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Review Article

Epidemiological Ins and Outs of Helicobacter pylori: a review

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Abstract

Helicobacter pylori infection is now recognised as a worldwide problem. It is the most common cause of chronic gastritis, and is strongly linked to peptic ulcer disease and gastric cancer. A comprehensive understanding of epidemiological ins and outs of H. pylori infection is very important in solving the patho-physiological enigma and might help in leading towards better management and prognosis of infection. This article presents a review of the literature on the epidemiology of H. pylori infection from 2006 to 2011. The authors used Medical Subject Heading (MeSH) terms 'Helicobacter' with 'epidemiology,' 'transmission' or 'risk factor' to search PubMed database. All relevant studies identified were included. Despite extensive medical advancement, many questions on Helicobacter pylori epidemiology still remain unanswered. Further studies are, therefore, required to gain a better understanding of the transmission pathway of this notorious pathogen.

Keywords: Helicobacter pylori, Epidemiology, Incidence, Prevalence, Transmission, Risk Factors, Re-infection.

Introduction

The gram-negative bacterium Helicobacter pylori persistently colonise the human stomach and also have been the focus of basic biochemical and clinical research since its discovery. The bacterium has infected almost 50% of the world's population; although most infections are asymptomatic.[1] Since the first culture of H. pylori the epidemiologic patterns, diagnosis and treatment strategies have changed dramatically. Although effective antimicrobial therapy is available, there is still no ideal treatment for H. pylori-induced gastric cancer. A comprehensive understanding of epidemiological ins and outs of H. pylori infection is very important in solving the patho-physiological enigma and might help in leading towards better management and prognosis of the infection.

This article presents a review of the published literature from year 2006 to 2011. The topics of main concerns were current epidemiological status of H. pylori, modes of transmission and risk factors that govern H. pylori infection as well as public health implications arising from infection with the bacterium. The authors used MeSH terms "Helicobacter" with "epidemiology," "transmission," or "risk factor" to search PubMed database. All relevant studies identified were included and are described under marked subheads.

Prevalence:

The prevalence rate of H. pylori and associated diseases has been highly inconsistent worldwide. In industrialised countries there is generally a low prevalence of H. pylori infection and yet a relatively high prevalence of gastric cancer. On the other hand, some countries with high H. pylori prevalence rates have low gastric cancer prevalence, particularly among the Asian countries. Prevalence of H. pylori infection is high in less developed Asian countries like India, Bangladesh, Pakistan, and Thailand, and is acquired at an early age than in the more developed Asian countries like Japan and China. The frequency of gastric cancer, however, is very low in India, Bangladesh, Pakistan and Thailand compared to that in Japan and China. Similar enigma has been reported from Africa as compared to the West.[2]

The search identified 24 population-based studies reporting frequency of Helicobacter pylori infection primarily from Asia and the Middle East (Table).[3-26] Several studies used stool antigen testing,[3,9,14,17,24-26] others used serologic testing,[5,6,10,11,13,15,18,19,21,23] carbon-13 urea breath testing[4,8,12,16,20,22] or urine antigen testing.[7] Prevalence of infection with H. pylori varied between 7% in a study conducted among asymptomatic children in the Czech Republic,[24] to 92% in Pakistani population.[20] Prevalence in European studies[14,24] varied between 7 and 33%, between 48 and 78% in South American studies,[22] and between 37.5 and 92% in Asian studies.[3,19,20,26] A study was conducted in China on children and adults in two regions of China with both a low and a high incidence of gastric cancer, reported that the prevalence of H. pylori was significantly lower in 2006 when compared to the early 1990s, with a decrease in the prevalence between 5 and 28%, depending on the population under study.[26] Only one study compared prevalence of H. pylori infection within the same population using different diagnostic tests and

Table: Population based studies reporting frequency of Helicobacter pylori infection.

Authors (year published)	Location	Age range of subjects (years)	Frequency (%)
Mishra et al (2008)[3]	India	0.67-60	45.7
Mohammad et al (2008)[4]	Egypt	6-15	72.4
Monno et al (2008)[5]	Albania	16-64	70.7
Moujaber et al (2008)[6]	Australia	1-59	15.4
Naito et al (2008)[7]	Japan	4-10	5.3
Zagari et al (2008)[8]	Italy	>32	58
Kori et al (2009)[9]	Israel	0.25-5	24.7
Nouraie et al (2009)[10]	Iran	18-65	68.3
Sasidharan et al (2009)[11]	Malaysia	10-70	14.2
Acosta Garcia et al (2009)[12]	Venezuela	4-14	74
Arslan et al (2009)[13]	Turkey	Mean 25.5	41.5
Breckan et al (2009)[14]	Norway	18-85	33
Cartagenes et al (2009)[15]	Brazil	1-12	50
Chi et al (2009)[16]	Taiwan	Mean 14.3	55
Dube et al (2009)[17]	South Africa	0-60	87
Jackson et al (2009)[18]	United Kingdom	18-70	26
Jafri et al (2010)[19]	Pakistan	1-15	47
Javed et al (2010)[20]	Pakistan	15-65	92
Mansour et al (2010)[21]	Tunisia	25-55	63
Santos et al (2010)[22]	Bolivia	5-8, 6-14, 4-13	74, 48, 78
Shimoyama et al (2010)[23]	Japan	Mean 57.7	61
Sykora et al (2010)[24]	Czech Republic	0-15	7
Yucel et al (2010)[25]	Turkey	2-12	31
Zhang et al (2010)[26]	China	8-15 and 40-79	66

reported no statistically significant difference in the prevalence of infection when the stool antigen test was used, compared with serologic testing.[23]

In developing countries, where majority of children are infected before the age of 10, the prevalence in adults peaks to more than 80% before 50 years of age. In developed nations, serologic evidence of H. pylori is rarely found before 10 years of age, but increases to 10% in those between 18 and 30 years of age and to 50% in those older than 60.[18] Within any age group the infection appears to be more common in Hispanics and the blacks compared to the white population; these differences are probably in part related to socioeconomic factors.[1]

The increased prevalence of infection with age was initially thought to represent a continuing rate of bacterial acquirement throughout one's lifetime. However, epidemiologic evidence now indicates most infections are acquired during childhood even in developed countries. Thus, the frequency of H. pylori infection for any age group in any locality reflects that particular cohort's rate of bacterial acquisition during childhood years.[27]

Incidence:

Four relevant studies examined the onset of new infection or re-infection. The Japanese study reported a decrease in 12-month incidence with age, 0.65% among 10-year-olds, 1.3% among 7-year-olds and 2.6% among 4-year-olds.[7] A study from Bangladesh examined new infections from birth to 2 years of age in 258 children. They observed that children showing evidence of infection at 6 months of age increases to 49% by 2 years of age.[28] An Israeli study[29] showed less than 1% of new and re-infection in adult patients. However, the small sample size in this study limits preciseness of the estimate. An Italian study investigating the source of H. pylori infection in the neonatal period examined 172 new-borns for the onset of new infection or re-infections.[30] According to this study, at 1 month 3% children were positive for H. pylori, but by 18 months all the infants had cleared the infection spontaneously.

Epidemiological evidence has shown that H. pylori is one of the most important pathogens for a wide spectrum of gastroduodenal diseases, including gastric malignancy. The incidence of gastric cancer varies with different geographic regions. Approximately 60 percent of gastric cancers occur in developing countries. The highest incidence rates are in Eastern Asia, the Andean regions of South America, and Eastern Europe, while the lowest rates are in North America, Northern Europe, and most countries in Africa and South Eastern Asian (Figure).[1,2]

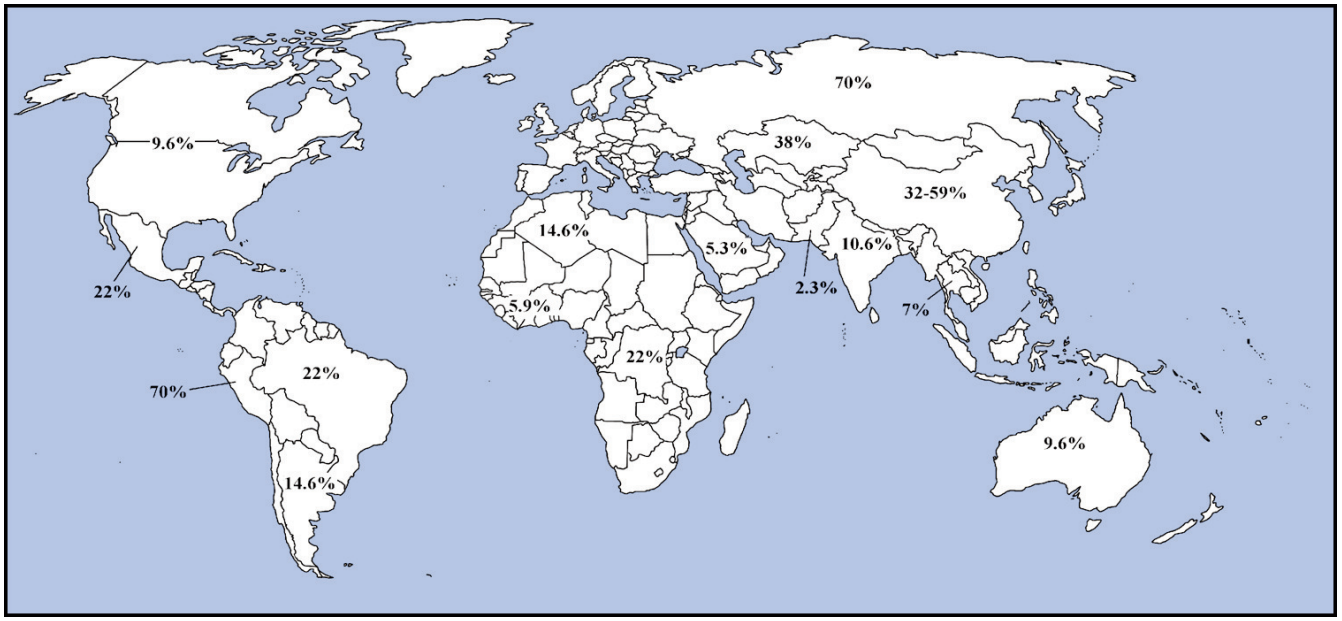

Figure: Global incidence of gastric cancer, age-standarized rate/100,000 population.

Transmission:

Despite extensive elaboration in literature of a variety of factors delineating the causative links of H. pylori infection been discussed in epidemiologic studies, the knowledge of transmission modes and reservoirs remain poor. However, some routes, such as gastro-oral, faeco-oral, oral-oral and iatrogenic transmission have been described.[31]

Intra-familial transmission has long been thought to be a major mode of transmission. Weyermann et al[32] determined the independent contribution of mothers, fathers and siblings in German population to acquirement of H. pylori during childhood. Chances among children for having an infected father or sibling were decreased in German population when compared to other studies. Infection status of siblings appears to matter more in populations where large families are common. Compared to other family members, the infection status of mother is more strongly associated with household hygiene and other risk factors.[32] A Brazilian cross-sectional study demonstrated that infected mothers were almost 20 times more likely to have an H. pylori-positive child, particularly mothers infected with CagA-positive strains.[15] A study in Turkey[25] screened asymptomatic children for H. pylori and reported a higher prevalence of infection in mothers of infected children. All of these studies concluded that the spread of infection is from person-to-person which seems to occur predominantly within families and the most probable cause of intra-familial transmission are mothers.

Iatrogenic transmission has been documented following the use of a variety of inadequately disinfected gastric devices, endoscopes, and endoscopic accessories. Adequate sterilisation and disinfection of endoscopes has reduced the incidence of transmission. In addition, gastroenterologists and nurses appear to be at increased risk for acquiring H. pylori; this is most probably due to occupational exposure to infected gastric secretions.[33]

Faeco-oral transmission and oral-oral transmission of bacteria is also possible. Contaminated water supplies in developing countries may serve as an environmental source of bacteria. Children who regularly swim in rivers, streams, pools, drink stream water, or eat uncooked vegetables are more likely to be infected.[31] Organisms have been identified in dental plaque, and the habit of feeding children with pre-masticated food commonly transmits the bacteria.[34]

Re-infection:

Re-infection with H. pylori following successful bacterial cure is unusual. Recurrence of infection most commonly represents recrudescence of the original bacterial strain. In adults, re-acquisition of bacteria occurs in less than 2% of persons per year, a rate that is similar to primary adult acquisition of infection. The low re-infection rate in adults supports the lower risk for infection during adulthood, although acquired immunity conferred by primary infection may also be important.[1]

It has been hypothesised that the re-infection rates may be higher in children in developing countries, and in those from low socio-economic status. However, a study from Ireland found a low annual re-infection rate in children older

than 5 years of age, regardless of socio-economic status.[35]

Risk Factors:

Potential risk factors for H. pylori infection among recruited subjects were reported in several studies. Most of the studies examined cross-sectional associations between various risk factors and the probability of being infected at the time of screening, which may not differentiate the determinants of acquisition from the determinants of persistent infection.

Among Israeli children in a day care, low socio-economic status was associated with H. pylori infection. The study collected data on family size, residential crowding, parent's education, and the country of birth, but the basis for classifying low status was not specified.[9] Among Egyptian children, H. pylori prevalence was highest in children attending school in socially-deprived areas. Inhabitants of Cairo residing in an overcrowded home had the highest prevalence among the locations studied.[4] A study on Taiwanese high-school children demonstrated no effect of the number of siblings, household size, educational level, or family income on the likelihood of infection.[16] A large Pakistani cross-sectional survey, containing almost 2000 children, showed that seropositivity was associated with increasing age, lower socio-economic status, and lower educational status of the child's father.[19] A study on university employees in India demonstrated a relationship between those living in semi-urban slums and H. pylori status classified by Polymerase Chain Reaction (PCR)-based stool and saliva tests.[3] A Chinese study of 2480 school-aged children identified an association with the lack of formal education of the mother, and an Iranian study of 851 individuals found low education of the mother, father and the subject to be associated with H. pylori infection.[10]

An Albanian study on 1391 individuals without detailed data on number in household correlated only female gender and subjects greater than 40 years of age with H. pylori seropositivity.[5] In a Chinese study conducted among adults and children in low- and high-incidence regions for gastric cancer, no association between gender and H. pylori infection was demonstrated, but the prevalence of infection in children increased with age.[26]

In a large cross-sectional survey of adults in the United Kingdom, male gender, increasing age, shorter height, tobacco use, and lower socio-economic status were all significantly associated with positive H. pylori serology.[18] In a study conducted in two communities in Norway, older individuals were again more likely to test positive for the bacterium.[14] A Czech cross-sectional survey conducted among children reported that two or more children in the household, lack of formal education of the father, and institutionalisation of the child were all significantly associated with infection after multivariate analysis.[24]

A Turkish study of asymptomatic children and their mothers demonstrated a positive correlation between H. pylori infection and lower educational status of the mother, lower family income, poor living conditions (defined according to domestic living space), and higher number of siblings.[25] In a study conducted in the Eastern Cape of South Africa, prevalence of H. pylori increased with increasing age, but the authors also demonstrated that female gender and higher socio-economic status were associated with the presence of infection.[17] Finally, a Turkish case-control study that compared the prevalence of infection in obese and non-obese individuals reported a significantly higher prevalence in those who were obese.[13]

Conclusion

In spite of the large number of studies published on the epidemiology of H. pylori, little has been added to our current understanding of the subject. The risk factors for developing the infection are similar in most of the studies and are in concordance with previous data. Much that was known before has just been confirmed. However, many questions, such as the cause of Asian/African enigmas, role of environmental factors and variation of H. pylori infection/gastric cancer prevalence in different regions within the same country, are some of the queries that still need to be answered on H. pylori epidemiology and related diseases. Further studies are, therefore, required to gain a better understanding of the transmission pathway of this notorious pathogen to combat and prevent associated disorders.

More depressingly, in spite of the projected increase in the incidence of gastric cancer, already the second most common cause of cancer death worldwide, and the knowledge that H. pylori is the underlying carcinogen, no public health measures have yet been instituted to treat infected individuals in the populations at risk, especially in developing countries like Pakistan where H. pylori prevalence is at an alarming level.

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