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STUDY OF THE CORRELATION BETWEEN HELICOBACTER PYLORI INFECTION AND URIC ACID

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Article Info

Abstract

This study examines the intricate relationship between Helicobacter pylori (H. pylori) infection and elevated uric acid levels, investigating their combined impact on metabolic pathways and the development of chronic diseases. H. pylori, notable for its colonization of the stomach lining, is closely associated with gastritis and peptic ulcers due to its production of urease, which alters the gastric environment, potentially leading to inflammation and ulcers. Various demographic factors, including age, race, ethnicity, and socioeconomic status, contribute to the rates of H. pylori infection across diverse populations. On the other hand, uric acid, a byproduct of purine metabolism, plays a critical role in numerous physiological processes. Dysregulation of uric acid levels, whether from impaired renal function or increased production, has been linked to conditions such as gout, kidney stones, and metabolic syndrome. This investigation delves into the mechanisms through which H. pylori infection and chronic inflammation influence uric acid metabolism. Chronic inflammation may lead to elevated purine production and hinder the excretion of uric acid by the kidneys. Furthermore, immune cell activity and tissue breakdown contribute to increased availability of uric acid precursors. Elevated uric acid levels have been associated with an increased risk of cardiovascular diseases, metabolic syndrome, and kidney disease, thereby posing significant health risks. Additionally, this study explores the potential link between elevated uric acid and insulin resistance, a known precursor to type 2 diabetes and cardiovascular diseases. Insights into the disruption of insulin signaling pathways and mitochondrial function shed light on the intricate interplay between H. pylori infection, uric acid levels, and metabolic dysregulation. Our study comprised of 249 patients out of which 140 were tested positive for H. Pylori. Among those positive tested patients, 46 were found to have elevated uric acid levels in their blood. This showed the clear correlation of the two and that H. pylori is capable of increasing uric acid levels in the body.

Keywords:

Helicobacter pylori, uric acid; chronic inflammation; metabolic syndrome; insulin resistance; purine metabolism; renal function; cardiovascular disease.

INTRODUCTION

Helicobacter pylori (H. pylori) is a bacterium renowned for its ability to colonize the stomach lining, often leading to gastrointestinal ailments such as gastritis and peptic ulcers. The discovery of H. pylori's role in gastric pathologies, recognized by the Nobel Committee's award to Barry Marshall and Robin Warren in 2005, marked a significant advancement in understanding digestive health. This bacterium's adaptation to the acidic gastric environment, facilitated by urease production, alters the stomach's protective mechanisms, making it susceptible to inflammation and injury. Various demographic factors, including age and race, influence susceptibility to H. pylori infection, highlighting the complex interplay between biological predisposition and environmental influences.

Concurrently, uric acid, a metabolic byproduct of purine breakdown, holds crucial physiological functions in the human body. However, dysregulation of uric acid levels, whether due to overproduction or impaired renal excretion, poses significant health risks. Elevated uric acid levels are commonly associated with conditions such as gout and kidney stones. Moreover, emerging research suggests a potential link between elevated uric acid and broader metabolic disturbances, including insulin resistance and cardiovascular diseases. (1)

H. pylori Infection and Uric Acid Metabolism

The impact of H. pylori infection on uric acid metabolism constitutes a multifaceted process with far-reaching implications for health. Chronic inflammation induced by H. pylori infection can disrupt purine metabolism, leading to increased uric acid precursor availability. Moreover, the bacterium's influence on gastric mucosal integrity can compromise renal function, affecting uric acid excretion. Iscan et al. (1997) highlight the role of inflammation in impairing renal uric acid handling, underscoring the intricate relationship between H. pylori-induced inflammation and uric acid homeostasis.

In addition to renal dysfunction, immune cell-mediated tissue breakdown contributes to elevated uric acid levels in the context of H. pylori infection. Macrophages, activated during inflammation, release substances that promote purine breakdown, thereby elevating uric acid production. These processes collectively underscore the role of chronic inflammation in disrupting uric acid metabolism and promoting its accumulation in the bloodstream. (1)

Implications for Metabolic and Chronic Diseases

Elevated uric acid levels, often observed in the context of H. pylori infection and chronic inflammation, are associated with an increased risk of metabolic and chronic diseases. The intricate interplay between uric acid and insulin resistance is particularly noteworthy. High uric acid levels can induce inflammation and oxidative stress, impairing insulin signaling pathways crucial for glucose metabolism. Disruption of insulin signaling through pathways such as PI3K/Akt can lead to insulin resistance, a precursor to type 2 diabetes and cardiovascular diseases. (2)

Furthermore, the activation of xanthine oxidase by elevated uric acid levels contributes to increased uric acid production, perpetuating a cycle of metabolic dysregulation. Mitochondrial dysfunction, influenced by high uric acid levels, further exacerbates insulin resistance and glucose metabolism impairment.

Notably, individuals with uric acid-induced diabetes have tested positive for H. pylori infection, suggesting a potential synergistic relationship between these factors in metabolic disturbances. (2)

Around 25-30% of the world population is affected by Non-alcoholic fatty liver disease NAFLD. NAFLD can lead to diseases such as NASH, liver fibrosis, and cirrhosis, affecting mortality and morbidity rates in masses. It was found out that patients who test positive for H. Pylori are often diagnosed with a fatty liver. Studies indicate that the infection of H. pylori speeds up the progression of a fatty liver, and for the disease to be cured, the infection must be treated first. People with the hepatitis C virus have been found to have a higher risk of cirrhosis if they also have an H. pylori infection. Gamma-glutamyl transferase (GGT), Alanine and aspartate transaminase, and alkaline phosphatase (ALT and AST and ALP) are commonly used serum enzymes in liver function testing. Elevated levels of serum ALT, which is a marker for liver damage, have been linked to various risk factors such as diabetes, metabolic syndrome, cardiovascular diseases, high blood sugar, obesity, abnormal lipid levels, raised blood pressure, and fatty liver disease (NAFLD). (3)

There's probably an interconnection between raised blood pressure, cardiovascular diseases, NAFLD, and metabolic syndrome. This is because these conditions have been linked to serum uric acid and liver enzymes, specifically ALT and GGT. So, these parameters are likely to be interconnected. (4)

Recent scientific research has revealed a compelling and robust correlation between the concentration of serum uric acid and the prevalence of nonalcoholic fatty liver disease in a multitude of individuals. This noteworthy connection strongly suggests that elevated levels of serum uric acid can indeed play a pivotal role in the initiation and development of NAFLD. (4)

In conclusion, this thesis elucidates the complex interplay between H. pylori infection and elevated uric acid levels, highlighting their combined impact on metabolic pathways and the development of chronic diseases. Chronic inflammation induced by H. pylori infection disrupts uric acid metabolism, leading to its accumulation and associated health risks. The link between elevated uric acid and insulin resistance underscores the broader implications of this relationship for metabolic syndrome, type 2 diabetes, and cardiovascular diseases. Future research should delve deeper into the molecular mechanisms underlying these interactions to develop targeted therapeutic interventions addressing both H. pylori infection and uric acid-related metabolic disturbances. (5)

MATERIALS AND METHODS

This research entails an observational study, with a focus on selecting patients exhibiting diversity in demographics, including age and medical conditions. Rigorous measures were taken to uphold patient's confidentiality, privacy, and ethical considerations throughout the study. A group of patients were enrolled, with their participation contingent upon informed consent. The investigation was centered on measuring anti-*H. pylori* IgG levels utilizing the ELISA test. Subsequently, patients were categorized into two groups:

1. H. pylori-infected group (HP+), denoting the positive group.
2. H. pylori-negative group (HP-), functioning as the control group.

To mitigate confounding variables, patients taking uric acid-lowering medications and those with underlying disorders such as diabetes, renal failure, cirrhosis, cardiovascular diseases, respiratory deficiency, and cancer were excluded from the study.

H. pylori Detection: Elisa Technique was used for H. pylori detection. Kit manufacturer's instructions were followed for sample preparation and detection.

Preparation of Samples

Stool samples were collected and stored at temperatures below 0°C to preserve the stability of the H. pylori antigen. Upon thawing, the samples were homogenized to achieve uniformity. A microplate, pre-coated for the assay, was allowed to reach room temperature. The wells of the microplate were washed with a washing buffer to eliminate any unbound substances or debris. To prevent non-specific antibody binding, the wells were then blocked with a blocking buffer. Stool samples were diluted in a dilution buffer to ensure the antigen concentration fell within the assay's detection range. The appropriately labeled diluted samples were added to the wells. The microplate was incubated at a controlled temperature for a specified period to enable antigen-antibody binding. Following incubation, the wells were washed several times with washing buffer to remove any remaining unbound material and minimize the risk of contamination.

Secondary Antibody Incubation

Enzyme-conjugated secondary antibodies, such as anti-IgG, IgM, or IgA, were introduced into the microplate wells. The microplate was then incubated again to facilitate the binding of the secondary antibodies to any captured H. pylori antigen. After this incubation, the wells were washed to remove any unbound secondary antibodies. A substrate solution, like TMB substrate, was added to the wells, and the microplate was incubated in the dark to allow the enzymatic reaction to take place. The color development in the wells was closely monitored, as the intensity of the color was directly related to the amount of H. pylori antigen present in the samples. After the incubation period, a stop solution, such as sulfuric acid, was added to terminate the enzymatic reaction, changing the color of the reaction mixture. This color change enabled accurate measurement, and the absorbance of each well was recorded at 450 nm using an ELISA plate reader.

- **Data Analysis and Quality Control:**
- The mean absorbance values for triplicate wells of each sample were calculated, and a standard curve was constructed using known concentrations of H. pylori antigen standards. The concentration of H. pylori antigen in each sample was then determined by interpolation from this standard curve. Appropriate positive and negative controls were included in each assay to ensure validity. All reagents and equipment were thoroughly checked to confirm their proper function, and the assay's performance was further validated through parallel testing with other detection methods.
- **Serum Uric Acid Evaluation:**
- The serum analysis method was used to evaluate uric acid levels in the patient's blood.

- **Sample Collection**: A venous blood sample was obtained from the patient and collected into a vacutainer tube without an anticoagulant.
- **Sample Handling**: The blood sample was centrifuged to separate the serum from the cellular components, with the serum then being used for uric acid analysis.
- **Reagent Preparation**: Reagents for the uric acid assay were prepared following the manufacturer's instructions.
- **Calibration**: The uric acid analyzer was calibrated with standards of known concentrations to ensure accurate results.
- **Sample Analysis**: Serum samples were loaded into the uric acid analyzer, which measured absorbance or fluorescence and calculated the uric acid concentration based on a standard curve.
- **Data Interpretation**: Uric acid concentrations were recorded for each sample.
- **Quality Assurance**: Results were carefully reviewed for outliers or discrepancies, and any samples falling outside acceptable ranges were reanalyzed.
- **Reporting**: The results, including patient information and uric acid concentrations, were compiled into a comprehensive report.
- **Clinical Interpretation**: Uric acid levels were interpreted in light of the patient's clinical history, with elevated levels potentially indicating conditions such as gout or kidney disease, and low levels possibly suggesting certain medications or metabolic issues.
- **Consultation**: Results were discussed with the healthcare provider, and any necessary recommendations or follow-up actions were provided.
- **Documentation**: Every step of the analysis process, including instrument calibration, reagent preparation, and quality control, was thoroughly documented to comply with regulatory standards and for future reference.

Data Recording:

All procedures, observations, and results were carefully recorded to ensure thorough evaluation. Accuracy and consistency in data collection were maintained throughout the process.

Table 1: H.pylori infected patients

Summary		
Description	**Numbers**	**Remarks**
Positive Patient	**140**	
Weak Positive Patient	**2**	
Negative Patient	**107**	

Quality Control: SOPs were followed to maintain quality control for all diagnostic tests.

Statistical Analysis: All the data was collected in Excel Sheet and data was arranged according to the date of sampling. All the gathered data was processed in IBM-SPSS Version 22 to check the Statistical Significance.

RESULTS

This research was carried out at Children Hospital, Lahore. A total of 249 patients were tested for Helicobacter Pylori infection and uric acid levels in their bodies. All of the patients were males and there were no such specifications as age , ethnicity etc.

H. Pylori Infected Patients:

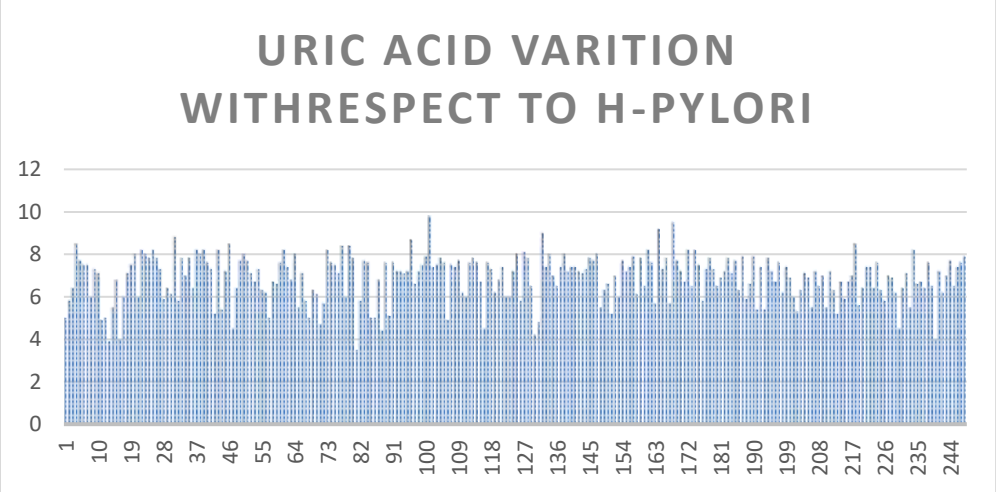
Out of 249 patients, 140 were tested positive for H. Pylori infection, 2 were weakly positive and 107 of them were tested negative for the infection.

The ratio can be seen as follows:

- Positive patients
- Negative patients
- Weakly positive patients

Variation of Uric acid level:

The normal value of uric acid level in males is between 3.40 to 7.20. Variation of uric acid level in both positive and negative patients can be seen as follows:



Out of these both positive and negative patients, 107 were found to have uric acid value higher than 7.2, the normal range. Whereas 142 had normal values of uric acid in their bodies.

Table 2 : uric acid levels in H. pylori infected patients

	Normal uric acid	**High uric acid**
H. pylori patients (positive + negative)	142	107

Variation of Uric Acid in H. pylori Positive Patients:

Furthermore, when Uric acid levels were observed in H. pylori positive patients in only. It was found out that there were a total of 140 positive patients out of which 46 were found to have uric acid levels above the normal range

Table 3: Uric acid levels in positive tested patients:

	Normal uric acid level	**High uric acid level**
H. pylori positive patients	94	46

DISCUSSION

Background on H. pylori Infection

H. pylori infection is a prevalent global health concern, affecting individuals across diverse demographic groups. While the bacterium's pathogenesis is multifaceted, its colonization of the gastric mucosa is a hallmark feature. The production of urease by H. pylori leads to the hydrolysis of urea, generating ammonia and bicarbonate ions, thereby neutralizing gastric acidity. This alteration of the gastric environment promotes bacterial survival and may contribute to the development of gastritis and peptic ulcers. Factors influencing H. pylori infection rates encompass a wide array of variables, including age,

ethnicity, socioeconomic status, and geographic location. Despite advancements in understanding its epidemiology and pathophysiology, the full scope of H. pylori-associated diseases and their interplay with other physiological processes, such as uric acid metabolism, remains incompletely understood.

Uric Acid Metabolism and Health Implications

Uric acid, a final product of purine metabolism, serves as a crucial antioxidant and scavenger of reactive oxygen species. While its physiological functions are diverse and essential, dysregulation of uric acid homeostasis can lead to pathogenic consequences. Elevated uric acid levels, often associated with conditions such as hyperuricemia, predispose individuals to the development of gout, a painful inflammatory arthritis. Moreover, uric acid deposition in joints and tissues can culminate in the formation of monosodium urate crystals, precipitating acute gouty attacks. Beyond its role in gout, elevated uric acid levels have been implicated in the pathogenesis of cardiovascular diseases, renal disorders, and metabolic syndrome. Understanding the intricate regulatory mechanisms governing uric acid metabolism is pivotal for elucidating its broader implications for human health.

Exploring the Correlation between H. pylori Infection and Uric Acid Levels

Our study, conducted at Children's Hospital, Lahore, involved the comprehensive evaluation of 249 male patients for both H. pylori infection and uric acid levels. Detection of H. pylori infection was accomplished through stool samples, while uric acid levels were quantified via blood samples. Among the patients examined, 140 tested positive for H. pylori infection. Notably, 94 of these individuals exhibited normal uric acid levels, whereas 46 presented with elevated levels exceeding the normal range. These findings suggest a potential association between H. pylori infection and perturbations in uric acid metabolism, with implications for the pathogenesis and management of associated disorders. While the precise mechanisms underlying this correlation warrant further investigation, our study underscores the importance of considering microbial influences on metabolic pathways and their implications for disease states.

CONCLUSIONS

The findings of our study offer valuable insights into the complex interplay between H. pylori infection and uric acid metabolism. By elucidating the potential correlation between these factors, we pave the way for future research aimed at unraveling the underlying mechanisms and identifying novel therapeutic strategies. Understanding how H. pylori infection influences uric acid levels may inform more targeted approaches to disease management, ultimately improving patient outcomes and quality of life. Moreover, the implications of our findings extend beyond the realm of gastroenterology, highlighting the interconnectedness of microbial infections and metabolic dysregulation in shaping human health. Continued exploration of this relationship holds promise for advancing our understanding of disease pathogenesis and developing innovative interventions to mitigate its impact.

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