ABSTRACT

*Helicobacter pylori* have been considered to be one of the most common pathogenic infections of the mankind. The infection rates are higher in developing countries with 70 to 90% of the population being infected. In developed countries, the prevalence of infection is lower ranging from 25 to 50%. In India the infection of *H. pylori* is high and recent reports indicated 80-95% as the infection rate, particularly in specific regions of the country. It has become clear that *H. pylori* infection has a natural history with the disease progressing into a chain of events in different groups such as peptic ulcers, variety of lymphoproliferative disorders, and chronic superficial gastritis proceeding to atrophic gastritis to the development of gastric cancer. *H. pylori* is able to colonize and persist in a unique biological niche within the gastric lumen. Extensive studies on this bacterium have cleared some doubts about the pathogenic mechanisms progressing to the disease stages.

The putative pathogenic determinants of *H. pylori* that contribute to the pathogenesis of *H. pylori* can be divided into two major groups as Virulence factors, which contribute to the pathogenic effects of the bacterium, and Maintenance factors, which allow the bacterium to colonize and remain within the host. Virulence factors contribute to the three major pathogenic effects of *H. pylori*, Gastric inflammation, disruption of the gastric mucosal barrier, and alteration of gastric physiology. Many *H. pylori* factors function as both virulence and maintenance factors in vivo. Major virulence factors include vacuolating cytotoxin, cagA, cag-pathogenicity island genes, Urease, lewis antigens etc., Vacuolating cytotoxin causes degeneration of cells by the vacuolation of gastric epithelial cells. The cagA is translocated in to gastric epithelial cells through type IV secretion encoded by the cag PAI and the first
reported bacterial virulence protein translocated by a type IV secretion system. This implies the role of cagA, representing a module inserted by bacteria in to eukaryotic signal transduction pathways, which is likely to play a role in *H. pylori*-host cell interactions and pathogenesis.

Despite its worldwide distribution, the pathogenesis of *H. pylori* associated gastroduodenal disease remains poorly understood. It has been suggested that phenotypic or genotypic differences among bacterial isolates may be important in disease. Intensive research on the pathogenesis of *Helicobacter pylori* infection has led to better understanding of the pathogenic mechanism and disease process. Several observations suggest that polymorphism of *vacA* genotypes may determine whether an *H. pylori* infected individual develops gastritis or an ulcer. With much clinical significance, the components of *Helicobacter pylori* that could play a role in its pathogenesis are not much clear. Although vast reports reveal the interplay between *Helicobacter pylori* and the host cell interaction, still there exists some uncertainties about the role of several factors that plausibly play a role in virulence. With this less-defined know-how of the pathogenesis of *H. pylori*, several *in vitro* models using cell lines mimicking the *in vivo* environment have been employed to estimate the role of virulence factors.

Bacterial surface components are constituents of the outer membrane, and frequently influence colonization and persistence of a pathogen as well as the disease process. Therefore a study involving an *in vitro* model with the outer membrane proteins (OMP) in a cell free system is a step towards understanding its role as a putative virulence associated factor. This study also contributed to the differentiation of the clinical isolates with regard to their degree of virulence by adherence and vacuolating activity assays. Cytotoxicity
and cytopathic effect of the outer membrane proteins were found to be highly significant when various fractions of the bacteria were analysed. Differences in the morphological changes in the host cell induced by the cytopathic effect of the OMP from characterized clinical isolates were also observed. An immunoblot assay with the OMP as a candidate antigen showed a reproducible immunoreactive pattern among different antigens analysed. Significant changes in the cytoskeletal network of the host cells were observed, with the actin depolymerisation and tubulin disruption in the OMP treated cells. Immunomodulatory effects of the OMP of the *Helicobacter pylori* was confirmed by Reverse-Transcriptase - Polymerase chain reaction (RT-PCR) which showed the increase in mRNA levels of the proinflammatory cytokines IL-6 and IL-8 in HEp-2 cells stimulated with whole bacteria and OMP. The involvement of NF-κB signalling pathway towards such an immunomodulatory event was shown by an electrophoretic mobility shift assay. Such a study threw light on the plausible role of OMP as virulence-associated factor with the activation of NF-κB transcription factor, playing a central role in inflammation through its ability to induce transcription of proinflammatory genes. Several research on the allelic variation of the two major virulence factors Vac A and CagA in different geographic location and its clinical significance exist. A PCR-based genotyping study of the *vacA* and *cagA* genes showed the different existing genotypes in this geographic location and its relationship to disease status. The study therefore highlights the significance of the outer membrane proteins as putative virulence associated factor in the host-pathogen interaction of *Helicobacter pylori* and the allelic variations of the known virulence genes in this geographic location is clearly shown.