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CLINICAL AND IMMUNOLOGICAL FEATURES OF CHRONIC HERPETIC STOMATITIS IN BREASTFEEDING WOMEN

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Abstract. Chronic herpetic stomatitis (CHS) is a common recurrent viral disease of the oral mucosa characterized by persistent inflammation and frequent relapses. In breastfeeding women, the clinical course of CHS demonstrates specific features associated with postpartum immune modulation. The aim of this study was to evaluate clinical manifestations and immunological characteristics of chronic herpetic stomatitis in breastfeeding women. Severity of oral mucosal inflammation, frequency of relapses, viral activity, and parameters of humoral and cellular immunity were assessed using clinical indices, real-time polymerase chain reaction, enzyme-linked immunosorbent assay, and lymphocyte phenotyping. The results revealed pronounced inflammatory changes, high prevalence of active herpes simplex virus replication, decreased mucosal immune protection, and dysregulation of cellular immune responses in breastfeeding women with CHS. These findings highlight the central role of immune imbalance in disease persistence and support the necessity of an integrated clinical and immunological approach to diagnosis and management of chronic herpetic stomatitis during lactation.

Keywords: chronic herpetic stomatitis, breastfeeding women, clinical features, immune imbalance, cellular immunity, humoral immunity.

Introduction. Chronic herpetic stomatitis (CHS) remains one of the most prevalent recurrent viral diseases affecting the oral mucosa and is characterized by persistent inflammation, pain syndrome, and a tendency to frequent relapses. The etiological agent, herpes simplex virus (HSV), establishes lifelong persistence in the host organism and periodically reactivates under conditions of impaired immune surveillance, leading to recurrent mucosal lesions and chronic disease progression [3,13,16].

The clinical significance of CHS is particularly pronounced in women during pregnancy and the postpartum period. Physiological immune modulation associated with pregnancy and breastfeeding creates favorable conditions for viral reactivation and persistence. Several studies have demonstrated that immune alterations during these periods contribute to increased susceptibility to herpesvirus infections and more severe or recurrent clinical manifestations [4,7,8].

Breastfeeding women represent a distinct clinical group in which immune regulation differs from that observed in both pregnant women and the general adult population. The postpartum period is accompanied by gradual restoration of immune reactivity; however, this process may be incomplete or dysregulated, leading to reduced antiviral defense mechanisms. As a result, chronic herpetic stomatitis in breastfeeding women often demonstrates prolonged inflammatory course, increased relapse frequency, and resistance to conventional therapeutic approaches [1,7,9].

Immunological disturbances in CHS involve both humoral and cellular components of the immune system. Previous investigations have reported decreased levels of immunoglobulin A, impaired interferon response, reduced $CD4^+$ T-lymphocyte counts, and diminished activity of natural killer cells, which play a key role in controlling herpesvirus replication [5,6,9]. These

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alterations compromise local and systemic antiviral immunity, facilitating viral persistence within the oral mucosa. Modern diagnostic approaches, including polymerase chain reaction (PCR), have significantly improved the detection of HSV DNA and enabled objective assessment of viral activity in recurrent forms of the disease. Studies have shown that PCR-based diagnostics allow differentiation between latent carriage and active viral replication, which is essential for adequate evaluation of disease severity and recurrence risk [2,10,12].

Despite the growing body of literature addressing herpetic stomatitis, most studies focus either on pediatric populations, pregnant women, or general adult cohorts. Data specifically evaluating clinical and immunological characteristics of chronic herpetic stomatitis in breastfeeding women remain limited. In addition, existing publications often analyze clinical manifestations and immune alterations separately, without comprehensive integration of these factors. Therefore, a detailed investigation of clinical features and immune status in breastfeeding women with chronic herpetic stomatitis is necessary to clarify disease pathogenesis and to improve diagnostic and therapeutic strategies for this specific patient population. Understanding immune mechanisms underlying recurrent disease during lactation may contribute to the development of targeted and safe management approaches.

Aim of the Study. The aim of the present study was to conduct a comprehensive assessment of clinical manifestations and immune status in breastfeeding women with chronic recurrent herpetic stomatitis in order to clarify the pathogenetic mechanisms underlying disease persistence and recurrence during the lactation period. Specifically, the study aimed to evaluate the severity of inflammatory changes of the oral mucosa, determine the frequency of active herpes simplex virus replication using molecular diagnostic methods, and analyze alterations in humoral and cellular immunity associated with chronic herpetic stomatitis in breastfeeding women. An additional objective of the study was to identify key immunological factors contributing to impaired antiviral defense and to substantiate the clinical significance of integrated clinical and laboratory diagnostics for optimizing management strategies in this patient population.

Materials and Methods

Study Design. This study was designed as an observational case–control study aimed at evaluating clinical and immunological characteristics of chronic herpetic stomatitis in breastfeeding women during the postpartum period.

Study Population. A total of 72 breastfeeding women aged 21–37 years were enrolled in the study and examined at the clinical facilities of the Tashkent State Dental Institute.

Participants were divided into two groups:

- Main group: 48 breastfeeding women diagnosed with chronic herpetic stomatitis.
- Control group: 24 clinically healthy breastfeeding women without inflammatory or viral lesions of the oral mucosa.

The groups were comparable in terms of age, lactation duration, and general health status.

Eligibility Criteria

Inclusion criteria (main group):

- confirmed diagnosis of chronic herpetic stomatitis;
- recurrent course of the disease (≥2 relapses per year);
- active breastfeeding at the time of examination;
- informed consent to participate.

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Exclusion criteria (both groups):

- acute infectious diseases;
- autoimmune or immunodeficiency disorders;
- recent antiviral or immunomodulatory therapy (within the last 3 months);
- severe systemic diseases.

Clinical Assessment. All participants underwent a comprehensive dental examination, including:

- evaluation of subjective complaints (pain, burning sensation, oral discomfort);
- assessment of oral mucosal lesions and inflammatory changes;
- classification of disease severity based on clinical findings.

Periodontal status was assessed using:

- the Papillary-Marginal-Alveolar (PMA) index;
- the oral hygiene index, calculated according to standard clinical methods.

Virological Examination. Detection of herpes simplex virus DNA was performed using real-time polymerase chain reaction (PCR).
Biological samples were collected from the oral mucosa by sterile scraping techniques.

Immunological Methods. The immune status of participants was evaluated by analyzing both humoral and cellular immunity.

- Humoral immunity: serum levels of IgA, IgM, and IgG were determined using enzyme-linked immunosorbent assay (ELISA).
- Cellular immunity: immunophenotyping of peripheral blood lymphocytes was carried out to determine $CD3^+$, $CD4^+$, $CD8^+$ T lymphocytes and natural killer (NK) cells.

Statistical Analysis. Statistical processing of data was performed using standard biomedical statistical methods.
Results are presented as mean ± standard error (M ± SE).

Intergroup comparisons were conducted using:

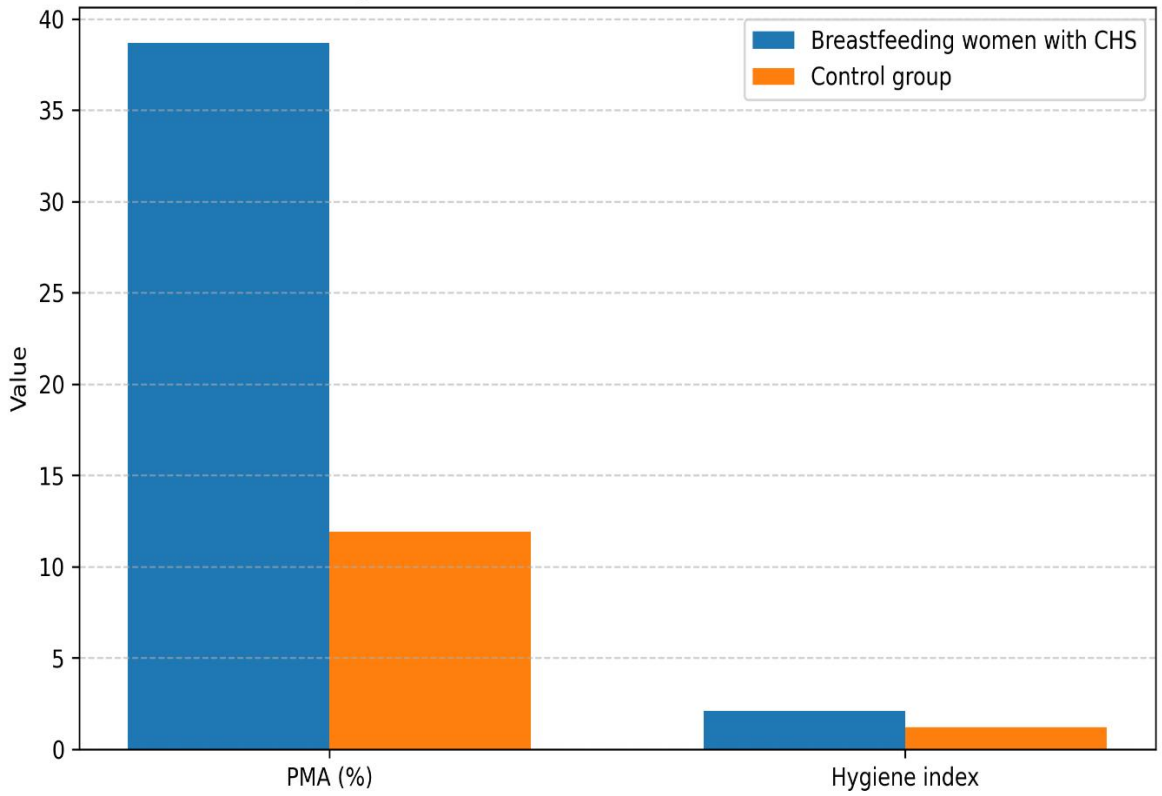
- Student's *t*-test for quantitative variables;
- χ^2 test for categorical data.

Statistical significance was defined as $p < 0.05$.

Results. *Clinical findings*. Clinical evaluation demonstrated pronounced inflammatory involvement of the oral mucosa in breastfeeding women with chronic herpetic stomatitis (CHS). The mean Papillary-Marginal-Alveolar (PMA) index in the CHS group reached 38.7%, significantly exceeding the control group value (11.9%, $p < 0.05$). The oral hygiene index was also markedly higher in the CHS group (2.1) compared with healthy breastfeeding women (1.2, $p < 0.05$), indicating persistent inflammatory activity and compromised periodontal status (Figure 1).

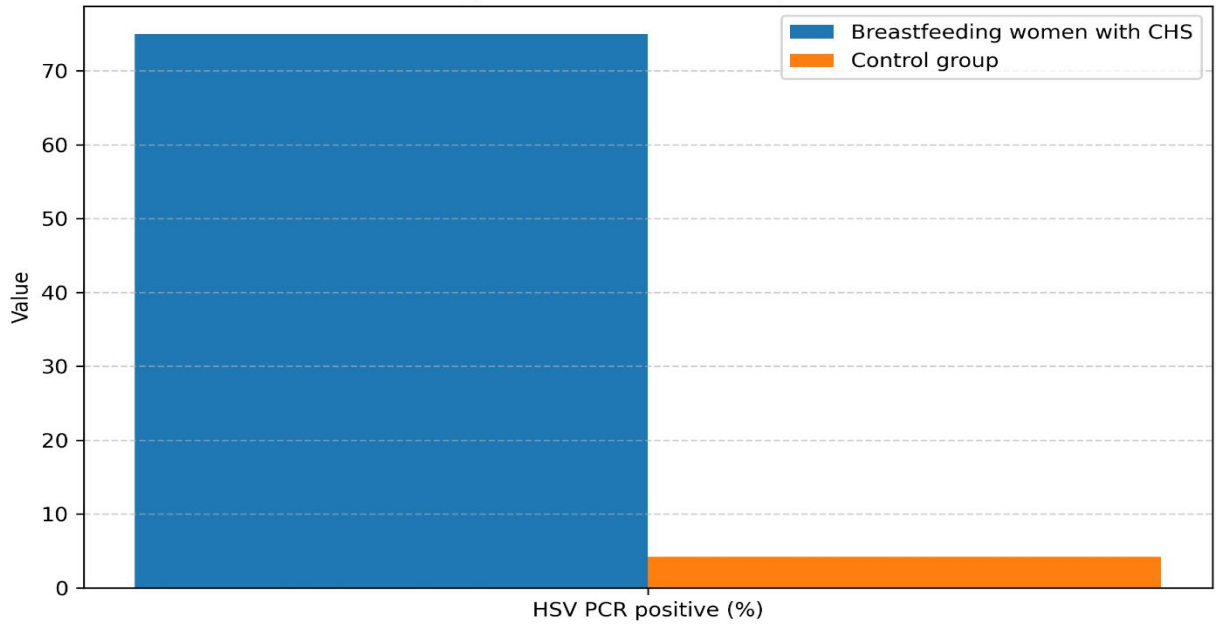
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Figure 1. Clinical indices of oral inflammation



Detection of herpes simplex virus by PCR. Real-time polymerase chain reaction analysis revealed active herpes simplex virus replication in 75.0% of breastfeeding women with CHS, whereas HSV DNA was detected in only 4.2% of control participants, consistent with latent viral carriage ($p < 0.001$) (Figure 2).

Figure 2. HSV detection by PCR



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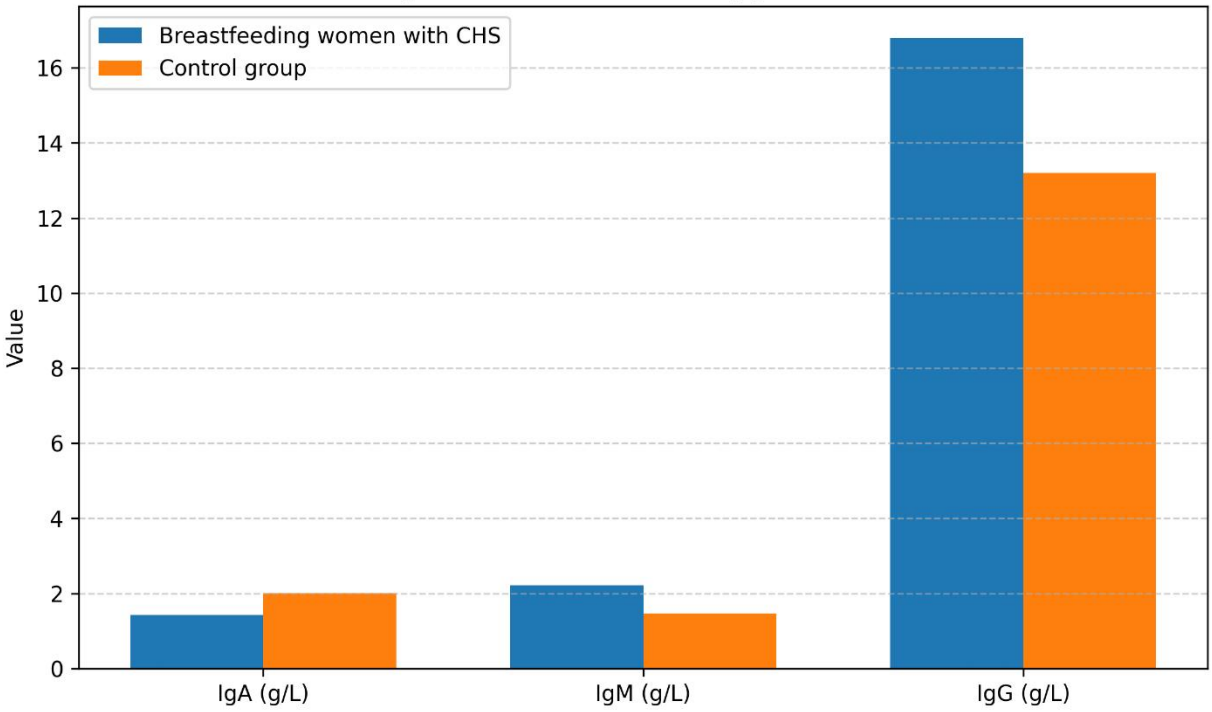
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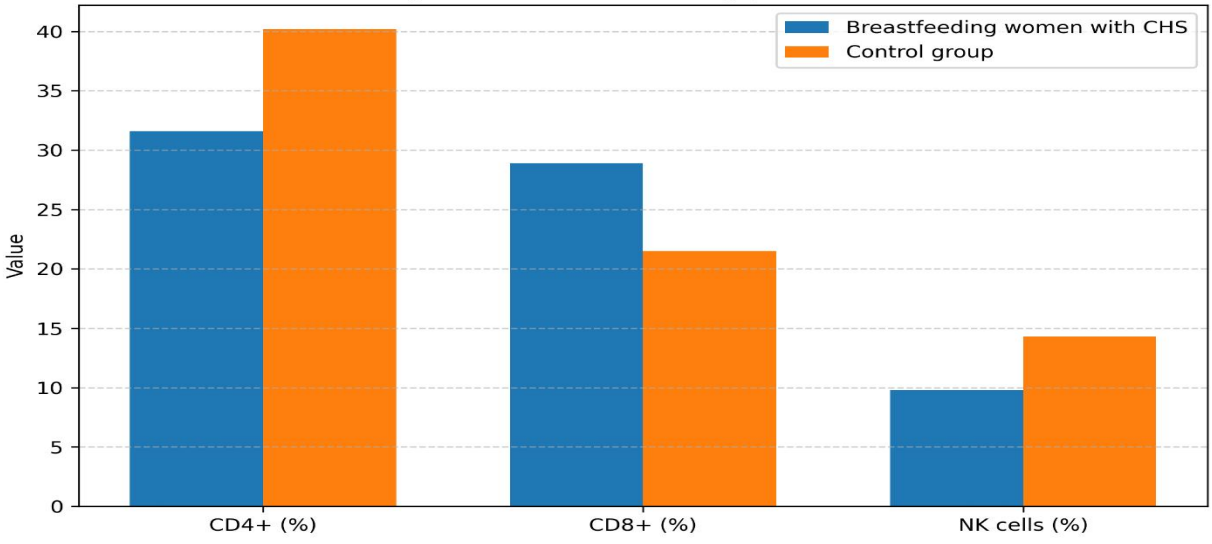
Humoral immunity parameters. Assessment of humoral immunity showed a significant decrease in serum IgA levels in the CHS group (1.42 g/L) compared with controls (2.01 g/L, $p < 0.05$). In contrast, IgM (2.21 g/L) and IgG (16.8 g/L) concentrations were elevated relative to healthy breastfeeding women (1.47 g/L and 13.2 g/L, respectively), reflecting chronic antigenic stimulation (Figure 3).

Figure 3. Humoral immunity parameters



Cellular immunity alterations. Cellular immunity analysis revealed a reduction in $CD4^+$ T-lymphocytes (31.6% vs. 40.2% in controls) and natural killer cells (9.8% vs. 14.3%, $p < 0.05$), accompanied by an increased proportion of $CD8^+$ T-lymphocytes (28.9% vs. 21.5%). These findings indicate dysregulation of antiviral immune surveillance in breastfeeding women with CHS (Figure 4).

Figure 4. Cellular immunity parameters



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Integrated interpretation of results. Taken together, the obtained results demonstrate that chronic herpetic stomatitis in breastfeeding women is characterized by a combination of severe local inflammation, high viral replication activity, suppression of mucosal immunity, and dysregulation of cellular immune responses. The concordant changes in clinical indices, PCR findings, and humoral and cellular immunity parameters underline the systemic nature of immune dysfunction associated with CHS during lactation.

Results and Discussion. The findings of the present study demonstrate that chronic herpetic stomatitis (CHS) in breastfeeding women is characterized by a complex interaction between pronounced local inflammation, active herpes simplex virus replication, and dysregulation of humoral and cellular immunity. Clinical evaluation revealed significantly elevated inflammatory indices in breastfeeding women with CHS , confirming persistent involvement of the oral mucosa and periodontal tissues. Similar increases in PMA and hygiene indices have been reported in women during hormonally vulnerable periods, indicating that immune modulation plays a critical role in maintaining chronic inflammation of the oral mucosa [6,10].

The high frequency of HSV DNA detection by real-time PCR in the CHS group indicates active viral replication rather than latent carriage. Previous studies have emphasized that immune suppression during pregnancy and the postpartum period facilitates herpesvirus reactivation, leading to recurrent and prolonged clinical manifestations [3,7,8].

In contrast, minimal PCR positivity in the control group reflects asymptomatic viral persistence, supporting the diagnostic value of PCR in differentiating active disease from latent infection [2,10].

Analysis of humoral immunity demonstrated a marked reduction in IgA levels in breastfeeding women with CHS. Secretory and serum IgA are essential components of mucosal immune defense, preventing viral adhesion and penetration into epithelial tissues. Decreased IgA concentrations observed in the present study are consistent with earlier reports describing impaired local immunity in chronic inflammatory diseases of the oral cavity and recurrent herpetic infections [5,7,11].

At the same time, elevated IgM and IgG levels reflect persistent antigenic stimulation and chronic immune activation, a characteristic feature of recurrent herpesvirus infections [12,15].

This imbalance suggests that systemic immune activation does not compensate for deficient local immune protection. Disturbances in cellular immunity further explain the chronic and recurrent course of CHS in breastfeeding women. Reduced $CD4^+$ T-lymphocyte counts observed in the CHS group indicate impaired immune regulation and insufficient coordination of antiviral responses. $CD4^+$ cells play a pivotal role in orchestrating both humoral and cellular immunity; their reduction has been associated with increased susceptibility to herpesvirus reactivation [6,12].

The relative increase in $CD8^+$ T-lymphocytes may represent a compensatory cytotoxic response; however, without adequate helper T-cell support, this response remains ineffective. Of particular importance is the significant decrease in natural killer (NK) cells detected in breastfeeding women with CHS. NK cells are key effectors of innate antiviral immunity and are responsible for early elimination of virus-infected cells. Previous investigations have demonstrated that reduced NK cell activity is strongly associated with frequent relapses and prolonged persistence of herpesvirus infections [12,18].

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The observed NK cell deficiency in the present study further supports the concept of impaired antiviral immune surveillance during lactation. Integrating clinical, virological, and immunological findings allows the formulation of a unified pathogenetic model of CHS in breastfeeding women. Lactation-associated immune vulnerability leads to suppression of mucosal immunity (IgA ↓), dysregulation of cellular immune surveillance ($CD4^+$ ↓, NK ↓), and persistence of active viral replication (HSV PCR ↑). These interrelated mechanisms form a self-perpetuating cycle of inflammation and viral reactivation, resulting in chronic and recurrent disease. The concordance of these findings with existing literature confirms that CHS during lactation should be regarded as a systemic immunologically mediated condition rather than a purely local oral pathology [1,3,6,7,11].

Conclusion. The present study demonstrates that chronic herpetic stomatitis in breastfeeding women represents a distinct clinical and immunological condition characterized by pronounced inflammatory activity of the oral mucosa, active herpes simplex virus replication, and significant dysregulation of both humoral and cellular immunity. Elevated clinical indices of inflammation, combined with high HSV PCR positivity, confirm that viral reactivation during lactation is closely associated with impaired immune control rather than latent viral carriage. The reduction of mucosal immune protection, reflected by decreased IgA levels, together with suppression of key cellular immune components such as $CD4^+$ T-lymphocytes and natural killer cells, indicates a state of lactation-associated immune vulnerability. This immune imbalance facilitates persistent viral activity and contributes to the chronic and recurrent course of the disease. Simultaneously, increased systemic immunoglobulin levels (IgM and IgG) reflect ongoing antigenic stimulation and chronic immune activation, further supporting the multifactorial nature of CHS pathogenesis in breastfeeding women. Taken together, the findings highlight that chronic herpetic stomatitis during lactation should be considered a systemic immunologically mediated disorder rather than a purely local oral infection. Comprehensive assessment integrating clinical examination, molecular virological diagnostics, and detailed immune profiling is essential for accurate diagnosis and for the development of effective, individualized management strategies. Future therapeutic approaches should focus not only on antiviral treatment but also on restoring immune balance in breastfeeding women to reduce recurrence rates and improve long-term outcomes.

Conclusion.

Breastfeeding women with chronic herpetic stomatitis exhibit significantly higher clinical indices of oral inflammation compared with healthy controls, indicating pronounced and persistent inflammatory involvement of the oral mucosa during lactation.

Active replication of herpes simplex virus is a characteristic feature of chronic herpetic stomatitis in breastfeeding women, as evidenced by a substantially higher rate of HSV DNA detection by real-time PCR.

Humoral immunity in breastfeeding women with chronic herpetic stomatitis is characterized by reduced IgA levels, reflecting impaired mucosal immune defense, alongside elevated IgM and IgG concentrations indicative of chronic antigenic stimulation.

Cellular immune alterations include a decrease in $CD4^+$ T-lymphocytes and natural killer cells, accompanied by a relative increase in $CD8^+$ T-lymphocytes, demonstrating dysregulation of antiviral immune surveillance.

The combined disturbances in clinical parameters, viral activity, and immune regulation suggest that lactation-associated immune vulnerability plays a central role in the pathogenesis and recurrence of chronic herpetic stomatitis.

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Comprehensive integration of clinical, virological, and immunological assessments is crucial for accurate diagnosis and effective management of chronic herpetic stomatitis in breastfeeding women.

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