Vol. 13, No.4 October-December 2021

HISTOPATHOLOGICAL CHANGES IN THE GUM EPITHELIUM OF PATIENTS WITH STOMACH ULCER

Valery Olenichuk [1], Iryna Sokolova[1], Olena Yaroshenko[1]

[1] Kharkiv National Medical University, Kharkiv, Ukraine, Educational and Scientific Institute for Postgraduate Training, Department of Dentistry

Corresponding author: Iryna Sokolova sdent_irina@ukr.net

All authors have the same contribution as the first author

ABSTRACT.

This study aims to study the histopathological changes in the epithelium of the alveolar processes in patients with gastric ulcer. Material and methods. Gums bioptats in stomach ulcers patients have been studied, and 10 of them had chronic cataract and 8 had chronic periodontitis. The morphological structure after staining of paraffin sections was studied using traditional histological and histochemical methods. Also microscopic cytophotometry video was done. Results. Histopathological restructuring of the papillary and reticular zone of the lamina propria was detected, and also increasing number of microspaces between the basal and spine layers in epithelial cells causes growing hydrodynamic disorganization in microcirculation system. The research has led to the conclusion that gingival epithelium alteration in patients with peptic ulcer disease is a local demonstration the systemic immune response to contamination of the mucous membranes in gastrointestinal tract with Helicobacter pylori, and inflammatory-dystrophic changes in the overlying layers of epithelial cells are secondary.

Keywords. *H.pylori*, stomach ulcer, chronic gingivitis, chronic periodontitis.

INTRODUCTION

In population morbidity structure in different age periods the digestive system pathology occupies a leading position [1, 2]. As the initial section of the gastrointestinal tract, the oral cavity is influenced by pathological processes associated with the internal organs system and it's esophago-gastro-duodenal segment particularly. The resulting changes, defining oral fluid physical and chemical properties, the local immunity state and teeth hard tissues, hygienic indicators, take on a mutually aggravating character. Although all oral cavity organs more - less are involved in the pathological process, the most manifest changes occur in an alveolar processes mucous membrane, from it's damage the cascade of increasing functional reflex reactions starts, this fact is ultimately leading to pathological structural and adaptive restructuring the entire periodontal complex. The peptic ulcer disease etiology and pathogenesis concept as a systemic disease with ulcer substrate localization in one or another part of the stomach has undergone significant changes over the last 30 years. Currently, infection is recognized as the leading cause of the ulcerative process genesis and development is *Helicobacter pylori (H. pylory). H. pylori* colonization in gastric epithelium begins with an oral cavity. Analysis of publications devoted to this topic shows, that *H.pylori* is determined in smears from the surface in mucous membrane of the cheeks, tongue, hard and soft palate. Meanwhile, the detection rate of the microorganism in dental plaque is the highest. [3, 4, 5, 6, 7, 8].

Rational treatment tactics of *H. pylori*-associated periodontitis is not possible without taking into account the mechanisms of

pathogenesis and underlying reaction of the mucosal system of the digestive tract in response to *H. pylori* infection. Thus, the **purpose of our study** is to study the histopathological changes in the epithelium of the alveolar processes in patients with gastric ulcer.

MATERIAL AND METHODS

Gums biopsies in patients with gastric ulcer were studied, among them 10 had manifestations of chronic gingivitis (CG) and 8 were diagnosticated with chronic periodontitis (CP). The selection criteria for patients were the dentoalveolar deformities absence, malocclusion, defects in the dentition. The study material was the gingival mucosa tissues, 2 x 5 mm in size (2 fragments in each observation), that were taken at the periodontal treatment stages after obtaining the informed patient's agreement. Samples were fixed in neutral 10% formalin. Tissue densification was achieved by wiring through alcohols increasing concentration, celloidin, chloroform and embedding in paraffin. For subsequent staining, sections with a thickness of $5\text{-}6\times10^{-6}$ m were prepared. The morphological structure after staining of paraffin sections was studied using traditional histological and histochemical methods: staining with hematoxylin and eosin, picrofuchsin according to van Gieson, a PAS reaction was performed to identify glycosaminoglycans. Microscope preparations were examined under a "Olympus BX-41" microscope with subsequent processing by the "Olympus DP-soft version 3.1" program, with it's help, besides determining the intensity of histochemical reactions, a morphometric study was also carried out with an optical density quantitative assessment of sections in the blue light spectrum with the help of video microscopic cytophotometry. The relative density of certain structural components was determined by additional superimposition of the meshes displayed on the computer monitor and subsequent counting that were done with the help of an Olympus DP-soft version 3.1 software. In each observation, 30 randomly selected fields of view were studied.

RESULTS

The study of biopsies made it possible to establish an irregular thickening of the epithelium due to the cells of the prickly and granular layers. In patients with CP, the thickening of the epithelial lining was combined with the immersion of epithelial elements into the lamina propria. In some fields, acantholytic cords anastomosed among themselves, disrupting the cytoarchitectonics of the epithelial layer. Acanthosis was more pronounced in patients with CG. The thickness of the epithelial layer in patients with CG was on average $750{,}3 \pm 4.5$ micron, in patients with CP $337{,}5 \pm 3{,}2$ micron $P \leq 0{,}01$ (fig. 1).

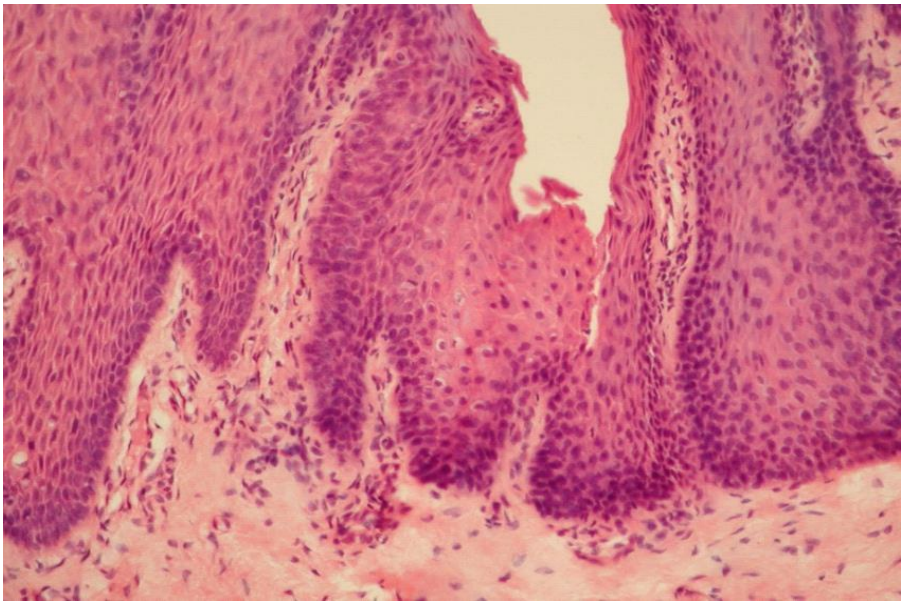

Fig. 1. Chronic Gingivitis. Acantholytic bands. Hematoxylin and eosin staining. ×200.

An epithelial cells heterogeneity was recorded in all preparations, manifested by the unevenness of their color and size variability. In an epithelial cells intercellular spaces of their basal and suprabasal layers were determined the expansion of the intercellular spaces and the formation of zones of spongiosis. Epithelium above-located areas were characterized by the presence of hydropic dystrophy zones in the form of light-optically "empty" cells (fig.2,3).

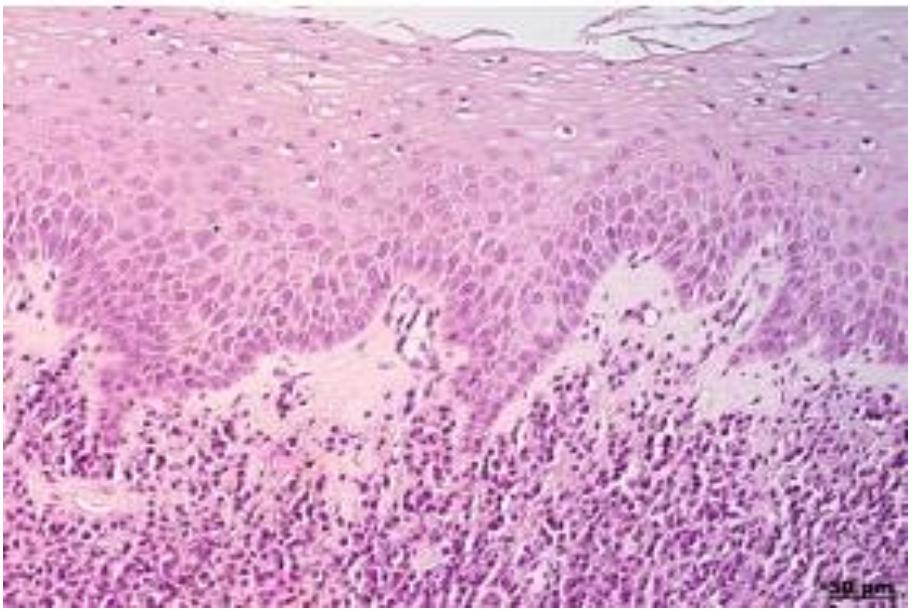

Fig. 2. Chronic Gingivitis. Hydropic dystrophy. Hematoxylin and eosin staining ×200.

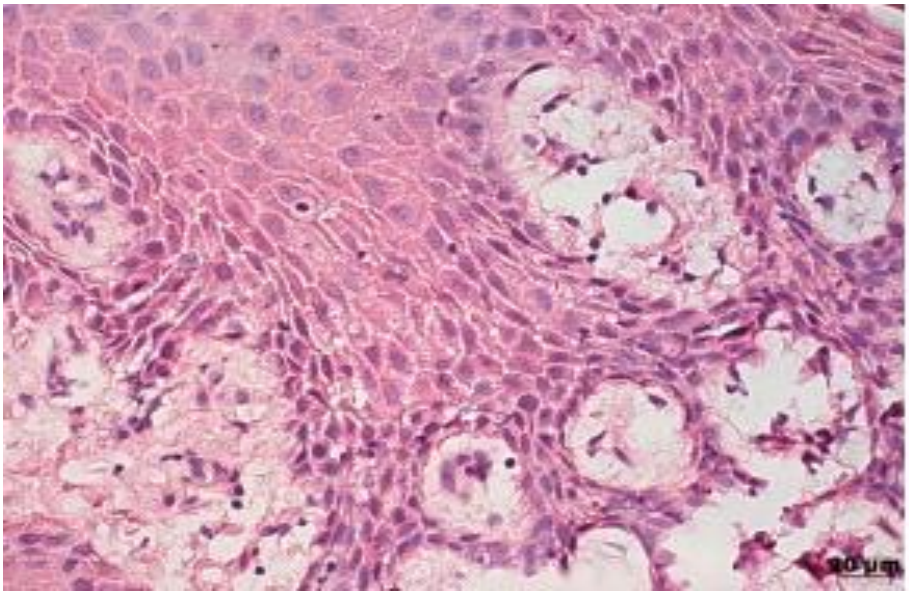

Fig. 3. Chronic Gingivitis. Intercellular edema, expansion of intercellular spaces. Hematoxylin and eosin staining. ×400.

In all preparations that were studied, we observed an inflammatory infiltrate whose substrate was lymphocytes, plasma cells, macrophages. The focus of localization is an intraepithelial and in the perivascular vessels spaces that are located most closely to the basement membrane. In lymphatic-plasma cell infiltration zones, lamina propria fibrosis is observed, in some cases, also the decreasement in lumen of the vessels diameter in microvasculature, up to their complete obliteration (fig. 4, 5).

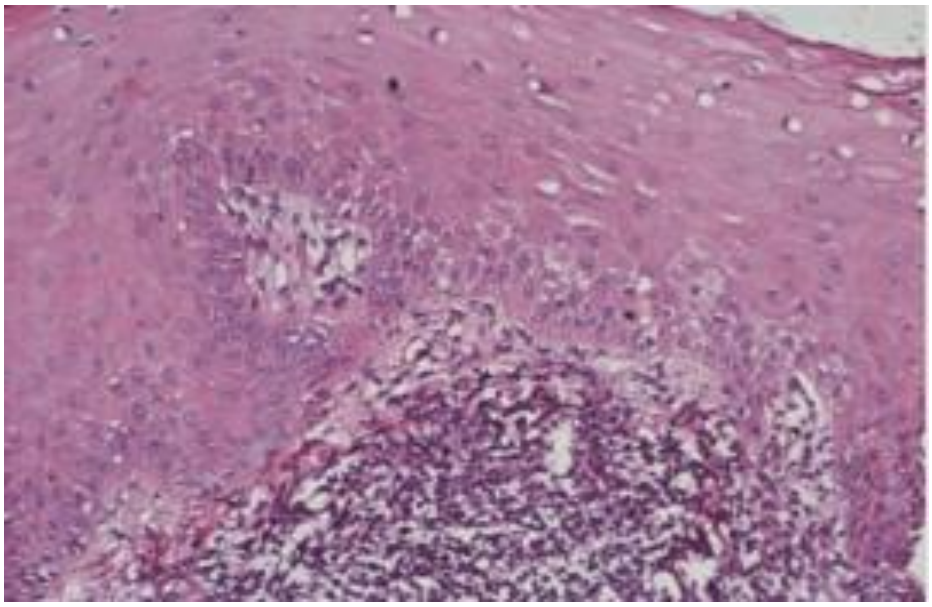

Fig.4. Chronic Periodontitis. Lamina propria infiltration in the epithelium with lymphocytes and plasma cells. Staining with hematoxylin and eosin. Increase × 400.

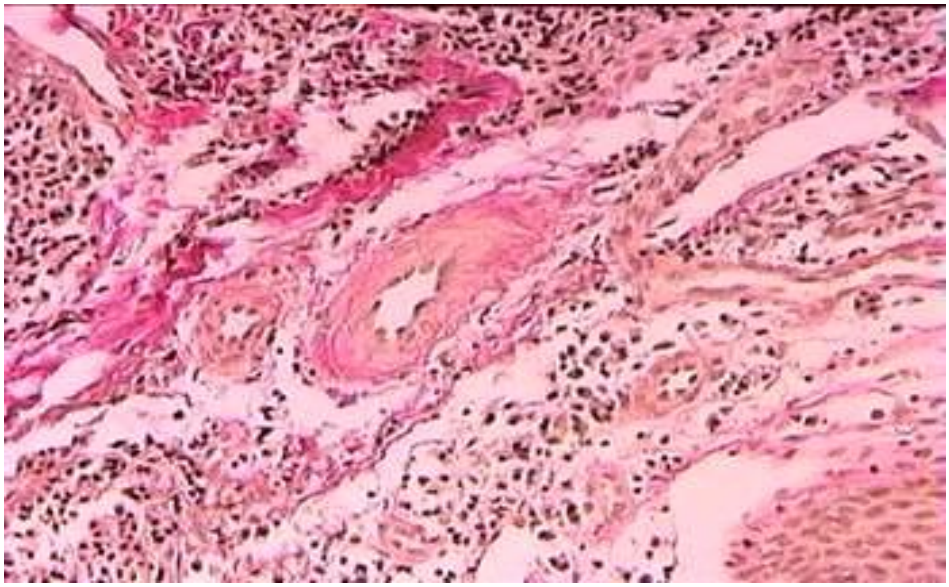

Fig 5. Chronic Periodontitis. Reducing the diameter of the lumen of the vessels. Staining with hematoxylin and eosin. Increase × 400.

The most indicative morphological sign of epithelial alteration in CP patients was the expansion of the intercellular spaces in the basal and prickly layers, due to the movement of excess volume of exudate from the hydrated interstitium of the lamina propria, followed by disintegration and destruction of epithelial cells of all layers. In micropreparations obtained from a biopsy material in patients with CP, areas of the epithelium were found, densely seeded with rod-shaped and spiral-shaped microorganisms (fig. 6).

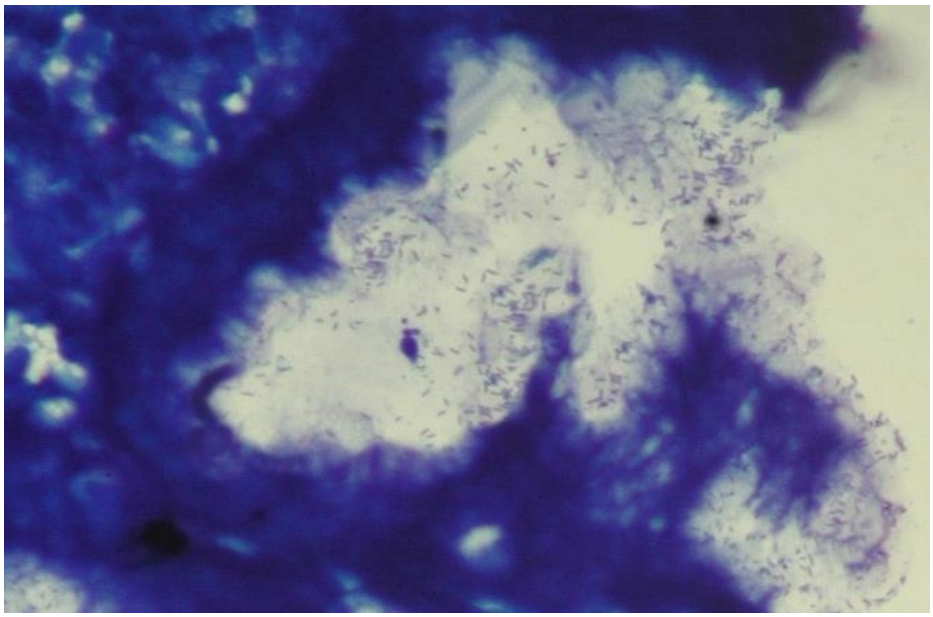

Fig.6. Chronic Periodontitis. Bacterial contamination in the surface layers of the epithelium. Romanovsky - Giemsa staining x400.

This is most likely due to the fact that keratocytes, exfoliated from the underlying prickly layer, form a substrate for microorganisms colonizing dental plaque, it evidenced by the visualized phenomena of adhesion of rod-shaped bacteria and their penetration to the prickly and basal layers, those intercellular spaces communicate with the interstitium of the lamina propria. In an amorphous substance, which is an accumulation of exudate between the cells of the prickly and granular layers, individual rod-shaped bacteria are clearly visible, well associated with cell detritus.

DISCUSSIONS

Results that were obtained, in our opinion, will be logical to interpret from the standpoint of immunology and tissue hydrodynamics. Recently, the concept of local immunity is generally recognized in immunology, implemented by immunocompetent cells associated with the tissue structures in mucous membranes of the body [9, 10, 11]. The works of J. Bienenstock and T. Tomasi (1979) proved the presence in immunity structure the mucous membranes autonomic immune system, in the implementation of that the leading role belongs to the secretory lgA. The immune responses mediated by secretory lgA and the mechanisms of its synthesis were designated as "secretory immunity". The results of subsequent studies made it possible to establish the regularities the functioning of local humoral and cellular immunity, morphological substrate of which is «mucosal associated lymphoid tissue» (MALT) [9, 10, 11].

The existence of inductive and effector divisions has been proven in MALT system. Antigenic stimulation occurs in inductive zones (Peyer's patches). Once in the lymphatic circulation, antigen-reactive T- and B- MALT-lymphocytes with the blood flow constantly migrate into the lamina propria of the mucous membrane - the effector zone. The result of this "resettlement" is the simultaneous activation of the immune response in all mucous membranes, regardless the focus of antigenic stimulation localization. The micropreparations that were obtained, demonstrating the lymph-plasma cell infiltration of the epithelial lamina propria in patients with CG and CP, (fig. 3.6) confirming this concept. The antigenic effect of *H. pylori* in peptic ulcer desease affects not only the epithelial membrane of the stomach, but also other parts of the gastrointestinal tract, including the oral mucosa. Two conclusions follow from the above. First, autoimmune processes play a significant role both in the initiation and in the chronicity of the periodontal diseases course in patients with peptic ulcer, associated with infection *H. pylori*; secondly, drug therapy aimed at destroying *H. pylori* is an effective tool in the treatment and prevention of periodontal tissue diseases in this contingent of patients.

It is known that the microcirculatory segment of the circulatory system is a closed system. Its tightness is provided by tight cell contacts. Normal interstitial fluid circulation is the result of the interaction of hydrostatic, oncotic pressure in capillaries and arteriovenular anostomoses on one side, and hydrostatic and oncotic pressure of tissue fluid on the other hand. There is normally a dynamic equilibrium between the volume of fluid filtered at the arterial end of the capillary and the volume of fluid reabsorbed at the venous end. If it is violated, there is an imbalance in filtration and reabsorption of the vascular-interstitial segment. As a result, there is an accumulation of fluid in the interstitial space, the occurrence of intercellular edema and hydropic dystrophy

appeared (fig. 2, 3). It is technically impossible to track the terminal sections of the microvasculature morphological rearrangement in transcapillary segment in dynamics. However, our observation (fig.4) allows you to represent the scenario of developing events. At the beginning, immunocompetent cells (antigen-reactive B - and T-lymphocytes) enter the perivascular spaces of the lamina propria. Then they are integrated into the epithelial layers. Biochemical processes of the immune response lead to a change in the structure of protein molecules on the surface of cell membranes and in the interstitial space, which leads to a decreasement in oncotic pressure in the lymphatic and venous sections of the microcirculatory module. As a result, the indicators of the difference in pressure drop are reduced. The result is the formation of zones of spongiosis, and the expansion of intercellular spaces in the epithelial cells of the basal and suprabasal layers. As the processes of obliteration of the arterial capillaries lumen increase, the pressure difference in the capillary and lymph-venous segments begins to level out, which makes the circulation of interstitial fluid in the interstitial space almost impossible. This situation is the physiological and morphological substrate in subsequent cascade of pathological compensatory processes, leading to restructuring of the epithelial barrier. It is obvious that the alveolar epithelium is an anatomical zone of increased mechanical, chemical, bacterial and antigenic load. Transcapillary metabolism violation inhibits the synthesis of proteins in epithelial cells desmosomes and leads to an increasing level in the permeability of the upper cell layers in epithelial lining. Dense obliterating contacts destruction between the layers of cells creates favorable conditions not only for active colonization by microorganisms in the intercellular spaces of the alveolar epithelium, but it is also the reason for a kind of "depressurization" in an interstitial space.

CONCLUSIONS

Our work confirms the existence of a pathogenetic relationship between peptic ulcer and involvement the mucous membranes of other body systems in the pathological process. The study also approves that the gingival epithelium damage in patients with peptic ulcer disease is the local manifestation of the systemic immune response to the mucous membranes contamination in gastrointestinal tract by *H. pylori*. Histopathological reconstruction of the papillary and reticular zone of the lamina propria, an increasing level between epithelial cells microspaces in the basal and thorny layers cause the growing hydrodynamic disorganization of the microcirculation system. Inflammatory-dystrophic changes in the overlying layers of epithelial cells are secondary. The consequence of the described processes is the destruction of obliterating contacts between keratinocytes, colonization in an intercellular spaces dental plaque microflora, constant sensitization and antigenic stimulation of inflammation in the alveolar epithelium.

REFERENCES

1. Kotilea K, Kalach N, Homan M, Bontems P Helicobacter pylori Infection in Pediatric Patients: Update on Diagnosis and Eradication Strategies. Paediatr Drugs. 2018; 20(4): 337-351. doi: 10.1007/s40272-018-0296-y.

2. Dumic I, Nordin T, Jecmenica M, Stojkovic Lalosevic M, Milosavljevic T, Milovanovic T. Gastrointestinal Tract Disorders in Older Age. Can J Gastroenterol Hepatol. 2019; Jan 17; 2019: 6757524. doi: 10.1155/2019/6757524.
3. Gisbert JP. Helicobacter pylori-related diseases. Gastroenterol Hepatol. 2016; Sep; 39 Suppl 1:36-46. doi: 10.1016/S0210-5705(16)30173-X.
4. Guevara B., Cogdill AG. Helicobacter pylori: A Review of Current Diagnostic and Management Strategies. Dig Dis Sci. 2020; 65(7):1917-1931. doi: 10.1007/s10620-020-06193-7.
5. Stein SC, Faber E, Bats SH et al. *Helicobacter pylori* modulates host cell responses by CagT4SS-dependent translocation of an intermediate metabolite of LPS inner core heptose biosynthesis. PLoS Pathog. 2017; 13(7): e1006514. https://doi.org/10.1371/journal.ppat.1006514.
6. Tegtmeyer N, Wessler S, Necchi V et al. (2017) Helicobacter pylori employs a unique basolateral type IV secretion mechanism for CagA delivery. Cell Host Microbe. 2017; 22(4):552-560.e5. doi: 10.1016/j.chom.2017.09.005.
7. Irani S, Esfahani AM, Zerehpoush FB. Detection of *Helicobacter pylori* in Oral Lesions. J Dent Res Dent Clin Dent Prospects. 2013; 7(4): 230–237. doi:10.5681/joddd.2013.037.
8. Adler I, Andrea Muiño A, Aguas S et al. *Helicobacter pylori* and oral pathology: Relationship with the gastric infection. World J Gastroenterol. 2014 Aug 7; 20(29): 9922–9935. Published online 2014 Aug doi:10.3748/wjg.v20.i29.9922.
9. Desbonnet L, Garrett L, Clarke G, Bienenstock J, Dinan T. The probiotic Bifidobacteria infantis: An assessment of potential antidepressant properties in the rat. J Psychiatr Res. 2008; 43(2): 164-74. doi: 10.1016/j.jpsychires.2008.03.009.
10. Suárez LJ, Arboleda S, Angelov N., Arce RM. Oral versus gastrointestinal mucosal immune niches in homeostasis and allostasis. Front Immunol. 2021; 5; 12:705206. doi: 10.3389/fimmu.2021.705206.
11. Wang F, Yang TB, Kim BS. The return of the mast cell: new roles in neuroimmune itch biology. J Invest Dermatol. 2020; 140(5):945-951. doi: 10.1016/j.jid.2019.12.011.