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The Relation between Helicobacter Pylori Infection and the Severity of Rheumatoid Arthritis

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Background: The cause of autoimmune disease is not well-known; it is suggested that environmental, viral and bacterial factors might trigger the immune system.

It was found that about 50% of the western and over 80% individuals in the developing countries are infected with Helicobacter pylori, a gram negative flagellated bacterium

Because of its ability to induce chronic immune response in the host, it has been suggested that H. pylori has a role in the development and aggravation of autoimmune diseases.

Objective: To evaluate the relation between H. pylori infection and the severity of rheumatoid arthritis.

Method: Hundred rheumatoid arthritis patients were tested for the presence of H. pylori infection using urea breath test, and were evaluated for the severity of rheumatoid arthritis using DAS 28/ESR, as well as the levels of ESR and C-reactive protein (CRP).

Results: There was no significant difference either clinically or laboratory between H. pylori positive and H. pylori negative patients in rheumatoid activity except in CRP.

Conclusion: There was no relation between H. pylori infection and rheumatoid arthritis activity.

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Rheumatoid arthritis is an autoimmune disease that affects small, medium and large joints ending in a destructive process, however multiple genetic and environmental factors contribute to the disease severity[1].

Pathogenesis of rheumatoid arthritis is not clear, but several viral and bacterial pathogens such as Epstein-Barr virus, Parvovirus B19 and mycobacterium tuberculosis may play a role[2].

Recently, Helicobacter pylori (H. pylori), a gram-negative, flagellated bacterium has been associated with autoimmunity. Chronic infection with H. pylori initiates antigenic process and can induce systemic inflammatory response[3].

H. pylori antigens were found to activate cross reactive T cells which can lead to autoimmune gastritis[4]. Chronic stimulation of B cells with ureas produced by H. pylori could generate autoantibodies including IgM rheumatoid factor[5]. A possible role of microbial heat shock protein (HSP) in the pathogenesis of autoimmune diseases has been postulated because of the high level of sequence homology with human HSP[6].

In this study we evaluated the severity of RA in patients with and without H. pylori infection to determine whether there is a link between the bacterium and the disease severity.

The aim of the study is to evaluate the relation between H. pylori infection and the severity of rheumatoid arthritis.

METHOD

All patients gave informed consent to participate in the study. Hundred seropositive RA patients were tested for the presence of H. pylori infection and were evaluated for the severity of RA.

The following investigations were performed for all patients: LFTs, urea and electrolytes, CBC, ESR, CRP as markers of inflammation, clinical activity of the disease will be assessed by 28-joint disease activity score (DAS28-ESR); it measures tender joint count (TJC), swollen joint count (SJC), patient global assessment-visual analogue scale (PGA-VAS) and ESR. The cut-off value representing remission was defined as <2.6[7-9]. The 13-C urea breath test (UBT) was used to diagnose H. pylori infection[10].

RESULT

The two groups of H. pylori-positive and H. pylori-negative RA patients in our study were well-matched regarding treatment protocol.

The prevalence of H. pylori in all RA patients was 48 (48%), 14 males (29.2%) and 34 females (70.8%).

The mean age for H. pylori positive patients was 48.4±2.3 years and in H. pylori negative was 57.6±4.1years.

C-reactive protein was the only parameter that showed significant difference between H. pylori positive and H. pylori negative patients, the mean value in H. pylori positive patients was 11.6±6.2 mg/dl, and in H. pylori negative patients was 6.4±3.7 mg/dl, P=0.01.

The mean value of ESR in H. pylori positive patients was 34.3±18.6 mm/hr, and in H. pylori negative was (34.9±21.1 mm/hr), P=0.9.

The clinical activity of RA was assessed by DAS28/ESR, the mean value in H. pylori positive patients was 3.39±1.5 and in H. pylori negative patients was 3.7±1.4, P=0.3.

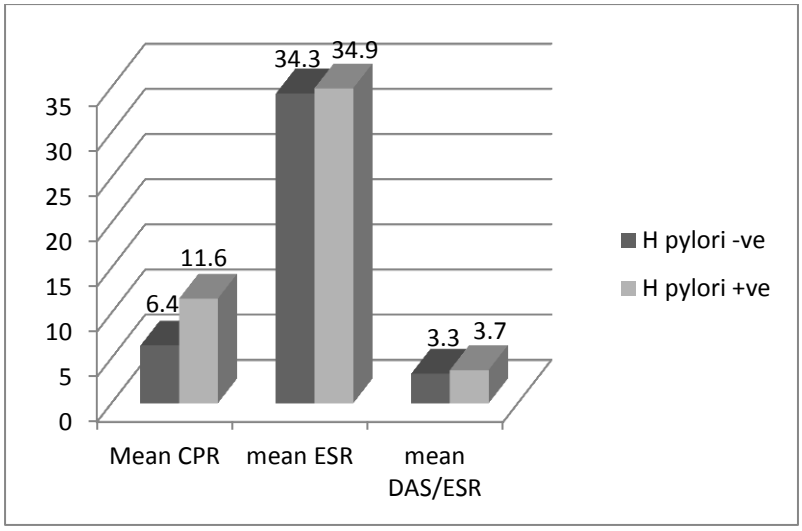

Figure 1: Laboratory and Clinical Parameters for Evaluation of Rheumatoid Arthritis Activity and Its Relation to H. Pylori Infection

DISCUSSION

We found the prevalence of H. pylori infection in RA patients to be 48% similar to the result of Zentilin study who found its prevalence to be 48% as well, and similar to the study of Tanaka; Tanaka studied the association of H. pylori infection and/or non-steroidal anti-inflammatory drug (NSAID) use with upper gastrointestinal ulcer. He found the prevalence of H. pylori in those with and without NSAIDs were 47.5% and 45.7% respectively[11,12].

The prevalence of H. pylori in autoimmune diseases is not high because it is known that H. pylori infection increased with age[11].

H. pylori infection rate detected by urea breath test was found to be 78% and 82% for men and women respectively[13]. In another study done by Marusic, there was also female predominance with H. pylori positive males about 670 (47.8%) and H. pylori positive female about 730 (52.2%)[14]. In our study, we found that H. pylori infection was also predominant in female patients because H. pylori positive females constituted 70.8% of the total H pylori positive patients; autoimmune diseases are known to be more common in females.

Marusic, found the majority of H. pylori infected patients are born between 1940 and 1979, with the highest point from 1950-1969 that is 45-64 years; in our study the highest point was between 48-58 years[14].

Zentilin et al found that patients with H. pylori positive have a tendency for severe clinical manifestations than H. pylori negative patients, which is indicated by increased number of painful joints and functional disability. In addition, the laboratory indices of activity including ESR and CRP were higher in H. pylori positive than in H. pylori negative patients because Zentilin et al found that the presence of continuous antigenic stimulation associated with the production of various cytokines; in our study no significant relation between RA activity and the presence or absence of H. pylori infection[11,15].

On the other hand, Nakamura found that the presence of a rheumatoid factor was inversely related to H. pylori infection and the value of the rheumatoid factor was lower in patients with the infection, concluding that H. pylori infection was not a major cause of gastrointestinal disorders in rheumatoid arthritis, and that the presence of rheumatoid factor significantly reduces the chance of H. pylori infection; in our study no significant correlation was found[16].

A study reported that RA patients possibly could suffer from an increase of disease activity manifested by rise of ESR, CRP and development of joints pain after eradication of infection[17]. This has been explained by disruption of oral tolerance against stress protein such as mycobacterial heat shock protein 65[17].

A study by Moriyama et al, investigated the role of H. pylori infection in RA patients during treatment with NSAID; the study showed that the infection could contribute to mucosal atrophy but does not affect the disease activity proved by the absence of change in clinical or laboratory markers between H. pylori positive and negative RA patients during the follow up period[18].

In our study, we used ESR, CRP as a marker of inflammation, and clinical activity of the disease which was assessed by 28-joint disease activity score using erythrocyte sedimentation rate (DAS28-ESR)[8]. We found that only CRP was significantly higher in patients with H. pylori infection.

There was no difference in the values of ESR or DAS28-ESR between H. pylori positive and H. pylori negative rheumatoid arthritis patients, as the cytokines released by the chronic infection with H. pylori were controlled by the immunomodulators given to the patients during the course of their treatment. Most important cytokine released during H. pylori infection is interleukin-8 which has a potent chemotactic activity and lead to activation and accumulation of polymorphic cells and monocytes in the gastric mucosa with production of other cytokines, such as interleukin-1, -6, -7 and -10 and tumor necrosis factor -α[11]. Because most of the patients with RA are treated with methotrexate that is known to generate less inflammatory type of circulating monocytes by inhibiting interleukin-1 and interleukin-8, the inflammatory response to H. pylori infection does not result in significant increase in cytokines and consequently does not result in an increased RA activity, which explain our findings[19].

CONCLUSION

There was no relation between H. pylori infection and rheumatoid arthritis activity.

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