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Analysis of the Limitations of Dynamic Changes in Serum *Helicobacter pylori* IgG Antibody Titer for Re-infection Detection

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Abstract: This study examines the limitations of detecting reinfection through dynamic changes in serum *Helicobacter pylori* (Hp) IgG antibody titers and proposes targeted optimization strategies. The analysis identifies three core challenges: antibody characteristics, diagnostic criteria, and individual variations. Clinical practice demonstrates that persistent antibody positivity, inconsistent diagnostic standards, and variations in immune responses and mucosal conditions are key obstacles. By optimizing monitoring timelines, establishing baseline calibrations, creating unified technical protocols, and developing multidimensional evaluation systems, the accuracy of reinfection detection can be significantly improved. Dynamic monitoring of serum Hp-IgG antibody titers requires standardized procedures and comprehensive assessment frameworks to provide reliable clinical support for reinfection prevention.

Keywords: *Helicobacter pylori*; IgG antibody titer; reinfection detection

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1. Introduction

Helicobacter pylori (Hp) is one of the microorganisms colonizing the acidic gastric environment. Infection of the gastric mucosa by Hp can lead to chronic gastritis, with prolonged persistent infection causing gastric mucosal atrophy and progressing to atrophic gastritis or even gastric cancer. Hp infection is one of the primary pathogens of peptic ulcers, with pathogenic mechanisms involving excessive gastric acid secretion, weakened protective effects of the gastric mucosa, impaired mucosal barrier, immune responses, and genetic factors. The positivity rate of Hp infection in peptic ulcers is relatively high, with risk factors related to patient age, household registration, smoking history, and personal hygiene. Hp infection serves as a significant contributing factor for chronic gastritis, gastric cancer, and other digestive diseases. Timely identification of reinfection after eradication therapy is crucial for blocking disease progression [1]. While serum Hp-IgG antibody titer testing is widely used for infection assessment due to its non-invasive and convenient advantages, it has notable limitations in detecting reinfection. In clinical practice, persistent antibody positivity, ambiguous diagnostic criteria, and individual variations often make it difficult to distinguish reinfection from previous infections, potentially

leading to missed diagnoses or overtreatment. Based on this, this study systematically analyzes the core limitations of dynamic serum Hp-IgG antibody titer changes in identifying reinfection and proposes actionable optimization strategies to standardize clinical reinfection diagnosis processes and improve diagnostic accuracy [2].

2. The biological characteristics of Helicobacter pylori, the harm of infection and the development of detection technology

Helicobacter pylori (Hp) is a microaerophilic Gram-negative bacillus that primarily colonizes the gastric mucosal epithelial cells. By producing ammonia through urease activity, it creates a localized alkaline microenvironment to resist gastric acid erosion. Pathogenic factors such as cytotoxin A and vacuolating toxin can compromise the gastric mucosal barrier, triggering chronic inflammatory responses [3]. Hp infection has become a global epidemic, being the primary cause of chronic gastritis and closely associated with gastric ulcers and cancer. Data indicates that over 90% of duodenal ulcers and approximately 80% of gastric ulcers are linked to Hp. Severe cases may induce precancerous lesions like gastric mucosal atrophy and intestinal metaplasia, potentially increasing gastric cancer risks. Timely identification of reinfection after eradication therapy is crucial for preventing disease progression. Current Hp detection methods include invasive and non-invasive approaches. The serum Hp-IgG antibody titer test, known for its non-invasive, convenient, and mass-screening advantages, is widely used in epidemiological studies. This method detects specific IgG antibodies produced by the immune system after Hp infection, with antibody levels fluctuating dynamically during infection. However, the lack of a precise differentiation system between reinfection and prior infection poses challenges for clinical reinfection identification [4].

3. The fluctuating serum IgG antibody titers cannot precisely determine Helicobacter pylori reinfection

3.1. The persistence of positive antibodies interferes with the distinction between reinfection and previous infection

After *Helicobacter pylori* (Hp) infection, the immune system produces IgG antibodies with long-term persistence. Even after achieving Hp eradication through standardized treatment, serum antibody titers do not rapidly decline to negative levels but instead show a gradual decay trend. Some patients may experience a decay period of 6–12 months, while a small number of individuals with stronger immune function may maintain positive status for over two years. This persistent positivity creates overlapping antibody signals between reinfection and previous infection: When patients are re-exposed to Hp after eradication and experience reinfection, serum IgG antibody titers may only show mild elevation or remain stable, failing to clearly distinguish from residual antibodies from prior infection. Clinically, this phenomenon is common, for instance, a patient with peptic ulcer who tests positive for serum antibodies one year after Hp eradication might have either a Hp reinfection causing mucosal inflammation recurrence or residual antibodies from previous infection. Relying solely on dynamic titers makes accurate differentiation challenging, directly impacting treatment decision-making accuracy.

3.2. The non-uniform determination criteria of titer changes lead to diagnostic deviation

Current clinical and research standards for re-infection determination based on dynamic changes in serum Hp-IgG antibody titers lack unified specifications, with significant variations in cut off values adopted by different institutions and studies. Some research uses a 20% increase from baseline levels as the re-infection criterion, while others set thresholds at 30% or 40%. Some institutions even directly use antibody positivity/negativity as diagnostic criteria, ignoring the clinical significance of titers' fluctuations. Additionally, differences in antigen coating concentrations and testing methods across reagent kits lead to incompatibility of titers measured at different institutions, further exacerbating diagnostic confusion.

For example, a patient with 25% titers increase from baseline six months after Hp eradication might be classified as re-infected under a 20% threshold, but would be deemed negative under a 30% standard. Such discrepancies may result in missed diagnoses for re-infected patients or unnecessary treatment for non-re-infected individuals, severely compromising the standardization of clinical practice.

3.3. Differences in individual immunity and mucosal status affect the accuracy of titer interpretation

Differences in immune function and gastric mucosal pathology directly lead to significant heterogeneity in the generation, peak, and decline patterns of serum IgG antibody titers following Hp infection. In immunocompromised individuals, insufficient lymphocyte activation results in low antibody production with suboptimal peak titers. When reinfection occurs, the titers show minimal elevation, making it difficult to reach diagnostic thresholds for missed diagnosis. Conversely, immunocompetent individuals maintain high antibody titers post-primary infection with no significant fluctuations during reinfection, rendering dynamic changes unidentifiable. Gastric mucosal pathology similarly affects antibody secretion: patients with atrophy exhibit reduced Hp colonization sites and impaired gastric gland function, leading to markedly decreased antibody production and slow titers during reinfection. Those with erosive gastritis or intestinal metaplasia may experience nonspecific antibody elevation due to mucosal inflammation, potentially misdiagnosed as reinfection. For instance, chronic atrophic gastritis patients maintain persistently low antibody titers after Hp eradication, with reinfection occurring only after a 15% increase six months later. In contrast, patients with rheumatoid arthritis demonstrate fluctuating antibody titers, making it challenging to distinguish between immune factors and reinfection.

4. Solutions to optimize the recognition efficiency of Helicobacter pylori reinfection

4.1. Optimize the timing sequence and baseline calibration for dynamic antibody titer monitoring to accurately distinguish reinfection from residual prior infection

To address the diagnostic challenges caused by persistent positive serum Hp-IgG antibody levels, the core clinical approach involves establishing standardized dynamic monitoring protocols and individualized baseline calibration systems. Standardized post-eradication monitoring nodes should be implemented: Collect the first serum sample 4 weeks after treatment completion to establish individualized antibody titers, followed by regular follow-up tests at 6, 12, and 24 months to generate complete titration curves. For patients with higher baseline titers, monitoring intervals may be shortened to every 3 months until titers stabilize at low levels. The “dual baseline comparison method” should be used for calibration: Use the eradication success titers as the initial baseline and the plateau-phase titers as the stable baseline. If subsequent test results show titers rising ≥ 30% above the stable baseline after excluding testing errors, this may indicate reinfection. To avoid interference from residual antibodies, pre-eradication antibody titers should be recorded. If suspected reinfection titers remain below 80% of pre-treatment peaks, additional tests should be conducted to confirm the diagnosis. Additionally, healthcare institutions can establish dynamic titration databases to analyze antibody decay patterns across age groups and treatment regimens through big data analysis. This enables personalized monitoring strategies, such as extending follow-up intervals for younger patients with faster antibody decline, while increasing monitoring frequency for elderly patients with slower antibody decay.

4.2. Establish unified criteria for determining titer changes and technical specifications for detection to reduce diagnostic deviations

To solve the problem of inconsistent decision criteria, it is necessary to implement it from three aspects: industry standard formulation, technical standardization and quality control system construction.

First, under the leadership of the Clinical Laboratory Standardization Committee, multi-center clinical studies with large sample sizes will be conducted, incorporating data from different regions and testing reagents to establish a unified reinfection determination threshold. Specifically, a patient can be diagnosed with reinfection if their serum Hp-IgG

antibody titer rises by ≥ 30% from the stable baseline and remains elevated for over two months, while excluding recent antibiotic or proton pump inhibitor use. For cases with 15–30% titer increases (the gray zone), they should be classified as suspected cases for further verification. Second, standardized testing protocols will be implemented: The only approved methods are enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay. Clear guidelines will specify antigen coating concentrations, sample processing procedures, and testing steps to ensure comparability across institutions. Additionally, quality control standards will require all clinical Hp-IgG antibody test kits to obtain certification from the National Medical Products Administration (NMPA), with each batch undergoing calibration verification.

Furthermore, implementing a mutual recognition mechanism for test results: Establishing a regional testing data sharing platform where medical institutions use standardized calibrated equipment and reagents. Test results are uploaded in real-time to the platform, which performs standardized conversion to eliminate diagnostic discrepancies caused by institutional variations. For example, titer values measured at primary care hospitals can be converted to standard values at central hospitals through the platform, ensuring consistent clinical decision-making.

4.3. Construct a multi-dimensional comprehensive judgment system based on individual characteristics to improve the accuracy of judgment

To address the impact of individual immunity and mucosal status differences, a multi-dimensional comprehensive judgment system of "serum titer + non-invasive detection + clinical characteristics + mucosal status" should be constructed to achieve personalized and accurate identification.

In serological testing, alongside Hp-IgG antibody titers, simultaneous detection of serum pepsinogen I (PG-I), pepsinogen II (PG-II), and gastrin-17 (G-17) is recommended. When elevated titers are accompanied by decreased PG-I and increased PG-II, with a PG-I/PG-II ratio (PGR) ≤ 3.0, this enhances the specificity for reinfection diagnosis. For immunocompromised populations, supplementary Hp-IgM antibody testing is advised. In diabetic patients, positive IgM results serve as crucial evidence, compensating for the limitations of less pronounced IgG titers.

In non-invasive testing, the dynamic changes in serum antibody titers are combined with the urea breath test. When titers reach the suspected threshold, a positive breath test confirms the diagnosis directly, while a negative result requires retesting after one month to rule out false negatives. For titers in the gray zone, fecal Hp antigen testing is used to validate results. This test directly reflects the status of live bacterial infection, effectively distinguishing between residual antibodies and reinfection.

In clinical and mucosal assessment, we developed a risk evaluation system incorporating eradication therapy plans, treatment adherence, lifestyle factors, and comorbidities. Through multivariate logistic regression scoring, patients with ≥ 6 points and elevated antibody titers showed significantly increased reinfection risks. For high-risk individuals, abnormal titers require endoscopic biopsy confirmation of reinfection and mucosal severity. Personalized monitoring profiles are established to track test results, symptoms, and medication history. Longitudinal analysis of titers reveals distinct patterns, such as a 25% spike in one patient's antibody levels, when combined with lifestyle factors, indicating reinfection risk. This multidimensional approach compensates for individual variations, enhancing the accuracy and reliability of reinfection detection.

5. Epilogue

This study identifies three core limitations in using serum Hp-IgG antibody titers to detect reinfection: persistent positive antibodies interfering with infection type differentiation, inconsistent diagnostic criteria causing measurement bias, and individual variations in immune status and mucosal conditions affecting interpretation accuracy. To address these challenges, proposed solutions, including optimized monitoring protocols with baseline calibration, standardized technical specifications, and multidimensional evaluation systems, demonstrate strong clinical applicability. Through standardized procedures, unified criteria, and personalized assessments, these approaches effectively compensate for the

limitations of single serological tests, enhancing reinfection detection precision. Future multi-center clinical trials will refine these solutions to provide more reliable technical support for Hp infection control and early diagnosis/treatment of gastrointestinal diseases.

Disclosure statement

The author declares no conflict of interest.

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