between periodontal disease (including gingivitis) and preterm birth. The risk of preterm birth appears to increase with the severity of gingivitis (5-8).
- Low Birth Weight (LBW): Similar to preterm birth, a correlation has been observed between gingivitis and low birth weight infants. Low birth weight is defined as babies weighing less than 2,500 grams (5.5 pounds). Studies have suggested that pregnant women with gingivitis are at a higher risk of delivering low-birth-weight infants compared to those with healthy gums (9).
- Preeclampsia: Epidemiological evidence also indicates a potential link between gingivitis and preeclampsia, a pregnancy-related condition characterized by high blood pressure. Several studies have reported increased preeclampsia among women with gingivitis or periodontal disease. However, the exact nature of this association is still being investigated (10-13).

These findings suggest that gingivitis is associated with an increased risk of adverse pregnancy outcomes, emphasizing the importance of oral health during pregnancy. It is important to note that epidemiological studies cannot establish causation alone. They provide valuable evidence to support associations between factors, but additional research, including experimental and clinical studies, is required to elucidate further the molecular and biological mechanisms involved (3, 6, 14).

Molecular pathogenesis of pregnancy outcomes related to gingivitis:

Gingivitis involves a complex interplay of molecular pathways that contribute to its development. Gingivitis is characterized by an inflammatory response triggered by the accumulation of dental plaque. This inflammatory process involves the release of various pro-inflammatory mediators. These molecules contribute to the recruitment and activation of immune cells, leading to local tissue damage and sustained inflammation. Gingivitis is also associated with increased reactive oxygen species (ROS) production, leading to oxidative stress (1, 15). To comprehend the molecular link between gingivitis and pregnancy outcomes, researchers have explored various mechanisms that may contribute to this relationship:

- Systemic Inflammation: Gingivitis is characterized by an inflammatory response triggered by the accumulation of dental plaque. This inflammatory process involves the release of various pro-inflammatory mediators, such as cytokines (e.g., interleukin-1β, tumor necrosis factor-α) and prostaglandins. These molecules contribute to the recruitment and activation of immune cells, leading to local tissue damage and sustained inflammation. This chronic inflammatory response can induce an imbalance in immune regulation, potentially triggering adverse pregnancy outcomes (16-18).
- Bacterial Dissemination: The oral cavity harbors diverse bacteria, and gingivitis can lead to the proliferation of harmful oral pathogens. These bacteria can enter the bloodstream through inflamed gum tissues and reach the placenta, causing local and systemic inflammation. This bacterial dissemination may disrupt placental function and compromise fetal development (19-21).
- Immunological Responses: The immune system plays a crucial role in developing and progressing gingivitis. Oral bacteria in dental plaque induce an immune response, producing antimicrobial peptides, chemokines, and activation of immune cells

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like neutrophils and macrophages. Gingivitis-related inflammation can activate immune cells and alter the delicate immune balance required for a successful pregnancy. Dysregulated immune responses may impact placental development and vascular function, contributing to adverse outcomes (22-24).

• Oxidative Stress: Gingivitis-associated inflammation can increase oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) production and antioxidant defenses. Excessive ROS can damage cellular components and disrupt essential cellular processes, potentially affecting placental function and fetal well-being (25-27).

The inflammatory mediators, immune responses, bacterial-host interactions, oxidative stress, and hormonal influences in gingivitis can disrupt placental function, compromise vascular health, and trigger adverse pregnancy outcomes such as preterm birth and low birth weight. Understanding the molecular pathways of gingivitis provides a foundation for developing targeted interventions and preventive strategies (1, 3, 28).

Conclusion:

Recognizing the importance of oral health during pregnancy is crucial for promoting positive pregnancy outcomes and overall maternal and fetal well-being. Further research is warranted to develop targeted interventions and preventive strategies to minimize the impact of gingivitis on pregnancy outcomes. We believe this review's findings will help healthcare providers implement preventive measures, foster interdisciplinary collaboration, and optimize prenatal care to promote better oral health and improve pregnancy outcomes.

of endometriosis with acceptable accuracy with the help of a transvaginal ultrasound (TVUS) examination. Therefore, the surgeon can estimate the complexity of the operation before performing the surgery. UBESS was added as a backup to some other classification systems (16). One of the applications of classification based on imaging stereotypes is determining the extent of rectosigmoid involvement in endometriosis. Rectosigmoid involvement is seen in one-third of patients with deep infiltrating endometriosis. Researchers developed the ENDORECT scoring system based on four simple preoperative items. These include palpation of a posterior nodule on digital examination, UBESS score of 3 on TVUS, rectosigmoid infiltration on MRI, and blood in stool during menstruation (17).

Discussion

The present study explains ten different classification methods of endometriosis. These classification methods have tried to categorize situations where the endometrial tissue is located in a place other than its original location. Many studies show that different anatomical types of endometriosis may show distinct gene expressions. In gene expression, information encoded in genes produces functional products such as proteins that perform various biological functions in cells. Depending on changes in gene expression, endometriosis can develop, progress, and respond differently to treatment. Gene expression patterns in different anatomical types of endometriosis have been studied by researchers using various techniques such as microarray analysis and RNA sequencing. Studies have shown potential differences in the gene expression profiles of different forms of the disease, including deep infiltrating endometriosis, ovarian endometriomas (endometriomas), and superficial peritoneal endometriosis. Differentially expressed genes in specific anatomic types of endometriosis may reveal details about the underlying molecular mechanisms and suggest potential therapeutic targets. For example, several genes have been discovered to be dysregulated in endometriotic lesions. These genes are involved in inflammation, hormonal signaling pathways, angiogenesis and tissue regeneration (18). Examining endometriosis gene expression patterns has also helped classify and subtype this disease. Molecular subtypes of endometriosis have been identified through integrative analyzes combining gene expression data with clinical and pathological features. These molecular subtypes may affect prognosis and treatment selection (19). For example, Gueuvoghlanian-Silva et al. study showed that GITR, TNFRII, HLA-DR, ICOS CTLA-4, CD45RA, and CD45RO markers are significantly more expressed in regulatory T cells in cases of deep involvement (20). On the other hand, a study demonstrated that FOXO1A, MIG6 and CYP26A1 are more involved in cases where the superficial peritoneum is involved. As a result, each type of endometriosis illustrates very different behaviors. For example, superficial endometriosis usually affects only the surface of the peritoneum, and simultaneous deep involvement in the bladder or rectum is infrequent in this type. Similarly, in the case of deep involvement, the involvement of the peritoneal surface is not seen simultaneously (21). On the other hand, it seems that although the mentioned categories cover the common types of endometriosis, some types of endometriosis, such as involvement of the uterus and distant areas, which impose a significant burden on patients, have been neglected. Extrapelvic endometriosis refers to the presence of endometrial-like tissue outside the pelvic area. While endometriosis primarily affects pelvic organs such as the ovaries, fallopian tubes, and peritoneum, extrapelvic endometriosis can appear throughout the body. The most common sites involved are the digestive, urinary, and respiratory systems and surgical scars. The exact mechanisms of extrapelvic

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endometriosis are not fully understood, but several theories have been proposed, including retrograde menstruation, lymphatic or vascular spread, metaplasia, and iatrogenic factors. The clinical manifestations of extrapelvic endometriosis can vary depending on the location of the lesions, including symptoms such as gastrointestinal complaints, urinary dysfunction, breathing problems, and pain. Diagnosis of extrapelvic endometriosis can be challenging and often requires a multidisciplinary approach and integration of clinical evaluation, imaging studies, and histopathological confirmation. Treatment options may include medical management, surgery, or an interdisciplinary approach (22-24). As mentioned, endometriosis is usually a disorder in which tissue similar to the endometrium develops outside the uterus. Adenomyosis is defined as uterine endometrium growth towards the muscular wall of the uterus. Historically, adenomyosis and endometriosis have been considered separate entities. However, recent studies have suggested a possible link between the two conditions (25). It should be noted that in both adenomyosis and endometriosis, the abnormal growth of endometrial tissue is observed outside its usual place. Current literature has stated that both diseases share similar genetic, hormonal, and immunological factors, indicating a common underlying pathogenesis. Endometrial glands and stroma inside the myometrium in adenomyosis further support the notion that adenomyosis is a type of endometriosis (26). It should also be noted that adenomyosis and endometriosis have significant clinical overlap. These two diseases often appear simultaneously in patients. Also, women with adenomyosis often experience pelvic pain, dysmenorrhea, and heavy menstrual bleeding. These symptoms are similar to what is seen in endometriosis. The similarity in clinical manifestations indicates similar pathogenesis between these two conditions (27). Regarding imaging and histological findings, there are significant similarities between adenomyosis and endometriosis. Imaging methods reveal similarities in the appearance and distribution of lesions in both conditions. This manifestation is consistent with studies that claim that adenomyosis is a type of endometriosis. Histological investigations also show that endometrial glands and stroma are present in a similar way in both adenomyosis and endometriosis (28, 29). Finally, these two disorders have similarities with each other in terms of response to treatment. In other words, adenomyosis responds well to medical and surgical interventions that are usually used for endometriosis. Hormonal therapies, such as gonadotropin-releasing hormone (GnRH) agonists and oral contraceptives, are effective in the management of both adenomyosis and endometriosis mediate. Similarly, surgical methods such as laparoscopy and hysterectomy are used to treat both diseases (30, 31).

Conclusion

Present systematic review evaluated ten articles in the field of endometriosis classification. Despite the fact that a considerable period of time has passed since the identification of endometriosis, a comprehensive and integrated classification has not yet been proposed. We believe that according to the findings related to gene expression, in near future five disorders of superficial peritoneal endometriosis, cystic ovarian endometriosis (endometrioma), deep endometriosis, extra-pelvic endometriosis and adenomyosis will be classified as five similar disease, rather than five forms of a single diseases.

Ethical Issue

There was no ethical issue in this systematic review.

Conflict of interests

There was no conflict of interest in this study.

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