ABSTRACT
Dentistry is a branch of medicine that focuses on the health status of the oral cavity; it also strongly integrates with other areas of medicine, as the health of the oral cavity may influence the health condition of other organs of the body. The gastrointestinal system, in particular, can be influenced by the oral cavity, as the oral cavity serves as an initial entrance to the gastrointestinal tract. Oral and gastrointestinal diseases can affect each other. The major role of the oral cavity is biting, chewing and mixing of food particles with saliva to form ‘bolus’ ready for swallowing and passing through the pharynx and the esophagus to the stomach. Dentists and gastroenterologists anticipated to recognize and diagnose oral and gastric conditions associated with gastrointestinal system beginning from the oral cavity. The aim of the current review is to describe the oral manifestations of gastrointestinal (GI) diseases which are important in the screening of GI disorders which may otherwise be undiagnosed. The review includes peptic ulcer diseases, gastroesophageal reflux disease, coeliac disease, Inflammatory bowel diseases and syndromes affecting both the GI system and oral cavity.

Keywords
Coeliac disease, Gastroesophageal reflux disease, Inflammatory bowel disease, Oral diseases, Peptic ulcer diseases.

Introduction
The initial part of the digestive system is the oral cavity where food and other secretions go through the rectum. The oral cavity shows general health conditions of each person and particularly exhibits disorders of the digestive system [1]. Oral lesions may occur earlier, during or after the development of GI diseases. Oral lesions may be similar to GI lesions or induced by systemic changes of GI disorders such as those associated with malabsorption [2]. Therefore dentists and gastroenterologists anticipate to recognize and diagnose oral and gastric conditions associated within the gastrointestinal system which may have originally started in the oral cavity.

Diseases of the Upper Digestive Tract
Gastroesophageal reflux disease (GERD)
Gastroesophageal reflux disease (GERD) is described as an unusual reflux of gastric ingredients into the esophagus at least one time a week, which leads to heartburn and/or acid regurgitation, causing macroscopic impairment to the esophagus and finally influences the quality of life [3,4]. The dental effects of GERD are mainly erosion of the teeth, dental sensitivity, pulpitis, impairment of the taste sensation, erythema, mucosal atrophy and tooth loss [1,5]. Enamel erosion can also be detected in those with hiatus hernia and bulimia. As enamel erosion is completely related to the exposure period to gastric acid, a gastroenterologist can consider the frequency and length of the reflux problem by evaluating the amount of enamel loss [2]. Also, it is important to note that gastrointestinal transmission of Helicobacter pylori (H. pylori) is suspected amongst those who experience vomiting and GERD. Infections with H. Pylori may also take place through food ingestion or exposure to vomit-infected objects colonized by H. Pylori. Temporary colonization in the oral cavity may occur in mothers with reflux problem, and H. Pylori can be transferred from mother to child during tasting or chewing of their food before feeding [6]. Kaneko et al. [7] reported a patient suffering from GERD with temporomandibular joint displacement associated with excessive mouth opening while vomiting. The patient was 73 years old with a history of stroke. After oral hygiene improvement, the frequency
of temporomandibular joint protrusion decreased and eventually disappeared. Researchers demonstrated that GERD patients are at higher risk of developing dental erosion, severe periodontitis, halitosis and oral mucosal lesions [8-10]. Also, lower buffering capacity, salivary flow rate, and pH were found in the GERD group compared to healthy controls [11]. Spineti et al. [12] reported that the degree of micro-crystallization of saliva was substantially decreased and lower in children suffering from GERD when compared with healthy control group. The researchers stated that examination of the structural properties of a dried oral liquid drop in children with reflux disease revealed the markers of changes in the oral cavity. Seneff et al. [13] demonstrated a very strong relationship between gastroesophageal reflux and bisphosphonate-induced osteonecrosis of the jaw (ONJ). Overgrowth of acidophilic species, especially Streptococcus mutans, in the oral biofilm preserves the low pH that maintains damage to the mucosa. Significant associations between ONJ and Sjogren’s syndrome, adrenal insufficiency and vitamin C deficiency were found. Researches stated that pathogen-induced acidosis, hypoxia, and insufficient antioxidant defenses together induce ONJ.

**Diseases of the Lower Digestive Tract**

**Peptic Ulcer Diseases (Gastric and Duodenal Ulcer)**

Chronic active gastritis, peptic ulcer disease, and gastric carcinoma are the diseases mainly caused by *H. pylori* which is a Gram-negative, spiral or curve formed and motile bacteria [14]. Antibiotics are strongly used in the treatment of *H. Pylori* infections but this treatment protocol can not prevent the recurrence of the disease. Thus researchers have begun to seek other reservoir areas that are not affected by systemic antibiotic treatment such as dental biofilm and saliva. Oral cavity serves as an extra-gastric reservoir area for this pathogenic microorganism because low concentration of antibiotics reaches to the oral fluid, periodontal pocket, and dental plaque and this is not enough to eradicate *H. Pylori* present in the oral cavity [15-17]. Also, it was shown that oral presence of *H. pylori* causes many other oral diseases such as recurrent aphthous stomatitis, glossitis, halitosis and dental caries [16,17]. Thus, reinfestation may continue due to the presence of *H. Pylori* in the oral cavity even though gastric eradication is successful. So it is important to reduce and/or prevent the recurrence rate by regular dental plaque control has vital importance. Gastroenterologists should consider this aspect of treatment failure and advise their patients especially those infected with *H. Pylori* to visit their dentist at least 2 times per year [17]. On the other hand, *H. pylori* vaccines are a remarkable issue in the recent period. Vaccine for *H. pylori* can be useful with fewer side effects and can be a solution for *H. pylori* infection in the future [18].

**Coeliac Disease**

Coeliac disease is a form of enteropathy that occurs in genetically susceptible individuals induced by wheat gluten and related cereal peptides. The inflammation of the small intestinal mucosa and other damages repaired with a diet which does not contain gluten [19,20]. Coeliac is a multisystemic disease because almost any other systems may be involved, including the oral cavity. Dental enamel defects, delay of the eruption, recurrent aphthous stomatitis, dermatitis herpetiformis, oral lichen planus and mouth dryness have been determined in coeliac patients [21-23]. According to Aine [24], dental enamel defects occur chronologically and symmetrically in the same anatomical groups of teeth in all 4 quadrants of dentition. Single and asymmetrical changes are regarded as highly unspecific for coeliac disease. It is believed that enamel mineralization disturbances occur in conditions where calcium absorption is insufficient and because of a genetic disease that affects the immune system of patients suffering from coeliac disease. Aguirre et al. [25] showed more enamel defects among patients with coeliac disease. The lesions mainly involve the incisors and the molars. Patients with such characteristics should be evaluated for a possible coeliac disease. It is very important to recognize dental defects which are related to coeliac disease for an early diagnosis of especially asymptomatic forms of the disease.

**Inflammatory Bowel Diseases (Ulcerative Colitis and Crohn’s Disease)**

Ulcerative colitis and Crohn’s disease are inflammatory diseases of unknown origin which affect lining mucosa and submucosa of the colon, bowel wall and ileum. The oral findings of the disease are; aphthous lesions, pyostomatitis vegetans, chronic granulomatous stomatitis, indurated tag-like lesions, cobblestone-like gingival appearance, granulomatous inflammation of minor salivary gland ducts, continuing lip swelling, extensive linear ulcers of the mucosa, midline lip fissuring, candidiasis and lichenoid drug reaction [26,27]. Laranjeira et al. [28] reported that in the active phase of the disease, aphthous ulcers were the most prevalent type of lesions in the oral mucosa. The researchers found small differences in oral symptoms between ulcerative colitis and Crohn’s disease which were not statistically significant. Also, in recent years, an association was shown between oral *Campylobacter concisus* (C. Concisus) and inflammatory bowel diseases (IBD). It was shown that C. Concisus generally colonizes the human oral cavity, however, patients with active IBD are colonized with multiple oral C. Concisus strains supporting that these species may have unique virulence factors that are expressed in the lower parts of the gastrointestinal tract [29].

Preidl et al. [30] reported a 36 years old patient with a history of Chron’s disease. Also, she used steroids and had osteoporosis. After a while, she started using bisphosphonates and referred to the clinic with peri mandibular swelling on the right side, cervical lymphadenopathy, dysphagia and pain on the affected area. In the intraoral examination, exposed necrotic bone near the tooth 47 was detected. Researchers advised that patients with IBD and planned treatment with biological drugs and a history of bisphosphonate therapy should also be examined by a dentist before starting the treatment regimen.

**Diseases of the Hepatobiliary System**

Jaundice is a symptom which causes an excessive amount of bilirubin accumulation into the tissues. Because of the high amount of bilirubin in circulation, the color of mucous membranes such as oral mucosa, the sclera of the eye and skin change into yellow. Oral findings may be related to anemia and vitamin deficiencies;
Peutz–Jeghers syndrome is an autosomal dominant genetic disorder characterized by mucocutaneous pigmentation, gastrointestinal hamartomatous polyps, and oral manifestations such as hyperplastic papillae, angular cheilitis, pale oral mucosa, oral candidiasis, glossitis with different degrees of atrophy of fungiform and filiform papillae, and burning mouth syndrome [40].

**Gastrointestinal Syndromes**

**CHARGE Syndrome**

CHARGE syndrome is a hereditary disease causing coloboma of the eye, heart defects, atresia of the choanae, retardation of growth and development, genitourinary abnormalities, characteristic ear anomalies, cranial nerve dysfunction, and choanal atresia. Gastrointestinal complaints are the most frequently reported symptoms such as GERD, dysfunctional swallowing, excessive salivation, abnormal feeding behaviors, abdominal pain, and constipation. Cranial nerve dysfunction is thought to contribute to weak sucking, weak chewing, swallowing difficulties, GERD and chronic aspiration [32]. Harrison et al. [33] presented two cases with CHARGE syndrome in mixed dentition and clinically absent upper permanent incisor with no history of trauma. The solitary permanent central incisor would be a rather secondary finding in CHARGE syndrome.

**Gardner's Syndrome**

Gardner’s syndrome is a genetical disorder which includes intestinal polyposis, multiple epidermoid cysts, osteomas which may affect paranasal sinuses, skull and mandible and congenital hypertrophy of the retinal pigment epithelium [34]. Dental anomalies are; hypercementosis, supernumerary teeth, congenitally missing teeth, impacted teeth, fused roots of the first and second molars, long and tapered roots of posterior teeth, dentigerous cyst, and multiple caries [35-37]. Patient with osteoma should be evaluated clinically and their family and medical history should be recorded thoroughly to rule out Gardner’s syndrome [38]. In their case report, Pereira et al. [39] aimed to describe the main stomatological manifestations of Gardner’s syndrome and the importance of dentists in its diagnosis. The first patient was an 18 years old girl with two osteomas in the mandible and was suspected of having Gardner’s syndrome. The colonoscopy confirmed the presence of polyposis and Gardner’s syndrome diagnosis was confirmed. The second patient was a 49 years old woman with a late diagnosis of Gardner’s syndrome and developed a rectum adenocarcinoma. Other dental abnormalities such as supernumerary teeth, hypercementosis, and odontomas can also be observed.

**Plummer-Vinson Syndrome**

The syndrome is associated with microcytic hypochromic anemia, atrophic glossitis, dysphagia and esophageal webs as its main symptoms. Oral manifestations are; recurrent aphthous stomatitis, glossitis with different degree of atrophy of fungiform and filiform papillae, angular cheilitis, pale oral mucosa, oral candidiasis, erythematous mucositis, and burning mouth syndrome [40].

**Peutz–Jeghers Syndrome**

Peutz–Jeghers syndrome is an autosomal dominant genetic syndrome identified by a unique type of gastrointestinal hamartomatous polyp related with anal and oral mucocutaneous pigmentation. Detection of pigmentation on the lips and buccal mucosa can assist with early diagnosis [41]. In the intraoral examination, the lesions usually become visible as flat, brown pigmented painless patches on the tongue, buccal and/or labial mucosa [2]. In the case report of Bentley and Hal [42] 53-years-old patient presented complaints of abdominal pain and weight loss. Physical examination revealed mucocutaneous pigmentation around the lips and oral mucosa. Radiological and endoscopic examinations showed obstructing mass in the second part of the duodenum, and there were smaller pieces of soft tissue along the bowel. The histology of the biopsied specimens revealed architectural irregularity without the presence of dysplasia, as suggested by Peutz-Jeghers hamartomatous polyps.

**Cowden’s Syndrome**

Cowden’s syndrome is an autosomal dominant genetic disorder related to mutations in the phosphatase and tensin homolog (PTEN) gene which affect 3 germinative layers of the derivative tissues such as gastrointestinal tract, oral mucosa, skin, bone, eyes, central nervous and genitourinary systems [43]. Oral lesions are papillomatous and found generally on tongue, lips, and gums [44]. Flores et al. [45] reported that; oral manifestations of the disease are asymptomatic, smooth, whitish pink papules in the appearance of cobblestone or pebbles. In their case report; papillomatous lesions were found in different anatomic areas in 10 patients, and the tongue/gingiva were the most frequently affected areas. The presence of fissured tongue is also commonly considered as an oral characteristic in this syndrome.

**Melkerson–Rosenthal syndrome**

Melkerson–Rosenthal syndrome (MRS) is a rare granulomatous disorder with unidentified etiology represented by fissured tongue, recurrent facial paralysis, and orofacial swelling. Other manifestations of MRS are regional lymphadenopathy, fever, and visual disturbances. Also, localization on the upper lip causes a proboscis-like malformation called ‘tapirus mouth’[46]. Gonçalves et al. [47] reported a 17 years old patient with continuing swelling of the lips with fissured tongue due to MRS. Recent studies have considered MRS as the first sign of Crohn’s disease, therefore, these patients should be screened and observed for gastrointestinal symptoms.

**Conclusion**

Gastroenterologists should consider the health status of the oral cavity of patients with gastrointestinal disorders as a possible first line diagnosis approach. Early detection of gastrointestinal disorders by a dentist/gastroenterologist followed by multidisciplinary treatment may increase the chance for the successful treatment of both gastrointestinal and oral disorders.

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References
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