Review Article

The relationship of *H.pylori* infection with certain common diseases in the society

Fulya Bayındır Bilman

İzmir Menemen State Hospital, Department of Medical Microbiology, Turkey

Abstract: *H. pylori* is a gram negative bacterium which settles in the stomach mucosa and causes inflammation and infection. The infection is strongly related to duodenal ulceration, gastric ulceration, and from time to time gastric carcinoma. There are many studies in which the relationship between the infection of this quite old but current bacterium in stomach /duodenum and different extra-intestinal diseases has been investigated. Among the extra-intestinal diseases, the most common are asthma, rosacea, chronic idiopathic urticarial, atopy, coronary heart disease and migraine. In this review, it has been aimed to study the data obtained from the fields in this field, and the results have been assessed.

Introduction

H.pylori, a pathogen dating back to very old times in gastrointestinal system, is a gram negative bacterium in spiral structure (1). In the performed autopsy studies, it has been reported that H.pylori genome was detected even in people of thousands of years ago (2). Apart from the known classical infection, studies in different fields have been conducted in relation to *H.pylori* in the last two decades.

The foremost among them, the studies in which the relationship with asthma is investigated attract attention (3-5). In a meta analysis study cited by Wang et al. (3) by examining all studies published n 770 subjects 785 control group, they report that they could not come to a conclusion of a statistically significant relationship between H.pylori and asthma. In a study conducted by Annagür et al. (4) on a group with asthma attacks (n=37) and on 79 patients including children with stable asthma (n=42), they reported that there is no relationship between H.pylori presence and asthma. In addition to these, Blaser et al. (5) drew attention to the fact that the rarity of H.pylori in developed countries can be a factor that increases the risk of bronchial asthma with hygiene hypothesis. According to hygiene hypothesis, living in an environment surrounded with natural antigens is necessary for normal immune maturation. Therefore, it can be possible to get protected from asthma and allergic diseases. There are studies that have data to support this hypothesis (6.7). Chen et al. (6) determined that there is a statistically significant reverse relationship between H.pylori antigen positivity and asthma incidence in children under the age of 5. Again, a similar finding was reported by Reibman et al. (7). According to these findings, 318 adult asthma cases and 208 control cases were studied. The findings of the study indicated that the people colonized by CagA positive H.pylori were protected from asthma and it caused delay at the age of disease onset. Considering the data of a meta analysis obtained in recent years in this field, H.pylori positivity was reported by Zhou et

al. (8) to be present in asthma cases at much less levels when 14 articles were evaluated including 28.283 cases.

According to a study in which a hypothesis that H.pylori infection can be protective from atopy as well as in asthma cases was investigated, the risk of atopy development in the presence of H.pylori infection was found to decrease by 18% in a meta analysis report covering 21.348 cases (9).

Rosacea disease is a chronic dermatologic disease characterized by erythema, telangiectasia and pustular change. There are findings that some microbial agents can trigger this disease. Especially the findings on Demodex folliculorum and H.pylori verify these opinions (10-12). In a study carried out recently (12), whether there is a relationship or not between H.plyori and rosacea clinic has been investigated in the patients diagnosed with small intestinal bacterial overgrowth (SIBO) detected with H.plyori. In the course of this study, skin lesions displayed improvement by 97.2% and pronounced regression within 10 weeks (12) after implementing clarithromycin-containing sequential therapy. In a similar study including similar findings, it is suggested that a H.pylori analysis should absolutely be made in rosacea patients and positive cases will greatly benefit from eradication therapy for especially papulopustular sybtype (13). Ocular involvement is encountered in more than half of all rosacea cases (14). It was reported by Dakovic et al. (14) that a pronounced improvement was detected both in skin lesions and in ocular findings within 6 weeks after the H.pylori eradication treatment n 7 rosacea cases having positive H.pylori antigen test and also displaying ocular involvement. Jorgensen et al. included 928 rosacea patients and 1527 controls in the meta analysis report they published by examining 42 articles (15). The researchers emphasized that they detected a weak relationship with no statistical significance between rosacea clinic and treatment and H.pylori in contrast to previous studies. Yet, the pathological link between the two conditions

is stated to be related to other factors whose existence is unknown.

There are many studies investigating the clinic link between bacterial infections and peripheral vascular disease (PVD) and the roles in pathogenesis (16). Gout microbiota, periodontal bacteria, Chlamydia pneumoniae and H.pylori are important pathogens that come to mind in PVD pathogenesis. Although H.pylori is an infection agent known with direct cytotoxic and proinflammatory effects for upper digestive tract, it also affects brain-gut axis indirectly (17). Dedepending on H.pylori infection, the host's neuroendocrine-immunological reaction followed with changes in cognitive functions and immunological response differences are also observed (18). In a study including quite serious findings, Kowalski (19) detected H.pylori DNA in atheromatous plaque material in coronary vessels, on the other hand, emphasized a reduction in restenosis in coronary vessels after H.pylori eradication. In this study, the role of H.pylori infection in the inflammatory process has been discussed with several data in the progression of coronary artery disease (CAD). For example, H.pylori seropositivity rate was found in 69.79% of CAD group, while a statistically significant difference was found in the control group (40.62%). In addition, CagA IgG level was similarly found to be significantly high in CAD group. The data on the contraction of artery lumen was found at a more serious level in CagA positive H.pylori cases (19). In other studies, after the eradication treatment, the decrease in proinflammatory cytokine release and eradication of chronic inflammation have been interpreted as the indicators that explain the reduction in the risk of re-occurance of CAD (20,21).

Jha et al., having made a study about the important roles of such factors as C.pneumoniae, H.pylori, Cytomegalovirus in CAD pathogenesis, put forward that the traces belonging to these factors can be used as markers in the target audience (22). In this study, IgA and IgG levels of pathogen microorganisms and an important inflammatory marker C reactive protein levels n 192 CAD cases have been compared to the control group. Statistically significant results have been obtained in all of them. These data have assisted to enlighten the role of these microorganisms in CAD pathogenesis.

One of the extragastric manifestations of H.pylori infection is Diabetes Mellitus (DM). Even though DM cases do not have dyspeptic symptoms, H.pylori infection prevalence has been reported to be higher than the controls and to have a positive relationship with insulin resistance (IR) (23). Especially in type 2 DM patients, there are scientific papers informing that more susceptibility is seen towards H.pylori infections (24). Because DM has multifactorial pathogenesis, it is difficult to exactly determine the role of H.pylori in pathogenesis. However, a large number of studies, which inform that a significant difference is not seen in terms of glycemic control after the H.pylori eradication treatment, are presented in meta analyses (25-27). In addition, neuropathy incidence has been detected to be higher in diabetics with H.pylori infection. Vafaeianesh et al. reported that the eradication rate of H.pylori

with combination treatments is lower in patients with type 2 diabetes than non-diabetic ones (26). According to some reports, relationship between H.pylori and migraine disease has been reported (28). There are some data that recurrent headache can develop secondary to H.pylori infection and this situation depends on systemic vasospastic effects caused by pro-inflammatory substances released from infected gastric mucosa (29,30). In the meta analysis of the studies made in 2000-2013 on migraine patients, Su et al. found out that the prevalence of H.pylori infection in 903 migraine cases was 39.31%, and was significantly higher than controls (28). In a study in which headache severity level was assessed according to Headache Impact Test (HIT6) questionnaire, Ansari et al. detected a statistically significant correlation between IgG level against H.pylori and frequency and severity of migraine attacks. considering the consequences of eradication treatment, the treatment is reported to be promising in reducing the severity of migraine and the number of attacks.

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