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Ethnic and geographic disparities in Helicobacter pylori infection: Unraveling the complexities of gastric cancer prevalence

Annie Chen

New York University, 27 West Fourth Street, New York, NY 10003, USA

annie.chen980717@gmail.com

Abstract. This literature review delves into the complex relationship between Helicobacter pylori infection and gastric cancer, focusing on ethnic and geographic disparities. It examines the varying prevalence of H. pylori across different regions and ethnic groups, the pathogenicity of different bacterial strains, and the influence of genetic, dietary, and socio-economic factors on gastric cancer incidence. The review identifies critical research gaps and underscores the need for an integrated approach to understand these disparities better and develop targeted prevention and treatment strategies.

Keywords: Helicobacter pylori, Gastric Cancer, Ethnic Disparities, Geographic Variability, Socio-economic Factors

1. Background

Cancer is progressively emerging as a significant global health challenge, with its impact being felt across various nations around the world. As time progresses, this disease has become the foremost cause of health-related issues and a major impediment to achieving longer life expectancies in countries globally, signaling a need for increased attention and resources to combat it [1]. Based on the comprehensive statistics provided by Globocan 2020, which evaluated the incidence and mortality rates of 36 different cancers in a total of 185 countries globally, gastric cancer has been identified as the fifth most commonly diagnosed malignant tumor worldwide. Furthermore, it holds a concerning rank as the fourth leading cause of death among all cancer-related fatalities [2]. This data underscores the significant impact and widespread prevalence of gastric cancer on a global scale, highlighting its criticality in the context of international health concerns.

2. Global Prevalence and Variability of H. pylori Infection

Gastric cancer is associated with well-defined causative factors. Infection with Helicobacter pylori is a significant risk factor for developing gastric cancer, particularly the non-cardia type. In 1994, the World Health Organization's International Agency for Research on Cancer classified Helicobacter pylori as a class I carcinogen specifically for this type of cancer [3]. The high concentration of strong gastric acid in gastric juice generally makes it difficult for bacteria to colonize and multiply within the stomach [4]. Nevertheless, H. pylori can infiltrate the body and settle on the surface of the gastric mucosa. There, it produces ammonia and carbon dioxide, neutralizing the adjacent gastric acid and thus resisting its lethal

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effects. This adaptation enables the bacteria to colonize the stomach, primarily in the pyloric region [5]. H. pylori generates ammonia, which can erode the mucus layer protecting the gastric mucosa. This erosion allows acidic gastric juice from the stomach lumen to infiltrate and harm the mucosa [6]. Moreover, H. pylori strains carrying the CagA gene exhibit heightened pathogenicity. CagA contributes to the apoptosis of gastric mucosal epithelial cells and fosters chronic inflammation, a precursor to gastric cancer, as well as gastric and duodenal ulcers [7].

H. pylori is widespread worldwide, infecting over half of the global population [8]. However, its prevalence and the severity of gastric-related outcomes differ significantly across different regions and countries [9]. There is a strong correlation between the rates of infection and socio-economic status. The incidence of H. pylori infection is generally lower in developed countries compared to developing countries [10]. The highest rates of prevalence are found in the Americas, whereas the lowest are in Africa [11]. It is estimated that the prevalence of H. pylori among adults is 62% in China, 62% in Central America, 82% in Eastern Europe, 71% in Japan, between 60-70% in Jamaica, and 62% in Hispanic Americans, in contrast to a significantly lower 26% in non-Hispanic whites [12].

3. High H. pylori Prevalence in Asian Countries

Epidemiological research has revealed that the prevalence of H. pylori is notably high in Asian countries. However, there is a variation in the seroprevalence of this infection across these nations. Countries with less developed or developing economies, like India, Pakistan, Bangladesh, Vietnam, and Thailand exhibit higher seroprevalence rates. In contrast, more industrialized or developed Asian nations, including China, Japan, Korea, and Singapore, tend to have lower rates of seroprevalence [13]. Variations in H. pylori seroprevalence rates within countries are influenced by geographic and ethnic differences. For example, in Australia, Aboriginal populations have higher rates (68%) compared to Anglo-Celtic groups (38%) [14]. In China, higher seroprevalence correlates with increased gastric cancer incidence, as seen in Changle (80.4%) versus Hong Kong (58.4%) [15].Similarly, in Malaysia and Singapore, differences in seroprevalence rates are evident among ethnic groups, with certain groups showing higher rates [16]. In Vietnam, urban Hanoi has a higher rate (78.8%) than rural Hatay (69.2%). These patterns highlight the role of geographic and ethnic factors in H. pylori infection and its link to gastric cancer [17]. The higher incidence of gastric cancer in industrialized countries like China and Japan, despite their lower rates of H. pylori infection, contrasts with lower cancer rates in less developed countries with higher H. pylori prevalence [18]. This indicates that H. pylori infection alone is not the sole cause of gastric cancer. Understanding the incidence of gastric cancer requires a holistic view that encompasses not just the presence of H. pylori infection but also considers the specific bacterial strain, genetic predispositions of the population, and various lifestyle factors.

4. Variability in H. pylori Pathogenicity

Not all strains of H. pylori are equally pathogenic. The most virulent cluster, the cytotoxin-associated pathogenicity island (cag PAI), is present in many clinical strains in Europe, the United States, and Japan. Strains with cag PAI, particularly those with the cytotoxin-associated gene A (cagA), pose a higher risk for gastrointestinal disorders like duodenal ulcers and gastric adenocarcinoma [19]. The Vacuolating cytotoxin A (VacA) and the outer-membrane protein BabA are other significant virulence factors, with the former inducing apoptosis in epithelial cells and the latter linked to increased gastric adenocarcinoma incidence [20, 21]. Despite these insights, the exact relationship between H. pylori's genetic variation and disease outcomes remains complex, as evidenced by varying gastric cancer rates in different regions, such as the low incidence in India despite the presence of pathogenic strains [22]. Ethnic background also plays a role, particularly concerning gastric atrophy and acid secretion. For instance, the Japanese population generally has lower acid secretion compared to Western populations [23]. Since gastric atrophy, a precursor to cancer, occurs more frequently in individuals with lower acid secretion, this could partly explain the higher incidence of gastric cancer in Japan [24]. This link was further supported by studies showing that proton pump inhibitors, which reduce gastric acid secretion, can exacerbate H.

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pylori-associated gastritis [25]. This phenomenon indicates that gastric atrophy, influenced by ethnic differences in acid secretion, is a significant risk factor for gastric cancer.

5. H. pylori Infection of Traditional East Asia and South Asia Diets

The primary pathways for the spread of H. pylori are through fecal-oral, oral-oral, and gastro-oral transmission. Additionally, there is a significant tendency for H. pylori infection to occur within family clusters. Children of parents who are infected with H. pylori are at a considerably higher risk of contracting the infection compared to children from other families.

In areas with inadequate sanitation, there is a high likelihood of drinking water being contaminated with H. pylori. This increases the risk of infection through the consumption of raw vegetables washed in untreated sewage water [26]. Additionally, milk and meat are susceptible to H. pylori contamination, and consuming these products can further elevate the infection rates [27]. The consumption of pickled, preserved, and smoked foods, common in East Asian diets, is associated with increased gastric cancer risk [28]. These foods contain nitrosamines, which are known dietary carcinogens. Studies have shown that nitrosamine intake can augment H. pylori-associated gastric carcinogenesis [29]. The risk is further elevated by the consumption of fermented products like soybean pastes and kimchi, which are rich in nitrosated compounds. Additionally, a high-salt diet is prevalent in East Asia. Such a diet can diminish gastric acid secretion and impede the production of prostaglandin E, which plays a key role in bolstering the resilience of the gastric mucosa. The decreased synthesis of prostaglandin E renders the gastric mucosa more susceptible to damage from various harmful substances, leading to an increased likelihood of gastric lesions [30]. Additionally, a diet high in salt promotes the colonization of H. pylori, resulting in the depletion of parietal cells, gastric atrophy, and the development of intestinal metaplasia [31]. Different levels of salt can modify gene expression in H. pylori, especially affecting the cagA gene. Research conducted with Mongolian gerbils demonstrated that a mix of cagA+ H. pylori strains and a diet high in salt markedly elevate the risk of developing gastric adenocarcinoma [32].

In contrast, South Asian countries have a high prevalence of H. pylori infection but a low incidence of gastric cancer. In India, the prevalence of H. pylori infection is notably high, and there is a greater likelihood of both initial infection and re-infection with different strains [33]. This results in high genetic heterogeneity among H. pylori strains within the Indian population. The propensity for genetic exchanges among these diverse bacterial populations may lead to the evolution of more competitive and potentially more virulent H. pylori strains [34]. Furthermore, almost all infected cases in India involve individuals carrying multiple strains of H. pylori, highlighting the complexity and diversity of H. pylori infections in this region.[34] In South Asian countries, it is a common practice to include various spices and herbal medicinal plants like turmeric in the diet. Turmeric (Curcuma), in particular, is well-known for its anti-inflammatory effects. These effects are crucial as they help reduce the activation of NF-κB and the release of IL-8, both key players in the inflammation process triggered by H. pylori [35]. Furthermore, curcumin, the primary active ingredient in turmeric, plays a significant role in suppressing NF-κB activation and reducing the expression of AID, an enzyme deeply involved in the development of gastric cancer linked to H. pylori infection [36]. Therefore, Turmeric effectively interrupts the inflammation process triggered by H. pylori, thereby potentially preventing the onset of carcinogenesis.

6. Racial Disparities in H. pylori Sero-Prevalence in the United States

Research focusing on the racial disparities in the sero-prevalence of this bacterium in the United States provides critical insights into the varying impact of H. pylori across different racial groups, emphasizing the situation among African Americans and Whites. A study titled "Racial Differences in Helicobacter pylori CagA Sero-prevalence in a Consortium of Adult Cohorts in the United States" aimed to assess the prevalence of CagA-positive H. pylori infection over time by race. It revealed significant racial disparities, with African Americans being three times more likely to be H. pylori–CagA sero-positive than Whites. While sero-prevalence declined among Whites, it remained stable for African Americans, indicating a widening racial disparity in the prevalence of this virulent H. pylori form, a primary cause of gastric cancer [37]. The overall H. pylori prevalence in the United States is approximately 30%, but

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it is notably higher in African Americans, estimated at 50% to 60% [38]. This group exhibits a significantly higher seroprevalence of H. pylori compared to Whites, with a 2-to 6-fold increased odds of sero-positivity for key proteins like CagA and VacA, known markers for gastric cancer risk [39]. The increased risk in African Americans is primarily due to CagA sero-positivity, with an 8.1-fold increased odds. This trend is particularly pronounced in individuals with medium to high African ancestry, suggesting a genetic predisposition to more virulent H. pylori strains.[39] The presence of multiple H. pylori strains in African Americans, contrasting with the homogeneity in European and Western populations, complicates the understanding of infection dynamics and disease progression, potentially exacerbating the risk of gastric cancer due to the genetic diversity within bacterial populations [40]. Another study, "Race African Ancestry and Helicobacter pylori Infection in a Low-Income United States Population," found a high prevalence of H. pylori sero-positivity in a sample of 689 African American and White participants. This study highlighted that genetic variation or lifestyle factors related to African ancestry might contribute to increased susceptibility to virulent H. pylori strains [41]. The findings indicate a high prevalence of antibodies against virulence factors like CagA in African Americans, emphasizing the need for targeted prevention strategies [42].

7. Conclusion

The comprehensive analysis presented in the literature review reveals a critical research gap in understanding the ethnic and geographic variability in H. pylori infection and its correlation with gastric cancer prevalence. While existing studies have established the link between H. pylori infection and gastric cancer, particularly in relation to specific virulent strains like CagA, there is a need for deeper investigation into the ethnic and genetic factors that contribute to the disparity in infection rates and cancer outcomes. Notably, the paradox of high H. pylori prevalence but low gastric cancer incidence in South Asian countries, in contrast to the situation in African American populations in the United States, suggests underlying factors that are not fully understood. This gap underscores the need for a more nuanced approach in exploring the interplay between genetic predisposition, lifestyle, dietary habits, and socio-economic status in different ethnic groups. Future research, therefore, must pivot towards a more integrated approach, combining molecular genetics, epidemiology, and cultural studies. This holistic perspective is crucial for unraveling the nuances of H. pylori infection and its varied impact on different populations. By bridging these research gaps, we can aspire to develop more tailored, effective strategies in the prevention, diagnosis, and treatment of gastric cancer.

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