Diagnosis of Helicobacter Pylon Infection - the Search goes on

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Helicobacter pylori (a spiral shaped gram negative rod) is a common human pathogen implicated in gastrointestinal diseases[1]. H. pylon causes gastritis and peptic ulcer disease and has been associated with gastric malignancies[2]. Infection with H.pylori is very common throughout the world occurring in 40 to 50% of the population in the developed countries and 80 to 90% of population in the developing regions[3]. H. pylori infection is mainly acquired in children and may predispose to peptic ulcer or gastric ulcer later in life. A strong association of H. pylori and antral gastritis has been noted in lower socioeconomic class[4], crowding, large family sizes, ethnic group (more in blacks and hot and humid climate[5]. Interestingly in Africa H.pylori acquisition is early but reinfection is low and gastric carcinoma was less although seroprevalence was high[6]. The International Agency for Research on Cancer in World Health Organization defined H.pylori infection as group I carcinogen. Cag A gene is one of31 genes of pathogenicity island called Cag PA[7] H. pylon strains are diagnostic of more severe gastric inflammation and high gastric cancer risks. Eradication of H.pylori can lead to regression or even cure of Malt Lymphoma[8,9].

The diagnosis of H. pylori is an essential element in the management of many common gastrointestinal pathogens. Previously diagnosis was dependent on the availability of endoscopic biopsy samples. Several techniques both invasive and non-invasive have been developed to diagnose H pylon infection. Various tests used are culture, which is possible, but viable organisms are present in a small percentage of cases. Culture though time consuming, is useful in determining sensitivity patterns and line of treatment[10]. Other tests are histology, biopsy, unease test, 13 urea breath test (12CUBT), serology and HpSA test[11] and PCR[12]. The advent of non invasive assay such as C^{13} urea breath test and ELISA serbiogy have enabled diagnosis and treatment to be undertaken in the primary care setting. The urea breath test is based on the detection of labeled carbon dioxide (labeled with carbon 13 or Carbon 14) in expired air as a result of H. pylon urease activity[13]. It gives results of treatment efficacy after few weeks of treatment. Although 13C UBT gives accurate results in both pre treatment and post treatment cases but expensive instrumentation and specialized technique required are not suitable for infants and very young children and patients with certain neurological disorders.

Serological tests are based on the detection of specific anti-H. pylori immune response mostly by IgG antibodies in patient's serum. Detection of IgG antibodies is accurate in the diagnosis of infection and there is a decline in IgG titters after successful eradication. Serum antibody persists even after H. pylori infection is eradicated and the role of the antibody test in diagnosing active infection or following therapy is therefore limited. H. pylon serology either qualitative or quantitative will yield false positive results in patients who have previously been treated for H. pylon and should therefore not be used to determine infection status in the population[14]. The antibody titers do not decrease sufficiently for accurate predication of the effect of eradication therapy until 12 months after successful eradication. Titres of antibody are known to fall after the bacteria are eradicated[15]. Continuing exposure to H. pyiori in developing countries may prevent disappearance of antibody[16].

Non-invasive diagnostic tests are particularly useful in children as screening tests and epidemiological studies but their accuracy has to be tested against invasive tests in symptomatic patients before they are used in any particular population. Of the common noninvasive test now available serological testing is not accurate in young patients and the 13C urea breath test is expensive[17]. Invasive and non-invasive tests have been developed for the diagnosis of H. pylori infection as H, pylon infection is acquired in

childhood and adolescence, hence accurate diagnosis of the infection in the pediatric population is important[18]. For screening of young patients and to decrease the workload of gastroenterologists and resultant financial saving, H. pylon status may be assessed after treatment by a non-invasive technique obviating the need for endoscopy. Recently another non invasive test based on the detection of H.pylori antigen in stools specimens was introduced[19-21]. Unlike serological and urea breath test the possibility of searching H. pylon in feces has been scarcely investigated but it seems to be a reliable method for predicting H. pylon status in untreated patients. Hp SA test is potentially useful for the diagnosis of H. pylon infection 4 weeks after eradication therapy[22]. Non-invasive low cost H. pylori antigen test can replace urea breath test in children with comparative reliability and accuracy[23].

Accuracy of the test was assessed in a large number of patients both before and after treatment by comparing results with gastric antral and body biopsies with special stains as well as culture and rapid urease testing[24]. The test appears less suitable for evaluating the outcome of the eradication treatment. It is unlikely to be accepted for the primary diagnosis of H. pylon status particularly in dyspepsic young patients[25]. HpSA test is not useful for early monitoring of treatment efficacy at 6 weeks or 6 months post treatment. It lacks accuracy as compared to UBT for evaluating the outcome of the eradication treatment[26].

Although HpSA is valuable in the assessment of H. pylon infection but short term Omeperazole treatment decreases the accuracy of HpSA and UBT but 2 weeks after therapy the HpSA gives positive results[27]. Recently a novel antigen EIA Fentol Lab H pylon using monoclonal antibody detection against Helicobacter antigen was developed[32].

Staff working in endoscopic unit is at greater risk of H. pylon infection as they are exposed to gastric secretions. Among the endoscopy personnel 13/14 (93%) of endoscopy assistants were positive and had a significantly higher prevalence of H. pylon antibodies. No correlation was found between positive serology and symptoms of dyspepsia[28].

In Pakistan overall infectivity of H. pylon was 83% in adult patients undergoing upper GI endoscopy for various reasons[29]. Colonization of H. pylon was found in all types of lesions and in apparently normal upper GI tract the CLO colonization was 76%[30]. Scanning Electron microscopy of local biopsy specimens showed striking concentration of H. pylon in the intracellular areas of epithelial cells. Transmission Electron microscopy studies also show clustering of bacilli in the intracellular areas, decrease of microvilli where bacilli were present[31]. With antigen made from local strains of H. pylori, Immunofluorescence test was positive at litres of 1:1046[32].

Strong correlation was found between CLO positivity, histological gastritis and presence of bacteria in tissue. Urease test yields result in 15 minutes, this test being easy, rapid and sensitive should be used for screening of H.pylori infection followed by histology for further confirmation[33]. However, care should be taken in interpreting urease based tests as they no longer remain diagnostic after commencement of treatment[34]. Commercially prepared CLO was tested against locally made tests and positive results were obtained in 80% of cases[35]. Non- invasive test include antibody detection in serum screening of patients revealed 17/37(46%) CLO antibody positive while 13/17(76%) were urease positive as well leaving only 4 as negative. Out of 20 LO antibody negative in 12/20 (60%) cases which were urease positive and antibody negative indicate infection or suppressed immunological responses[36]. Correlation of H, pylon was observed with histology, CLO of dental plaque and saliva of patients undergoing upper GI endoscopy[37]. Overall exposure rate to H. pylori antibody in children was 33%[38], Clinical trials with Bismuth Salicylates showed 77% clearance but clearance of H. pylori to triple drug regimen has changed with time[39]. Local isolates have shown 81% resistance to Metronidazole[40].

At Pakistan Medical Research Council a preliminary study is being conducted to evaluate the efficacy of HpSA test. Patients with gastroduodenal problems are screened and those found positive for CLO test and/or IgG antibody are included in the study. Detection of H. pylon antigen in stools by means of HpSA assay is a new, effective, non invasive means of diagnosis which can be performed in routine laboratory settings, as it is simple to perform and has possible advantages over other non-invasive tests.

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