



ABSTRACTS: VOLUME 8, SPECIAL ISSUE {8th Undergraduate Conference}

INVESTIGATING GENETIC POLYMORPHISMS IN TLR GENES AND THEIR ASSOCIATION WITH THE VARIATION OF CLINICAL OUTCOMES OF *HELICOBACTER PYLORI* INFECTION IN HEBRON DISTRICT.

Maya Musleh¹, AbdulMajeed Nasreldeen¹

Supervisor: Dr. AbdulMajeed Nasreldeen¹

¹ Natural Sciences, Al-Quds Bard College, Al-Quds University, Palestine

Abstract

Background: *Helicobacter pylori* is a Gram-negative, flagellated bacterium that colonizes the inner mucus layer of the stomach. It survives the acidic gastric environment and disrupts the protective mucosal lining through the production of virulence factors, leading to common but potentially severe infections such as chronic gastritis, peptic ulcer disease (PUD), and gastric cancer. Single-nucleotide polymorphisms (SNPs) in genes involved in immune regulation, particularly Toll-like receptors (TLRs), may influence host responses to *H. pylori* and contribute to variability in clinical outcomes. The global prevalence of *H. pylori* infection was estimated at 43.9% in 2022, while in the Eastern Mediterranean Region, including Palestine, prevalence ranges from 22% to 87.6%.

Objectives: This study aimed to develop a one-tube next-generation sequencing (NGS) approach for detecting genetic polymorphisms in TLR genes and to investigate their association with susceptibility to *H. pylori* infection and its clinical outcomes in a Palestinian population. It also sought to explore the relationship between host genetic variations and disease severity to support improved diagnostic and preventive strategies.

Methods: A total of 30 oral saliva swab samples were collected and categorized into three groups: 9 patients with severe clinical outcomes, 11 with mild outcomes, and 10 uninfected individuals. Genomic DNA was extracted and amplified targeting TLR polymorphisms (TLR1_rs4833095, TLR4_rs4986790, TLR5_rs5744174, TLR9_rs187084, and TLR10_rs10004195) using multiplex PCR. This was followed by magnetic bead purification, index PCR (barcoding), pooling, additional purification, and NGS analysis. Statistical analysis was conducted to evaluate genotype–phenotype associations.

Results: A statistically significant association was identified between the TLR5_rs5744174 (A>G) polymorphism and infection status and severity. The wild-type AA genotype was associated with increased susceptibility and more severe clinical outcomes, likely due to heightened immune and inflammatory responses. In contrast, the G allele appeared to confer a protective effect, possibly by moderating excessive



immune activation. No significant associations were observed for TLR1 and TLR9 polymorphisms. TLR10 failed to amplify during PCR, and no genotypic variation was detected for TLR4 among participants, leading to its exclusion from final analysis.

Conclusion: This study provides the first comprehensive genetic analysis of TLR polymorphisms associated with *H. pylori* infection in Palestine. The significant association of TLR5_rs5744174 highlights its potential as a host genetic biomarker for susceptibility and disease severity. Additionally, the developed NGS-based assay represents a promising tool for large-scale population screening and personalized risk assessment. Further studies with larger sample sizes are required to validate these findings and clarify underlying mechanisms.

Keywords: *Helicobacter pylori*, Toll-like receptor (TLR), single-nucleotide polymorphism (SNP), next-generation sequencing (NGS), host immune response.