

# Helicobacter Pylori Associated Autoimmune Diseases

Awad Ahmed Ahmed Hamedelnile  
Sudan, Khartoum, Alemarat, Postal code 12217.

**Abstract:-** *Helicobacter pylori* (*H.pylori*) can cause a wide array of gastric disorders such as chronic gastritis, peptic ulcer, and gastric cancer. In fact recent studies and accumulating evidence implicate *helicobacter pylori* in various extra intestinal autoimmune mediated diseases such as: chronic urticaria, psoriasis, schonleihenoch purpura, behcet's disease, immune mediated thrombocytopenic purpura, food allergy, and multiple sclerosis, which will be discussed here. Various immunopathological theories was conceived in an effort to clarify this relationship between the *helicobacter pylori* and autoimmune diseases. However even these theories are not bases on solid experimental data. But *helicobacter pylori* eradication was shown to improve symptoms of these diseases and improving the quality of life. I wrote this research to arise some ambiguity in this topic and to be a constant draw attention to this topic.

**Keywords:-** *H. pylori*, Autoimmune Disease, Chronic Urticaria, Immunomodulation, *H. pylori* eradication.

## I. INTRODUCTION

Since *helicobacter pylori* was identified in 1983 it was believed to be a major cause of wide spectrum gastro intestinal diseases which will not be discussed here. More recent study and data collected from epidemiological and experimental recourses reveal a relationship between *H. pylori* infection and several allergic and immunological disorders, Among different infectious agent implicated in different autoimmune disorder *H. pylori* have got particular attention that because it was found to be induced the development of organ specific and non organ specific autoimmune diseases(1). *H. pylori* is a wide spread microbe that present in nearly 50% of the western world population and over 80% of those who live in developing countries are infected(2).

This organism has amazing ability to chronically persist in the host for many decades even if it was asymptomatic colonization This chronic persistence of the infection imperative a prolonged interaction between the bacteria and host immune system which makes it a possible autoimmune triggering agent. Autoimmune disorder was suggested being regulated by several environmental and genetic factors that play significant role in determining different clinical outcome.

The object of this review will focus the potential role of *H.pylori* infection in different autoimmune mediated diseases by a systemic approach, and also to draw attention of researchers to this inevitable relationship.

## II. POTENTIAL PATOPHYSIOLOGICAL MECHANISMS OF INFECTION RELATED AUTOIMMUNITY

Several virulence factors allowing this spiral shaped gram negative bacterium to chronically colonizing gastric mucosa. This virulence factors including: urease enzyme that allowing the bacteria overcome highly acidic environment in the stomach, also flagella are present in all infectious strains and important in colonizing the gut mucosa. The other important virulence factor associated with organism pathogenesis are cytotoxin-associated gen A (*Cag A*) and vaculating cytotoxin A (*Vac a*) toxin(3).

Several potential mechanism are suggested in effort to clarify the autoimmune disorder manifested in *H.pylori* infected patient. One of this mechanism are increase in gastric vascular permeability during atrophic gastritis caused by *H.pylori* that may increase the exposure to alimentary antigen. In addition to that chronic inflammatory process triggered by the microbe cause releases of inflammatory mediators and molecular mimicry to the circulation. Anti-gastric auto-antibody have been found in more frequently in patient with *H.pylori* infection (4).

Microbes can causes autoimmunity by inducing loss of self tolerance to self –antigen such as molecular mimicry in which common amino acids sequence are shared between the bacteria and host cells. This will affect causing generalized immune response against both the host proteins and microbe antigen (5). Other suggested mechanism are polyclonal activation, epitope spread and by standard activation and superantigen phenomenon (6).

An interesting medical note was the observation of the effect of antibiotic therapy against the *H.pylori* which was found to reduces the clinical acuity of some autoimmune and allergic disorders. Studies on innate and acquired immune response to *H.pylori* found out that result of activation of toll like receptors by bacterial antigen are anti-inflammatory mediator production, for example the effect of lipopolysacharid(LPS) of *H.pylori* on toll- like receptors was less potent than the activation of toll-like receptors by (LPS) of *escherichia coli* and result in poor

proinflammatory response(7) . Similarly H.pylori flagellin evades recognition by toll-like receptors(8) .

In fact H.pylori vaculating cytotoxin (VacA) was found to affect CD4+helper lymphocytes by blocking its proliferation by interfering with T-cell receptor interleukin (IL-2) signalling pathway (9) .In addition preferential priming of naive T-cells into T-regulatory lymphocytes which are anti inflammatory regulator was influenced by H.pylori also H.pylori infection was found to cause anarching growth of CD5+B lymphocytes that produces poly and auto reactive IgM and IgG3 antibodies(10).

In fact autoantigen H+,K+ adenosine triphosphate (h+/K+.ATP ase) was detected and activation of CD4+ T-lymphocytes were shown to cross react with H+ ,K+ -ATP ase and H.pylori antigen as occur in autoimmune mediated gastritis (AIG) (11).

#### ➤ *H. pylori and Chronic urticaria*

Chronic urticaria (CU) are classified according to the aetiology to chronic spontaneous urticaria (CSU) and chronic inducible urticaria (CIU) , CSU may be due to known(autoantibody) or unknown causes.

Pathogenetic mechanism of H.pylori inducing urticaria are poorly understood ,but several hypothesis are developed regarding this link between the organism infection and chronic urticaria. However immunomodulatory role of H.pylori in chronic urticaria is section of intense study as example:IgG and IgA antibodies to IgKDaH.Pylori associated lipoprote in was found to be implicated in pathogenesis of chronic urticaria (12).

This auto- antibodies causing release of histamine when it react with IgE epitopes or with alpha chain of FcεRI receptors(13) .Clinical assessment of this autoantibody is done autologous serum skin test (ASST),if ASST is positive this indicate chronic urticarial exacerbation(14).

However the best evident of association of H.pylori with chronic urticaria is the improvement of the patient after H. pylori eradication .besides studies reveals that H.pylori eradication in patient with antihistamine medication resistant chronic urticaria, will decrease the urticaria activity score and causes complete loss of urticaria symptoms (15).Recent experimental data suggest that H.pylori virulence genotype in the patient with chronic urticaria don't affect the clinical course of the disease(16) .

#### ➤ *H. pylori and Psoriasis*

Psoriasis is chronic autoimmune mediated disease characterized by abnormal patches of the skin which are red, dry, Itch, and scaly (17).Recent studies suggest that h.pylori infection might act as triggering agent in psoriasis (18),(19). However this relationship are not based on solid experimental data.

But several causes were reported in which psoriatic lesion cleared up following successful eradication of H.pylori (20) ,(21) . And patient show less severe symptom compared to those with anti H.pylori antibodies serotype (22) . An extensive study are need to rule out this suspicious co-existence of H.pylori infection and psoriasis disease.

#### ➤ *H. pylori and Vasculitides*

After considerable studies in the last years, taking about association of H.pylori infection and various vasculitides are becoming acceptable now.

#### • *Schoenlein –Henochpurpura*

Schoenlein –henoch purpura (SHP)is disease characterized by inflammation involving small blood vessels of the skin, intestine, and joint, and the main symptoms is rash and burusing.SHP is the most common vasculitic disease in children but less common in adult (23) .Studies reveals that after H.pylori eradication therapy symptoms of SHP were resolved(24) ,(25).

#### • *Behcet's Disease*

Behcet's disease (BD) is a multi system inflammatory disease of blood vessels that causes mouth sore, eye inflammation, skin rash, and genital ulcer, the exact causes remain enigmas but epidemiological studies suggests an autoimmune background (26), (27).A study on Turkish journals report the increase seropositivity of H.pylori cytotoxin-associated gen –A in patient with BD (28).Eradication of H.pylori is shown to reduce the clinical manifestation of the disease(29).

#### • *Immune Mediated Thrombocytopenic purpura*

Immune thrombocytopenic purpura (ITP) is an idiopathic decrease in the number of circulating platelets, manifested by bleeding tendency easy bruising and petechial hemorrhage.

Interestingly, anti CagA antibodies cross react with peptides present on platelets of ITP patient (30). This molecular mimicry here is not new as antibodies against H+/K+ \_ATP ase were detected in autoimmune gastritis (12). Improvement of clinical symptoms and elevation in platelets count was reported in this patient after H. pylori eradication (31),(32).

#### ➤ *Autoimmune Thyroid Diseases*

Although several studies support a role for H.pylori in autoimmune thyroid diseases this relation remain controversial. Cross reaction autoimmunity between the H.pylori and thyroid antigen has been proposed as a mechanism in H.pylori induced autoimmune thyroid diseases (AiTD)(33).

Intact similar amino acids sequences are shared between the CagA of *H.pylori* and thyroid peroxidase were reported(34). Recent study detected reduction in thyroid autoantibody after *H.pylori* eradication(35). Another research on Korean journal of internal medicine reveals that prevalence of thyroid peroxidase antibody positive is more frequent in patient with *H.pylori* infection which may role out the association of *H.pylori* with AiTD (36).

De Luis et al demonstrate that the titer of anti *H.pylori* immunoglobulins G (IgG) antibody in grave's disease and hashimoto thyroiditis patient was much higher compared with controls (37).

#### ➤ *Multiple Sclerosis*

*H.pylori* infection is considered as triggering agent of some neurological disorder such as multiple sclerosis, neuromyelitis optica, Alzheimer's disease, Parkinson's, migraine, and cerebrovascular diseases(38).

Multiple sclerosis is multifactorial neurodegenerative inflammatory disease of the central nervous system. Recent studies report the presence of immune modulating feature of Sydney strain -1 antigen administered in an experimental model of multiple sclerosis suggesting the potential role of *H.pylori* in the mechanism of these diseases(39). In contrast to that recent data reports negative correlation between *H.pylori* infection and multiple sclerosis particularly in western countries(40).

This conflicting findings may be due to ethnical and variation in the methods of analysis. However more studies are required to detect this bogging concomitantly coexistence of *H.pylori* and multiple sclerosis.

#### ➤ *H. pylori and Food Allergy*

Multiple mechanisms are suggested regarding the immunological response to food antigens. In genetic predisposed subject IgE are produced as a response to exposure to food antigens. Circulating IgE molecules binds high affinity receptors (FcεRI) present on mast cells resulting in release of various mediators such as serotonin, prostaglandins, leukotrienes and platelet activating factors (PAF)(41).

Experimental data suggest that *H. pylori* can facilitate passage of antigen across the epithelium which cause immune response against it. Also, *H.pylori* was shown to be distorting the gastric barriers against food antigens which is formed by gastric mucosa that act as insulator against this antigen (42).

### III. CONCLUSION

*H. pylori* are now considered to be one of the most important triggers of autoimmune disorders and the pathogenesis of this organism with no doubt could explain this relation. Further research is needed to rule out the possible role of *H.pylori* infection in autoimmune disorders.

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