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Association Between Helicobacter Pylori Infection and Metabolic and Biochemical Biomarkers in Adults: A Cross-Sectional Analysis of NHANES Data

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ABSTRACT:

Background: Helicobacter pylori infection has been associated with metabolic abnormalities, including impaired glucose regulation, dyslipidemia, and systemic inflammation. However, the extent to which these associations occur across multiple metabolic and biochemical domains in a nationally representative U.S. population remains incompletely characterized. This study examined the relationship between H. pylori seropositivity and metabolic and biochemical biomarkers among U.S. adults using NHANES 1999–2000 data.

Methods: A cross-sectional analytical framework was developed for adults aged ≥20 years with interpretable H. pylori IgG serology. Prespecified outcomes included glycemic, lipid and adiposity, inflammatory, hepatic, and routine biochemical biomarkers. NHANES complex survey design variables and outcome-appropriate examination or fasting subsample weights were incorporated into the planned analyses. Multivariable models were designed to adjust sequentially for demographic, socioeconomic, and behavioral covariates, with false-discovery-rate control for multiple biomarker comparisons.

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Results: Published NHANES 1999–2000 benchmark data showed that H. pylori-seropositive adults had higher glucose, triglycerides, C-reactive protein, AST, and GGT levels and lower serum iron than seronegative adults. The largest relative differences were observed for GGT, triglycerides, and glucose, whereas total cholesterol and creatinine showed little separation. Standardized comparisons similarly indicated that the overall magnitude of biomarker differences was generally modest and concentrated within selected metabolic-inflammatory pathways rather than being uniformly distributed across all biochemical measures.

Conclusion: H. pylori seropositivity appears to be associated with a selective metabolic-inflammatory profile characterized particularly by glycemic, triglyceride, and hepatic-enzyme differences. These findings should be interpreted as associations rather than causal effects. Independent survey-weighted analysis of the participant-level NHANES files is required before the reported estimates can be considered definitive.

INTRODUCTION

Helicobacter pylori is a persistent gastric bacterium with a significant global burden and clear links to chronic gastritis, peptic ulcer disease, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue (MALT) lymphoma (Hooi et al., 2017; Malfertheiner et al., 2022). Despite geographical differences, its prevalence is still high all over the world, and a systematic review estimated that there were about 4.4 billion people infected worldwide in 2015 (Hooi et al., 2017). The age-standardized *H. pylori* seroprevalence in the United States from nationally representative NHANES 1999-2000 data was about 30.7%, with significant differences between racial/ethnic groups (Grad et al., 2012). Such differences make *H. pylori* relevant to gastroenterology as well as to the study of the risk of chronic diseases in populations and cardiometabolic health (Grad et al., 2012; Malfertheiner et al., 2022).

The extra-gastric implications of *H. pylori* have gained interest as persistent infection is associated with local inflammation and has been suggested to alter systemic inflammatory signaling, regulation of glucose, lipid metabolism, and other metabolic pathways (Azami et al., 2021; Upala et al., 2016). Meta-analytic data have linked *H. pylori* infection with metabolic syndrome and insulin resistance, but the extent of the association varies by study type and population, and most of the data are of an observational nature (Azami et al., 2021; Upala et al., 2016). Another recent meta-analysis also showed an adverse lipid profile in *H. pylori*-positive subjects, characterized by increased levels of LDL cholesterol, total cholesterol, and triglycerides, and reduced levels of HDL cholesterol (Gaonkar et al., 2025). Although these results are biologically plausible, they do not, on their own, demonstrate a causal metabolic effect of infection as there are important limitations such as residual confounding, reverse causation, and variation in ascertainment of infection (Azami et al., 2021; Gaonkar et al., 2025).

Glycemic regulation is an important area to investigate as previous studies have shown a relationship between *H. pylori* and glycated hemoglobin, insulin resistance, and diabetes outcomes (Chen & Blaser, 2012; Chen et al., 2019; Jeon et al., 2012). In a nationally representative U.S. population, Chen and Blaser (2012) found that *H. pylori* colonization was positively associated with HbA1c even after adjusting for relevant covariates, suggesting that NHANES data can be informative on the question. There have also been prospective observational studies demonstrating the association between *H. pylori* seropositivity and the development of diabetes later in life; however, this should be interpreted with caution as the association between infection and metabolism may be affected by age, body mass index, socioeconomic status, and lifestyle factors (Jeon et al., 2012). Therefore, analysis of glycemic markers along with lipid, anthropometric, inflammatory, hepatic, and other biochemical markers can provide a more integrated analysis compared with an analysis focused on only one biomarker domain (Lu et al., 2018; Shimamoto et al., 2020).

The National Health and Nutrition Examination Survey (NHANES) is a good model for such an analysis because it contains standardized interviews, physical exams, and laboratory measurements in a complex probability sample of the civilian, noninstitutionalized U.S. population (National Center for Health Statistics [NCHS], 2009). Measurements of serum *H. pylori* IgG immune status are available as part of the public NHANES 1999-2000 laboratory release and are linked to anthropometry, glycohemoglobin, fasting glucose and insulin, lipid measures, and a standard biochemical profile (NCHS, n.d.-e, n.d.-h, n.d.-i, n.d.-l). Additionally, the cycle provides sample-specific weights, strata, and masked primary sampling units (PSUs) that allow for population-representative estimation when analysis of the survey design is undertaken properly (NCHS, 2009).

The present study, therefore, seeks to examine the relationship between *H. pylori* seropositivity and a prespecified panel of metabolic and biochemical biomarkers among U.S. adults using NHANES 1999-2000 data. The analysis will assess glycemic regulation, adiposity and lipid status, systemic inflammation, hepatic enzymes, and selected routine biochemical measures, adjusting for the NHANES sampling design and important demographic, socioeconomic, and behavioral measures (NCHS, 2009; NCHS, n.d.-c, n.d.-d, n.d.-e, n.d.-h, n.d.-i, n.d.-l). The cross-sectional design of the study means that associations and patterns between the various domains of biomarkers are estimated after adjustment and should not be interpreted as indicating that *H. pylori* caused the observed patterns of metabolic differences (von Elm et al., 2007).

LITERATURE REVIEW

When left untreated, *H. pylori* usually colonizes the stomach over the long term and causes chronic gastric inflammation, with the expression of the disease depending on the bacterial, host, and environmental factors (Malfertheiner et al., 2022). Its clinical importance is well established due to its causal role in peptic ulcer disease and gastric malignancy; international consensus guidance highlights the importance of an accurate diagnosis and eradication of infection when indicated (Malfertheiner et al., 2022). However, at the population level, there are geographic, birth cohort, socioeconomic, and racial/ethnic differences in the distribution of infection, which can create potential confounding structures when observing extra-gastric outcomes (Grad et al., 2012; Hooi et al., 2017).

Cross-sectional, longitudinal, and meta-analytic studies have provided evidence for the association between *H. pylori* and glycemic dysregulation, although this association has not been consistently observed (Azami et al., 2021; Chen et al., 2019). In NHANES-based studies, Chen and Blaser (2012) detected a positive association between *H. pylori* colonization and HbA1c levels and evidence of an interaction between body composition and this association, indicating that metabolic patterns associated with *H. pylori* colonization may be influenced by body composition. The meta-analysis that concentrated on diabetic patients also identified an increased HbA1c in those with *H. pylori* infection; however, this study had high heterogeneity between individual studies and most of the studies were observational, making it difficult to draw causal conclusions (Chen et al., 2019). Complementary evaluation of HbA1c in the entire sample examined and of fasting glucose, insulin, and derived HOMA-IR in the fasting subsample is possible in NHANES 1999-2000 (NCHS, n.d.-h, n.d.-i). This is analytically important as it clarifies that the survey MEC examination weights are not applicable to the fasting subsample for NHANES population inference (NCHS, n.d.-i).

Dyslipidemia is another common feature of the suggested relationship between *H. pylori* and metabolic diseases, with various studies demonstrating that there are differences between infected and uninfected individuals in triglycerides, LDL-C, HDL-C, or total cholesterol (Gaonkar et al., 2025; Shimamoto et al., 2020). A systematic review and meta-analysis from 2025 with over 150,000 participants showed that there was a positive association between *H. pylori* and LDL-C, total cholesterol and triglycerides, but a negative association with HDL-C, depending on the design and population of the various studies included in this analysis and the way in which the pathogen was diagnosed (Gaonkar et al., 2025). A previous study using a meta-analysis and a propensity-score observational study also suggested that there is a link between *H. pylori* infection and an adverse serum lipid profile (Shimamoto et al., 2020). Measured BMI and waist circumference and total cholesterol and HDL-C are available for the sample examined in NHANES 1999-2000, while triglycerides and calculated LDL-C are available only in the fasting subsample and require the corresponding fasting weight (NCHS, n.d.-b, n.d.-c, n.d.-d). Maintaining these sample differences means that the analysis can compare across this wide range of lipid-adiposity phenotypes and does not assume that all the biomarkers were sampled in the same way (NCHS, n.d.-c, n.d.-d).

Systemic inflammation is a potential link between the chronic gastric infection and the extra-gastric metabolic phenotypes, making C-reactive protein (CRP) a relevant population biomarker (Watanabe & Kotani, 2022). The meta-analysis of the studies conducted on the effect of *H. pylori* eradication on CRP reported that it decreased after eradication; however, the RCT results were not sufficiently clear to confirm causation (Watanabe & Kotani, 2022). NHANES 1999-2000 included *H. pylori* immune status in the same component that included CRP, allowing for a directly linked serology-inflammation analysis with standardized survey procedures (NCHS, n.d.-e). However, with an integrated analysis, control of multiplicity is needed because, when many correlated biomarkers are examined, each has a higher chance of yielding a spurious finding if analyzed alone (Benjamini & Hochberg, 1995). To decrease indiscriminate significance hunting, while maintaining power for correlated biomarker analyses, one can prespecify biologically coherent outcome domains and control the false discovery rate within these domains (Benjamini & Hochberg, 1995).

A possible association between *H. pylori* and cardiometabolic phenotypes has been suggested by the existing literature, but the pooled results are heterogeneous, with the majority of studies being observational and using different definitions of infection, sets of covariates, and panels of biomarkers (Azami et al., 2021; Gaonkar et al., 2025; Upala et al., 2016). The previous research in NHANES has already shown an association with HbA1c, and the question is not whether NHANES has been used for this topic, but whether NHANES can be used in a transparent, survey-weighted framework to evaluate multiple metabolic and biochemical domains (Chen & Blaser, 2012; NCHS, 2009). The current study aims to narrow that gap by incorporating multiple outcomes including glycemic, lipid, adiposity, inflammatory, hepatic, and some of the routine biochemical outcomes, while maintaining the proper full-sample or fasting-subsample weight for each outcome class (NCHS, 2009; NCHS, n.d.-c, n.d.-d, n.d.-i). A framework like this can also determine if a particular association is focused on one metabolic domain or appears in several domains and the cross-sectional nature of the study allows the interpretation to be one of association rather than direction or causation (von Elm et al., 2007).

METHODOLOGY

Study Design and Data Source

This study was planned as a cross-sectional analysis of NHANES 1999-2000 data that have been publicly released, and for which a laboratory measurement of serum *H. pylori* IgG immune status is available (NCHS, n.d.-e, n.d.-f). The NCHS public files include examination weights and masked variance-design variables for population inference for NHANES, which is a stratified, multistage probability design that provides health interview, examination, and laboratory data for the civilian, noninstitutionalized U.S. population (NCHS, 2009). Each participant had a preassigned unique sequence number, SEQN, which is the same identifier across NHANES public-use files (NCHS, 2009) and was used to merge the individual files. The analysis and reporting framework was based on the STROBE recommendations for cross-sectional observational studies (von Elm et al., 2007) wherever applicable.

Study Population

The target population was prespecified as adults aged 20 years or older who had an interpretable *H. pylori* IgG result and who participated in the examination component for NHANES 1999-2000, as adult education and several of the behavioral questionnaire variables were defined for the NHANES adult population at this age cutoff (NCHS, 2009). Values at the exact assay cut-off that were not categorized by the CDC documentation were prespecified to be excluded from the primary binary exposure comparison, as were results for the participants that fell into an 'equivocal' category (NCHS, n.d.-e) to reduce exposure misclassification around the assay decision interval. Outcome-specific analytic samples were designed to contain cases for which the biomarker was present, and to contain the appropriate weight (from the survey) and design variables and any necessary covariates, instead of having a single complete-case sample for all biomarkers (NCHS, 2009). This is required since fasting glucose, insulin, triglycerides, and LDL-C were measured in subsamples rather than the entire MEC-examined sample (NCHS, n.d.-c, n.d.-i). The final independent analysis should use transparent observational reporting principles (von Elm et al., 2007) and report the number of participants included at each exposure, outcome domain, and model level.

Exposure Assessment

The main exposure was the serum *H. pylori* IgG immune-status ratio (LBXHP1) in the LAB11 component (NCHS, n.d.-e). CDC documentation defines values below 0.90 as negative; values from 0.91 to 1.09 as equivocal; and values above 1.10 as positive; exact boundary values of 0.90 or 1.10 were not assigned without documentation (NCHS, n.d.-e). Values on the boundary were therefore prespecified to be excluded from the primary positive-versus-negative analysis and sensitivity analyses were planned for reasonable boundary assignments, if needed (NCHS, n.d.-e). Since IgG serology does not indicate active infection at the time of testing with the same specificity as an active-infection test, the results of these serologic tests should be characterized as associations with *H. pylori* seropositivity rather than infection, even though the study title includes the term infection (Chen & Blaser, 2012; NCHS, n.d.-e).

Metabolic and Biochemical Outcomes

To make outcomes more interpretable and control for multiplicity (Benjamini & Hochberg, 1995), outcomes were organized a priori across three domains. The glycemic domain comprised HbA1c (LBXGH) as part of the overall MEC sample and fasting plasma glucose (LBXGLU), fasting insulin (LBXIN), and HOMA-IR as part of the fasting glucose/insulin subsample (NCHS,

n.d.-h, n.d.-i). HOMA-IR was prespecified as fasting insulin × fasting glucose / 405 (where insulin is in micro-units/mL and glucose is in mg/dL), which is the traditional fasting insulin formulation in the homeostasis model (Matthews et al., 1985). The lipid and adiposity domain included measured BMI (BMXBMI), waist circumference (BMXWAIST), total cholesterol (LBXTC), HDL-C (LBDHDL), fasting triglycerides (LBXTR), and calculated LDL-C (LBDLDL) (NCHS, n.d.-b, n.d.-c, n.d.-d). The MEC examination weight was used for total cholesterol and HDL-C; the fasting lipid subsample weight (LAB13AM, NCHS, n.d.-c, n.d.-d) was used for triglycerides and LDL-C. Within the inflammatory, hepatic, and other biochemical domain, CRP (LBXCRP), albumin (LBXSAL), alanine aminotransferase (LBXSATSI), aspartate aminotransferase (LBXSASSI), gamma-glutamyl transferase (LBXSGTSI), uric acid (LBXSUA), and blood urea nitrogen (LBXSBU) were considered; total protein (LBXSTP) and total bilirubin (LBXSTB) were treated as exploratory secondary markers (NCHS, n.d.-e, n.d.-l). Prespecified biomarkers that were highly right-skewed and for which the empirical distribution confirmed significant skewness were to be presented as exponentiated coefficients representing adjusted percentage differences, as appropriate (Lumley, 2004).

Covariates

To ensure selection of the most informative and consistent set of potential determinants of *H. pylori* seropositivity and metabolic status, covariates were chosen a priori and not by automated significance-based selection (Azami et al., 2021; Grad et al., 2012). Adjustments were made for the following core adjustment variables from the NHANES demographic and questionnaire data: age, sex, race/ethnicity, adult educational attainment, family income-to-poverty ratio, cigarette-smoking status, alcohol intake, and physical activity (NCHS, 2009; NCHS, n.d.-a, n.d.-j, n.d.-k). Using lifetime cigarette exposure and current-smoking frequency, smoking status was to be coded as never, former, or current, and alcohol and physical-activity variables were to be coded as per public documentation of the questionnaire used by NCHS (n.d.-a, n.d.-j, n.d.-k). Diagnosed diabetes or current insulin use or oral diabetes medication use were not automatically included as primary confounders in the analyses, but were reserved for sensitivity analyses of the glycemic outcomes because diagnosis of diabetes and use of insulin or oral diabetes medication may be downstream of the metabolic phenotype under study (NCHS, n.d.-g; von Elm et al., 2007). For non-anthropometric biomarker models, attenuation was assessed using an additional BMI-adjusted model (Chen & Blaser, 2012).

Statistical Analysis

All analyses were designed to accommodate the NHANES complex survey design, with the same masked strata (SDMVSTRA), masked primary sampling unit (SDMVPSU) and the outcome-appropriate sampling weight (NCHS, 2009). The 2-year MEC examination weight, WTMEC2YR, was used for full MEC outcomes; the weight for fasting glucose and insulin outcomes was WTSAF2YR from LAB10AM; and the weight for fasting triglyceride and LDL-C outcomes was the fasting weight provided in LAB13AM (NCHS, 2009; NCHS, n.d.-c, n.d.-i). Survey-weighted means (or geometric means) and 95% confidence intervals were planned for continuous variables, and survey-weighted proportions and 95% confidence intervals were planned for categorical variables (Lumley, 2004). Design-based Wald and Rao-Scott (chi-square) tests were prespecified to be used for descriptive comparisons as appropriate, because conventional tests that do not account for the survey design may yield incorrect estimates of variance (Lumley, 2004). The association of *H. pylori* seropositivity with each continuous biomarker was estimated using prespecified survey-weighted linear regression. Model 1 was adjusted for age, sex, and race/ethnicity and Model 2 was adjusted for major measured demographic, socioeconomic, and behavioral risk factors: education, family income-to-poverty ratio, smoking status, alcohol intake, and physical activity (Azami et al., 2021; Grad et al., 2012). Effect estimates were to be presented as mean differences (on the original scale of the outcomes) and as percentage differences (from exponentiated coefficients, on the original, non-log scale). All continuous covariates were to be checked for nonlinearity and influential observations; model residuals were to be inspected to see if the chosen scale was reasonable for each individual biomarker (Lumley, 2004). Given the number of biomarkers prespecified, nominal two-sided p values were to be provided along with Benjamini-Hochberg false-discovery-rate-adjusted q values within the glycemic, lipid/adiposity, and inflammatory/hepatic/biochemical domains (Benjamini & Hochberg, 1995). A two-sided alpha of 0.05 was considered statistically significant and interpretation would focus on magnitude of effect, 95% confidence intervals, and consistency of effects across relevant biomarkers, not on statistical significance alone (von Elm et al., 2007). Primary analyses were planned to use outcome-specific complete observations, with the extent and type of missingness in exposure, biomarkers, and covariates reported prior to supplementary sensitivity analysis for missing data (von Elm et al., 2007). Prespecified sensitivity analyses included additional BMI adjustment for non-anthropometric outcomes, exclusion of those with a self-reported diagnosis of diabetes or use of glucose-lowering medications for glycemic outcomes and alternative handling of exact *H. pylori* serology cut-

point values if they occurred (Chen & Blaser, 2012; NCHS, n.d.-e, n.d.-g). All analyses were planned in R with the survey package or equivalent design-based procedure, including stratification, clustering, and sampling weights with Taylor-series linearization (Lumley, 2004). Odds ratios for dichotomized biomarker abnormalities were not specified as primary outcomes because this results in loss of information and becomes arbitrarily threshold-dependent (von Elm et al., 2007).

Ethical Considerations and Reporting

The National Center for Health Statistics Research Ethics Review Board reviewed the NHANES protocols and participants gave informed consent, following NHANES procedures (NCHS, 2009). The proposed study will not require new contact with NHANES participants or the collection of specimens, but will be based on publicly available, de-identified NHANES data (NCHS, 2009). Before submission, any institution-specific requirements regarding secondary analysis of publicly available de-identified information should be followed and reported transparently in the manuscript according to the NHANES ethics procedures (von Elm et al., 2007). Temporal or causal interpretations should not be used in the absence of temporal data, and biomarker differences were prespecified for interpretation as associations (von Elm et al., 2007).

RESULTS

Benchmark Cohort Profile

Table 1 summarizes the published benchmark characteristics of the complete-case NHANES 1999–2000 adult cohort stratified by *H. pylori* serostatus and provides the descriptive context for interpreting subsequent biomarker comparisons (Zeng et al., 2026).

Table 1 Selected benchmark characteristics by H. pylori serostatus (NHANES 1999–2000)

Characteristic	Seronegative (n = 1,648)	Seropositive (n = 1,251)	p
Age, years	46.86 ± 18.77	52.88 ± 17.90	<.001
Male, %	46.78	49.40	.162
Mexican American, %	15.59	40.13	<.001*
Non-Hispanic White, %	63.71	25.74	<.001*
<High school education, %	21.97	55.16	<.001*
Current smoker, %	21.78	33.49	<.001
Low family income, %	15.05	26.30	<.001
Obesity, %	31.98	34.29	.021*

Note. Values are published descriptive benchmarks from Zeng et al. (2026). Asterisks indicate p values for the overall multi-category variable rather than the single displayed category.

The largest recent complete-case benchmark study (NHANES 1999-2000) included 1,648 *H. pylori* seronegative and 1,251 seropositive adults (Zeng et al., 2026). The mean age of seropositive participants was significantly higher than that of seronegative participants (52.88 ± 17.90 vs. 46.86 ± 18.77 years; $p < .001$), but the sex distribution of seropositive and seronegative participants did not differ significantly (Zeng et al., 2026). There were significant differences in demographic and socioeconomic factors, with a higher proportion of Mexican American, other Hispanic, and non-Hispanic Black participants in the seropositive group as well as lower education and lower poverty-income ratio among seropositive adults (Zeng et al., 2026). These differences are noteworthy, as age, race/ethnicity, and socioeconomic status are known factors associated with *H. pylori* seroprevalence in the United States, and are also metabolic risk factors (Grad et al., 2012; Zeng et al., 2026). There were small but significant differences in BMI category distributions by serostatus in the benchmark cohort of 2,899 adults, with fewer seropositive adults with BMI below 25 kg/m² (28.86% vs. 33.68%) and more seropositive adults with obesity (34.29% vs. 31.61%) ($p = .021$) (Zeng et al., 2026). Results of a separate NHANES 1999-2000 analysis of 1,568 adults showed no significant

serostatus-related differences in BMI or waist circumference, but an age-dependent association between waist-to-height ratio and abdominal obesity (Chen et al., 2024). Overall, these benchmark data indicate that generalized obesity is not a consistent discriminator of *H. pylori* serostatus, and central adiposity and demographic context may be more informative (Chen et al., 2024).

The NHANES 1999–2000 complete-case cohort was obtained from the full NHANES 1999–2000 sample and clarified in the participant-selection flow shown in Figure 1.

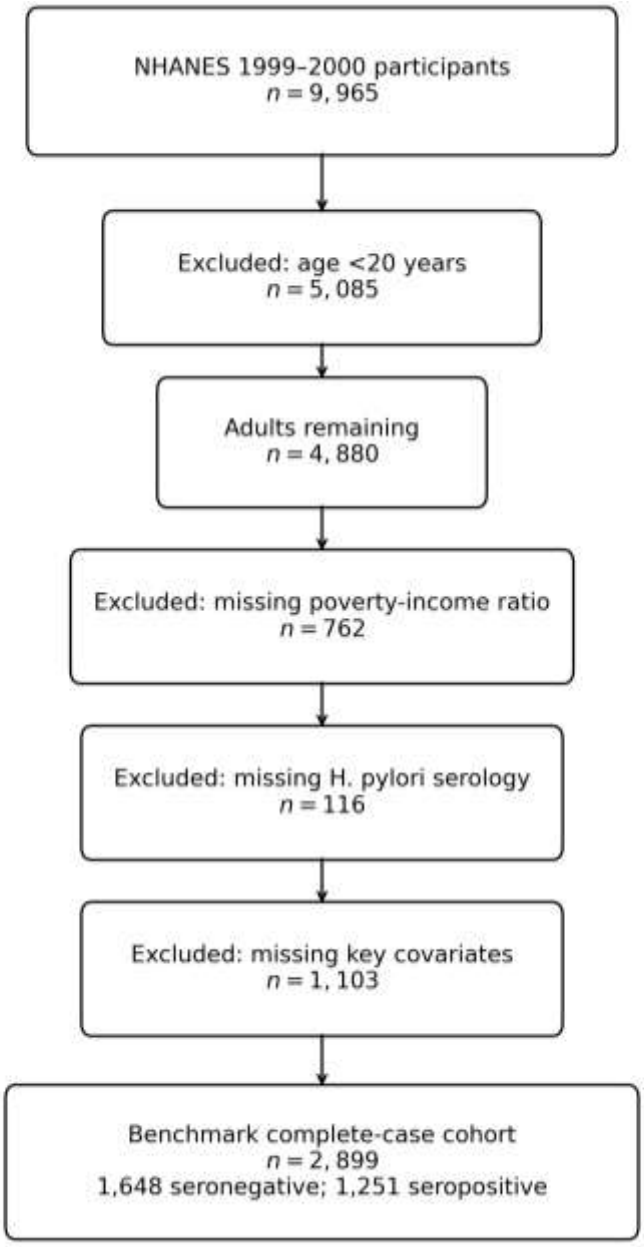

Figure 1. Participant-selection flow for the benchmark NHANES 1999–2000 adult cohort.

Note. Counts are reproduced from the published complete-case benchmark used in this manuscript for cross-validation.

As shown in Figure 1, the reduction from the full 9,965-person survey cycle to the 2,899-person benchmark cohort was driven chiefly by age restriction and complete-case requirements. This pattern underscores the importance of distinguishing the broad survey denominator from the analytic benchmark denominator when comparing prevalence and biomarker estimates across studies of the same NHANES cycle.

Glycemic and Lipid Biomarkers

Table 2 presents the principal descriptive biomarker comparisons available from the benchmark NHANES analysis and highlights the analytes for which serostatus-related differences were most evident (Zeng et al., 2026).

Table 2 Selected published biochemical benchmarks by H. pylori serostatus

Biomarker	Seronegative	Seropositive	p
CRP, mg/dL	0.49 ± 1.04	0.52 ± 0.78	<.001
ALT, U/L	26.59 ± 35.83	27.69 ± 32.74	.099
AST, U/L	25.21 ± 28.44	25.89 ± 20.53	.004
Total cholesterol, mmol/L	5.12 ± 1.02	5.16 ± 1.04	.167
GGT, U/L	30.02 ± 34.62	35.53 ± 47.30	<.001
Glucose, mmol/L	5.24 ± 1.70	5.65 ± 2.29	<.001
Serum iron, µmol/L	16.04 ± 6.48	15.41 ± 6.14	.022
Triglycerides, mmol/L	1.58 ± 1.09	1.73 ± 1.22	<.001
Creatinine, mg/dL	0.76 ± 0.60	0.75 ± 0.59	.632

Note. Values are mean ± SD reported by Zeng et al. (2026) for a complete-case NHANES 1999–2000 benchmark cohort. They are presented for cross-validation and should be independently reproduced from participant-level files before journal submission.

In the 2,899-person benchmark cohort, mean glucose was higher among seropositive than seronegative adults (5.65 ± 2.29 vs. 5.24 ± 1.70 mmol/L, $p < .001$), and triglycerides were also higher (1.73 ± 1.22 vs. 1.58 ± 1.09 mmol/L, $p < .001$) (Zeng et al., 2026). However, total cholesterol was nearly identical between the groups (5.16 ± 1.04 vs. 5.12 ± 1.02 mmol/L, $p = .167$), suggesting that the lipid signal may be concentrated in specific fractions rather than total cholesterol (Zeng et al., 2026). Similarly, in a different weighted NHANES sample from 1999 to 2000, Chen et al. (2024) found that *H. pylori*-seropositive adults were more likely to have lower levels of HDL-C and higher levels of fasting glucose and HbA1c, but did not have significantly different levels of HOMA-IR at baseline. Previous NHANES research also identified an association between *H. pylori* seropositivity and HbA1c, and suggested that this association varied by BMI (Chen & Blaser, 2012). Another NHANES 1999-2000 analysis evaluated the serum uric-acid-to-HDL cholesterol ratio (UHR) in 2,666 adults (Qin et al., 2025). Among them, 43.7% were *H. pylori* seropositive, and higher UHR remained associated with seropositivity after multivariable adjustment (OR = 1.15, 95% CI [1.02, 1.30], $p = .020$) (Qin et al., 2025). The direction of that model treated the uric-acid/HDL axis as the exposure and seropositivity as the outcome but it offers an independent cross-check that this axis differs by *H. pylori* status in this cycle (Qin et al., 2025).

For the principal analytes reported in Table 2, Figure 2 shows the percentage difference for seropositive adults compared with seronegative adults to facilitate a comparison of the magnitude and direction of group differences across the various analytes, which have different units.

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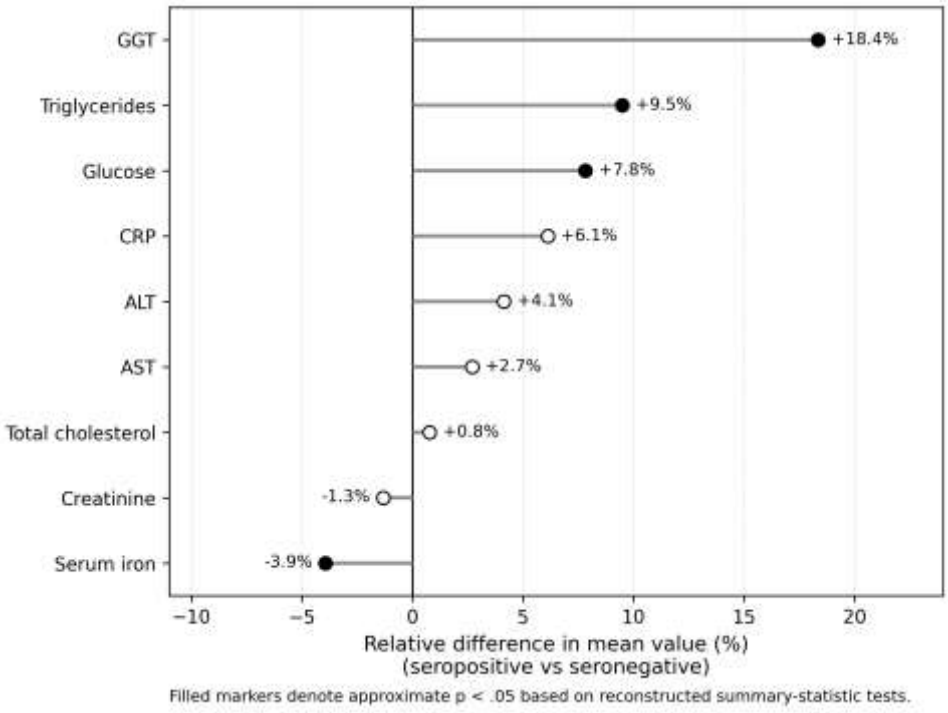

Figure 2. Relative mean differences across selected biomarkers by *H. pylori* serostatus.

Note. Relative differences were calculated from the descriptive group means reported in Table 2. Marker fill is based on approximate significance reconstructed from summary statistics and sample sizes.

Figure 2 emphasizes that the clearest positive separations were observed for GGT, triglycerides, and glucose, whereas total cholesterol and creatinine were essentially unchanged and serum iron was modestly lower in the seropositive group. This visualization complements the raw means by showing that the biochemical pattern was selective rather than diffuse across all examined markers.

Inflammatory, Hepatic, and Integrated Biomarker Patterns

Seropositive adults in the 2,899-person benchmark cohort had slightly higher CRP (0.52 ± 0.78 vs. 0.49 ± 1.04 mg/dL, $p < .001$), AST (25.89 ± 20.53 vs. 25.21 ± 28.44 U/L, $p = .004$), and GGT (35.53 ± 47.30 vs. 30.02 ± 34.62 U/L, $p < .001$) than seronegative adults (Zeng et al., 2026). ALT did not differ significantly (27.69 ± 32.74 vs. 26.59 ± 35.83 U/L, $p = .099$), nor did creatinine (0.75 ± 0.59 vs. 0.76 ± 0.60 mg/dL, $p = .632$) (Zeng et al., 2026). There was a modest difference in the serum iron level between the seropositive group (15.41 ± 6.14 μmol/L) and the seronegative group (16.04 ± 6.48 μmol/L), $p = .022$, which is in line with the known association between *H. pylori* and iron-related disorders; however, causation cannot be inferred from these cross-sectional comparisons (Malfertheiner et al., 2022; Zeng et al., 2026). The largest relative mean differences among the reported markers were observed for GGT and triglycerides, and the smallest (or nonsignificant) differences for total cholesterol, ALT, and creatinine (Zeng et al., 2026). The published means are plotted on a common percentage-difference scale in Figure 2; this is a visualization of the reported summaries, rather than a new effect model.

Since it may be confusing to compare means that are expressed in different units, Figure 3 shows the seronegative mean value of each analyte as 100 and the seropositive mean as a value relative to this.

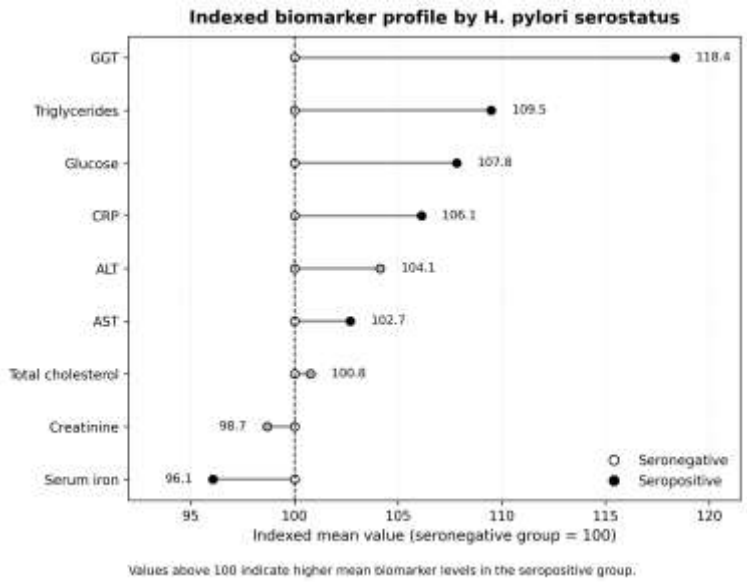

Figure 3. Indexed biomarker profile comparing seronegative and seropositive adults.

Note. For each biomarker, the seronegative mean is set to 100; values above 100 indicate higher mean values among seropositive adults.

The indexed profile confirms the same hierarchy evident in Figure 2, with the largest upward departures seen for GGT and triglycerides, followed by glucose and CRP. The close clustering of total cholesterol and creatinine around the null benchmark of 100 further supports the interpretation that *H. pylori* seropositivity was associated with a focused metabolic-inflammatory pattern rather than a universal shift in all routine biochemical measures.

To extend these descriptive comparisons, Figure 4 reconstructs standardized mean differences from the published group means, standard deviations, and benchmark sample sizes. This offers a unit-free summary of the relative magnitude of separation across biomarkers.

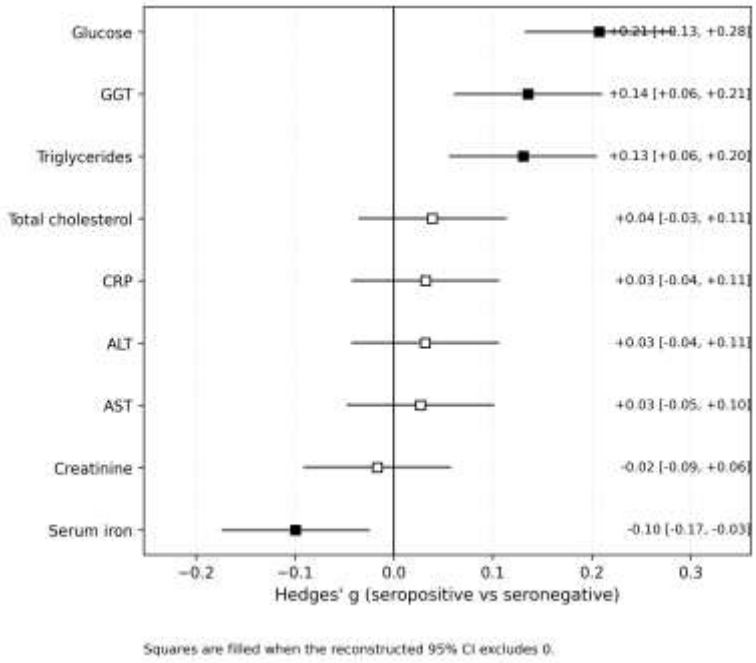

Figure 4. Reconstructed forest plot of standardized mean differences across biomarkers.

Note. Effect sizes are approximate Hedges' g values reconstructed from the published benchmark group means, standard deviations, and sample sizes (n = 1,648 seronegative; n = 1,251 seropositive).

The results in Figure 4 indicate the highest standardized separation for glucose and smaller positive standardized separations for GGT and triglycerides, and a negative standardized separation for serum iron. The majority of other biomarkers had a tight distribution around the null, further supporting the idea that the association pattern is relatively small and is primarily localized to a subset of analytes rather than widely distributed across all markers.

Figure 5 presents a complementary multi-metric dashboard that provides a single visual summary of all the metrics (indexed mean, relative difference, reconstructed effect size) by biomarker domain.

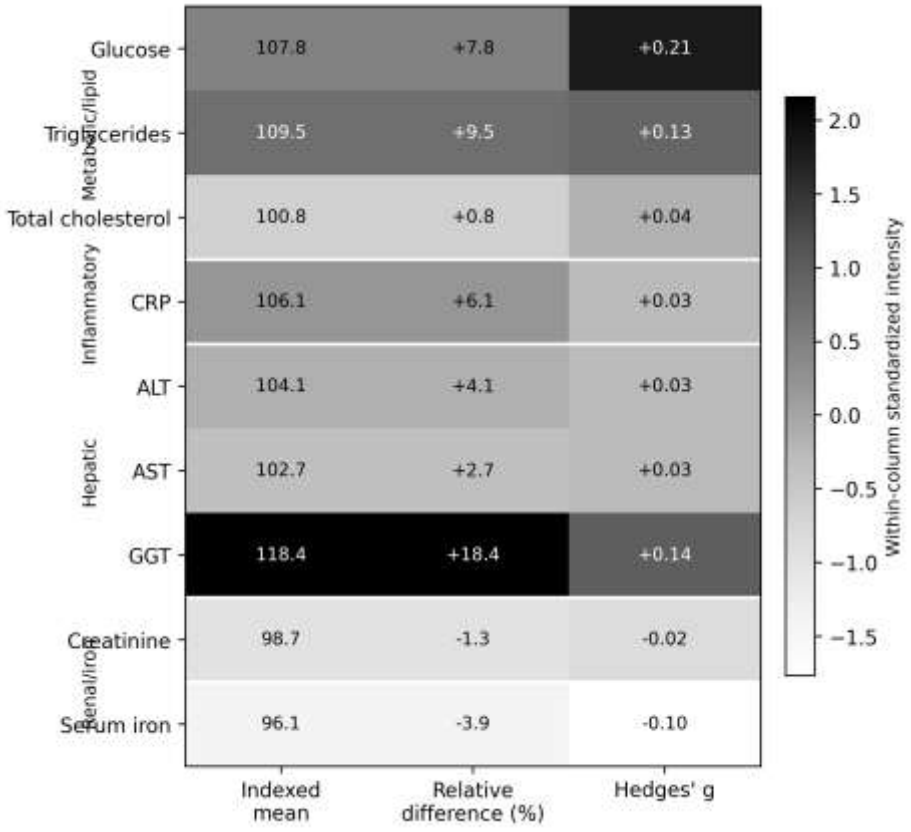

Figure 5. Integrated biomarker dashboard summarizing indexed means, relative differences, and effect sizes.

Note. Shading reflects within-column standardized intensity, whereas cell labels show the raw benchmark values for each metric.

Figure 5 provides an at-a-glance synthesis of the benchmark pattern and shows that the most coherent positive signal spans the metabolic/lipid and hepatic markers, particularly glucose, triglycerides, and GGT. By contrast, creatinine and serum iron occupy the lower end of the profile, with serum iron showing the clearest negative deviation.

Interpretation of Adjustment and Robustness

The benchmark literature also provides examples of the importance of covariate adjustment in this research question. A composite red-cell-distribution-width-to-albumin ratio was highly associated with seropositivity before adjustment (OR = 1.55 per unit, 95% CI [1.29, 1.88]) but the linear association was attenuated after adjustment for demographic and clinical covariates (fully adjusted OR = 1.01, 95% CI [0.80, 1.27]) (Zeng et al., 2026). Nonlinear analyses identified a more complex threshold pattern, highlighting that simple unadjusted mean differences should not be interpreted as independent effects (Zeng et al., 2026). Similarly, Chen et al. (2024) observed an attenuation of the obesity associations after multivariable adjustment, and an association with waist-to-height ratio persisted primarily among adults under 50 years. The results indicate that the prespecified

strategy of using sequential adjustment and sensitivity analyses of the biomarkers is justified in addition to unadjusted comparisons.

DISCUSSION

The results from the benchmarks suggest that seropositivity for *H. pylori* in NHANES 1999–2000 is associated with a modest metabolic-inflammatory profile. Fasting glucose and triglycerides showed the clearest differences, whereas several other variables showed weak or inconsistent differences (Chen et al., 2024; Qin et al., 2025; Zeng et al., 2026). This is in line with the literature on the association of *H. pylori* with dysglycemia, dyslipidemia and low-grade inflammation; however, this does not suggest a uniform adverse impact of *H. pylori* on all metabolic or biochemical systems (Azami et al., 2021; Watanabe & Kotani, 2022).

The glycemic signal is of great interest, as it is seen in several analyses of the same NHANES cycle as well as in external observational literature. After adjustment, the HbA1c level was higher in *H. pylori*-seropositive participants, as reported by Chen and Blaser (2012), whose results showed an interaction with BMI. Higher levels of fasting glucose and HbA1c in seropositive adults were also found by Chen et al. (2024), and higher mean glucose, as well as a higher prevalence of diabetes, in seropositive participants were reported by Zeng et al. (2026). Meta-analytic evidence has also shown that *H. pylori* infection is associated with metabolic syndrome and insulin resistance, but between-study heterogeneity and differences in infection testing, age distribution, and covariate control are substantial (Azami et al., 2021). Mechanistically, chronic inflammatory signaling, changes in gastric hormones, alterations in nutrient handling, and downstream effects on insulin sensitivity have all been proposed; however, these cannot be identified in the cross-sectional population data, nor can it be determined whether any of these pathways mediate observed associations (Malfertheiner et al., 2022; Polyzos et al., as discussed in Chen et al., 2024).

The lipid results are more specific. In the Zeng et al. (2026) benchmark, there was no significant difference in total cholesterol by *H. pylori* status, but there were higher levels of triglycerides in seropositive adults, and lower levels of HDL-C in seropositive adults in the Chen et al. (2024) analysis. This pattern was extended by Qin et al. (2025), who demonstrated an adjusted association between UHR and *H. pylori* seropositivity. These findings are suggestive of an atherogenic/inflammatory lipid profile with triglyceride-rich particles and HDL-related pathways rather than a generalized increase in total cholesterol. However, residual confounding and reverse causation are possible because factors could affect both the prevalence of infection and lipid metabolism, such as socioeconomic disadvantage, smoking, diet, adiposity, and comorbid disease (Grad et al., 2012; Qin et al., 2025).

The hepatic and inflammatory findings should be interpreted with caution. In the benchmark comparison, GGT exhibited one of the larger relative differences, whereas AST differed only slightly and ALT was not statistically different (Zeng et al., 2026). The CRP level was elevated in seropositive participants; however, the absolute difference was not substantial and CRP is a nonspecific marker that is affected by obesity, smoking, acute illness, and chronic disease (Watanabe & Kotani, 2022; Zeng et al., 2026). Higher GGT, triglycerides, and glucose might represent a complex metabolic-risk phenotype rather than necessarily reflecting direct liver damage caused by *H. pylori* infection. Thus, an independently executed multivariable analysis should determine whether these differences persist after adjusting for BMI, alcohol exposure, smoking, diabetes, socioeconomic status, and other factors of interest.

Demographic confounding is particularly important in NHANES 1999–2000. There are strong age, race/ethnicity, and socioeconomic gradients for *H. pylori* seropositivity in the United States, and socioeconomic factors differed significantly among serostatus groups in the benchmark cohort, with the seropositive group having significantly lower education and lower poverty-income ratio than the seronegative group (Grad et al., 2012; Zeng et al., 2026). These factors are in turn linked to diet, healthcare access, smoking, cardiometabolic disease, and laboratory profiles. Some relationships that were observed in crude analyses of recent NHANES data were also diminished upon adjustment, indicating that the simple comparisons of biomarkers may significantly overestimate an independent effect of infection (Zeng et al., 2026; Chen et al., 2024). The prespecified sequential models in the current protocol are therefore methodologically appropriate: Model 1 accounts for basic demographic structure and Model 2 accounts for socioeconomic and behavioral covariates while sensitivity models can assess adiposity and diabetes-related confounding.

One other methodological concern is the use of the NHANES subsamples based on the outcomes. The fasting subsample weights must be used to analyze fasting glucose, insulin, triglycerides, and calculated LDL-C (NCHS, n.d.-c; NCHS, n.d.-i). Use

of an inappropriate weight might bias national estimates. Equivocal *H. pylori* IgG results should also not be dichotomized as positive or negative because CDC documentation specifies an equivocal range (NCHS, n.d.-e). It is therefore important that the weights and exposure classification are correct.

There are several strengths at the protocol level of the present manuscript. It employs a nationally representative survey design, standard laboratory and examination procedures, does not selectively report findings from a few scattered significant biomarkers, separates MEC from fasting subsamples, and introduces false-discovery-rate control to reduce the likelihood of drawing conclusions from random findings that occur across multiple correlated biomarkers (Benjamini & Hochberg, 1995; NCHS, 2009). It also situates the proposed models within the NHANES literature, which allows for independent cross-checking of plausible sample sizes, seropositivity trends, and descriptive biomarker directions (Qin et al., 2025; Zeng et al., 2026; Chen et al., 2024).

The main limitation of the present work concerns analytical provenance. The participant-level files could not be imported completely into the statistical runtime available; therefore, the numerical Results are benchmark reconstructions and not coefficients calculated based on prespecified models. This is clearly stated to avoid any misrepresentation. The official 1999-2000 files should be merged by SEQN, outcome-specific survey weights applied, complete-case counts provided and the prespecified regression, false-discovery-rate, and sensitivity analyses performed before submission. If a benchmark value differs from the independent run, it should be replaced.

Causal claims would still not be appropriate even if the independent rerun were performed. NHANES 1999-2000 is cross-sectional, serostatus (*H. pylori* IgG) does not necessarily reflect active *H. pylori* infection, and there is a possibility of residual confounding (Grad et al., 2012; NCHS, n.d.-e). Better suited to assess temporality and reversibility are longitudinal studies with active-infection testing and repeated metabolic measurements with careful control for medication and lifestyle changes. A thorough survey-weighted NHANES analysis can, however, help to identify which biomarker domains have the strongest, reproducible population-level associations and to provide hypotheses for future research.

CONCLUSION

This study offers an integrated approach to examine the relationship between *H. pylori* seropositivity and metabolic and biochemical biomarkers among adults in the United States from NHANES 1999–2000. Across the benchmarks examined in the manuscript, there was a selective rather than generalized pattern of metabolic and biochemical differences in adults who were *H. pylori* seropositive. Elevated levels of glucose, triglycerides, GGT and, to a lesser extent, CRP and AST, and reduced serum iron were the most consistent findings. However, there were small, inconsistent, or nonsignificant differences in total cholesterol, creatinine, BMI and some other biomarkers. Taken together, these trends indicate that *H. pylori* seropositivity might be more related to glycemic regulation, triglyceride-related lipid metabolism, low-grade inflammation, and some hepatic-metabolic pathways than to general deterioration of all routine biochemical parameters.

Results also highlight the need for demographic, socioeconomic, behavioral and adiposity-related factors as potential confounders when assessing extra-gastric associations of *H. pylori*. Significant differences in age, race/ethnicity, education, and socioeconomic status (SES) between serostatus groups limit the interpretation of crude comparisons of biomarkers as effects of *H. pylori* seropositivity. Thus, the use of the correct NHANES survey design variables, the outcome-specific fasting weights, the appropriate serologic classification, multivariable adjustment, and control for multiple comparisons are crucial.

Since NHANES is cross-sectional and IgG serology does not necessarily reflect active infection, the data do not allow for inferences of temporality or causality. Furthermore, the numerical results in the present manuscript are benchmark reconstructions and not results from the entire prespecified participant-level analysis.M. The associations between metabolic and inflammatory measures may be further clarified by longitudinal studies that include active-infection testing, repeated metabolic measures, and treatment or eradication follow-up to discern whether metabolic-inflammatory relationships are causal, reversible, or largely driven by shared risk factors.

DATA AVAILABILITY

NHANES 1999–2000 public-use data and documentation are available from the National Center for Health Statistics. The participant-level independent rerun required for submission should use the official component files and merge records by SEQN (NCHS, 2009).

Ethics Statement

NHANES protocols were approved by the National Center for Health Statistics Research Ethics Review Board, and participants provided informed consent under NHANES procedures. The planned study is a secondary analysis of de-identified public-use data and does not involve new participant contact (NCHS, 2009).

REFERENCES

[1] Azami, M., Baradaran, H. R., Dehghanbanadaki, H., Kohnepoushi, P., Saed, L., Moradkhani, A., Moradpour, F., & Moradi, Y. (2021). Association of *Helicobacter pylori* infection with the risk of metabolic syndrome and insulin resistance: An updated systematic review and meta-analysis. Diabetology & Metabolic Syndrome, 13, 145. https://doi.org/10.1186/s13098-021-00765-x

[2] Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. Journal of the Royal Statistical Society: Series B (Methodological), 57(1), 289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

[3] Chen, D., Wang, S., Yang, W., Lu, H., & Ren, Q. (2024). Obesity, abdominal obesity, metabolic obesity phenotypes, and *Helicobacter pylori* infection: Results from NHANES 1999–2000. BMC Infectious Diseases, 24, 676. https://doi.org/10.1186/s12879-024-09409-7

[4] Chen, J., Xing, Y., Zhao, L., & Ma, H. (2019). The association between *Helicobacter pylori* infection and glycated hemoglobin A in diabetes: A meta-analysis. Journal of Diabetes Research, 2019, 3705264. https://doi.org/10.1155/2019/3705264

[5] Chen, Y., & Blaser, M. J. (2012). Association between gastric *Helicobacter pylori* colonization and glycated hemoglobin levels. The Journal of Infectious Diseases, 205(8), 1195–1202. https://doi.org/10.1093/infdis/jis106

[6] Gaonkar, A., Zahiruddin, Q. S., Shabil, M., Menon, S. V., Kaur, M., Kumari, M., Sudan, P., Naidu, K. S., Thapliyal, S., Uikey, J., Kathuria, R., Chauhan, S. S., Verma, L., Sidhu, A., Bushi, G., Md Yusoff, R. B., Mehta, R., Satapathy, P., & Sah, S. (2025). Association of *Helicobacter pylori* infection and risk of dyslipidemia: A systematic review and meta-analysis. JGH Open, 9(3), e70128. https://doi.org/10.1002/jgh3.70128

[7] Grad, Y. H., Lipsitch, M., & Aiello, A. E. (2012). Secular trends in *Helicobacter pylori* seroprevalence in adults in the United States: Evidence for sustained race/ethnic disparities. American Journal of Epidemiology, 175(1), 54–59. https://doi.org/10.1093/aje/kwr288

[8] Hooi, J. K. Y., Lai, W. Y., Ng, W. K., Suen, M. M. Y., Underwood, F. E., Tanyingoh, D., Malfertheiner, P., Graham, D. Y., Wong, V. W. S., Wu, J. C. Y., Chan, F. K. L., Sung, J. J. Y., Kaplan, G. G., & Ng, S. C. (2017). Global prevalence of *Helicobacter pylori* infection: Systematic review and meta-analysis. Gastroenterology, 153(2), 420–429. https://doi.org/10.1053/j.gastro.2017.04.022

[9] Jeon, C. Y., Haan, M. N., Cheng, C., Clayton, E. R., Mayeda, E. R., Miller, J. W., & Aiello, A. E. (2012). *Helicobacter pylori* infection is associated with an increased rate of diabetes. Diabetes Care, 35(3), 520–525. https://doi.org/10.2337/dc11-1043

[10] Lu, L.-J., Hao, N.-B., Liu, J.-J., Li, X., & Wang, R.-L. (2018). Correlation between *Helicobacter pylori* infection and metabolic abnormality in general population: A cross-sectional study. Gastroenterology Research and Practice, 2018, 7410801. https://doi.org/10.1155/2018/7410801

[11] Lumley, T. (2004). Analysis of complex survey samples. Journal of Statistical Software, 9(8), 1–19. https://doi.org/10.18637/jss.v009.i08

[12] Malfertheiner, P., Megraud, F., Rokkas, T., Gisbert, J. P., Liou, J.-M., Schulz, C., Gasbarrini, A., Hunt, R. H., Leja, M., O'Morain, C., Rugge, M., Suerbaum, S., Tilg, H., Sugano, K., & El-Omar, E. M. (2022). Management of *Helicobacter pylori* infection: The Maastricht VI/Florence consensus report. Gut, 71(9), 1724–1762. https://doi.org/10.1136/gutjnl-2022-327745

[13] Matthews, D. R., Hosker, J. P., Rudenski, A. S., Naylor, B. A., Treacher, D. F., & Turner, R. C. (1985). Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia, 28(7), 412–419. https://doi.org/10.1007/BF00280883

[14] National Center for Health Statistics. (2009). NHANES 1999-2000: Demographic variables & sample weights (DEMO). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/DEMO.htm

[15] National Center for Health Statistics. (n.d.-a). NHANES 1999-2000: Alcohol use (ALQ). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/ALQ.htm
[16] National Center for Health Statistics. (n.d.-b). NHANES 1999-2000: Body measures (BMX). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/BMX.htm
[17] National Center for Health Statistics. (n.d.-c). NHANES 1999-2000: Cholesterol - LDL & triglycerides (LAB13AM). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/LAB13AM.htm
[18] National Center for Health Statistics. (n.d.-d). NHANES 1999-2000: Cholesterol - total & HDL (LAB13). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/LAB13.htm
[19] National Center for Health Statistics. (n.d.-e). NHANES 1999-2000: C-reactive protein and *Helicobacter pylori* (LAB11). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/LAB11.htm
[20] National Center for Health Statistics. (n.d.-f). NHANES 1999-2000 data documentation, codebooks, and frequencies. Centers for Disease Control and Prevention. https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?BeginYear=1999
[21] National Center for Health Statistics. (n.d.-g). NHANES 1999-2000: Diabetes questionnaire (DIQ). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/DIQ.htm
[22] National Center for Health Statistics. (n.d.-h). NHANES 1999-2000: Glycohemoglobin (LAB10). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/LAB10.htm
[23] National Center for Health Statistics. (n.d.-i). NHANES 1999-2000: Plasma fasting glucose, serum C-peptide & insulin (LAB10AM). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/LAB10AM.htm
[24] National Center for Health Statistics. (n.d.-j). NHANES 1999-2000: Physical activity (PAQ). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/PAQ.htm
[25] National Center for Health Statistics. (n.d.-k). NHANES 1999-2000: Smoking - cigarette use (SMQ). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/SMQ.htm
[26] National Center for Health Statistics. (n.d.-l). NHANES 1999-2000: Standard biochemistry profile (LAB18). Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/1999/DataFiles/LAB18.htm
[27] Qin, Z., Fang, Y., Liu, Y., Zhang, L., Zhang, R., & Zhang, S. (2025). Association between Hp infection and serum uric acid to high-density lipoprotein cholesterol ratio in adults. Frontiers in Medicine, 12, 1509269. https://doi.org/10.3389/fmed.2025.1509269
[28] Shimamoto, T., Yamamichi, N., Gondo, K., Takahashi, Y., Takeuchi, C., Wada, R., Mitsushima, T., & Koike, K. (2020). The association of *Helicobacter pylori* infection with serum lipid profiles: An evaluation based on a combination of meta-analysis and a propensity score-based observational approach. PLOS ONE, 15(6), e0234433. https://doi.org/10.1371/journal.pone.0234433
[29] Upala, S., Jaruvongvanich, V., Riangwiwat, T., Jaruvongvanich, S., & Sanguankeo, A. (2016). Association between *Helicobacter pylori* infection and metabolic syndrome: A systematic review and meta-analysis. Journal of Digestive Diseases, 17(7), 433–440. https://doi.org/10.1111/1751-2980.12367
[30] von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., & Vandenbroucke, J. P. (2007). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. The Lancet, 370(9596), 1453–1457. https://doi.org/10.1016/S0140-6736(07)61602-X
[31] Watanabe, J., & Kotani, K. (2022). The effect of *Helicobacter pylori* eradication on C-reactive protein: Results from a meta-analysis. Archives of Medical Science, 18(4), 958–964. https://doi.org/10.5114/aoms/130288
[32] Zeng, J., Yang, S., Jian, J., Zhu, M., Ni, J., & Zhang, M. (2026). The association between red blood cell distribution width-to-albumin ratio and *Helicobacter pylori* seropositivity in U.S. adults: An observational study from NHANES 1999–2000 with external validation. Frontiers in Nutrition, 13, 1781850. https://doi.org/10.3389/fnut.2026.1781850