



Investigating the association between IL-20 gene rs2981572 polymorphism and *Helicobacter pylori* induced kidney disorders

Hussein Mahmood Abbas¹, Amer H. Abbas², Yasir B. Fadhil³, Anwar Abed Nasser Dhabaan³, Tahreer Hadi Saleh^{4*}

¹Department of Biology, College of Science, Al-Nahrain University, Baghdad, Iraq.

²Division of Biotechnology, Department of Applied Science, University of Technology, Baghdad, Iraq.3

³Department of Biology, College of Education, Al-Iraqia University, Baghdad, Iraq.

⁴Department of Biology, College of Science, AlMustansiriya University, Baghdad, Iraq.



ARTICLE INFO

Article history

Received 07 February 2025

Received revised 25 February 2025

Accepted 28 February 2025

Available online 1 March 2025

Corresponding Editors

Abas, M. W.

Amiri Fahliyani, S.

Abdullah, B.

Keywords

Chronic inflammation markers, cytokine polymorphism, genetic predisposition, host-pathogen interaction, immune response modulation, renal pathogenesis.

ABSTRACT

Half of the world's population has *Helicobacter pylori* diseases. This study evaluated Iraqi controls and patients to see if rs2981572 interleukin 20 gene polymorphism promotes renal disease. Half of 300 individuals were patients and half were controls in this study. Each participant supplied 8 ml of venous blood, however only 4 ml was immediately placed in EDTA tubes to capture DNA. The two trial groups used a gel tube to coagulate and separate serum for IL-20 measurements. Forward and reverse primers were used to amplify the IL-20 gene and rs2981572 polymorphism using tetra primer amplification refractory mutation. The ELISA test measured IL-20. The Results were shown In relation to rs2981572, the TT genotype was protective (OR = 0.54, 95% CI = 0.34–0.85, P = 0.025) and the TG genotype risky. GG genotype did not increase disease risk (OR = 1.2, 95% CI = 0.50–3.10, P = 0.58). The T and G alleles had substantial protective factors (OR = 0.67, 95% CI = 0.48–0.93) and risk factors (OR=1.49, 95%CI=1.07–2.08) (P = 0.023). We identified a strong link between *H. pylori*-related urological illnesses and rs2981572 polymorphism genotypes and allele frequencies. Both studies estimated IL-20 from whole blood serum. IL-20 levels were significantly higher in cases compared to controls (1348.24 ± 29.09 vs. 812.91 ± 29.63 pg/ml, P = 4.7×10^{-20}). IL-20 was high in 63% of people. The TG genotype and G allele in the rs2981572 polymorphism may be linked to *H. pylori* infections in renal disease patients.

Published by Arab Society for Fungal Conservation

Introduction

Helicobacter pylori is a Gram-negative, microaerophilic bacterium responsible for diseases such as chronic gastritis, gastric cancer, and peptic ulcers (Sun et al., 2023). Remarkably, much literature has emerged confirming the association of these bacteria with causing urological problems which may eventually lead to more severe diseases such as bladder lymphoma (Al-Marhoon, 2008). In

addition, the infection with this bacterium can cause kidney problems, as studies have shown a relationship between these pathogenic bacteria and a number of kidney diseases (Alhoufie et al. 2022). So, the infection via *H. pylori* is now of great medical interest. *H. pylori* infections contribute to both gastrointestinal and extra intestinal disorders. Among the disorders associated with the gastrointestinal tract are gastric adenocarcinoma, and lymphoma, as well as chronic atrophic gastritis and duodenal ulcer. As for the extra

*Corresponding author Email address: dr.tahreer80@uomustansiriya.edu.iq (Tahreer H. Saleh)



intestinal disorders, they include diseases of the blood vessels, respiratory system, liver, skin, and kidneys (Pellicano et al. 2004; Pan et al. 2019) noted that patients with stomach ulcers caused by the bacteria may have kidney damage. This means that the bacteria have been identified as a risk factor contributing to this damage. Several health complications have been linked to this bacterium. *H. pylori* is responsible for nearly 50% of bacterial infections globally, particularly those affecting the gastrointestinal system, this bacterium was linked to the development of cancer, which represents the third leading cause of death globally, so it is a health concern (Ali et al.2024). In addition, gastric cancer is often caused by an infection of *H. pylori* (Usui et al. 2023). Moreover, the most common infections recorded worldwide are those caused by *H. pylori*. Furthermore, epidemiological data have shown that this bacterium may be increasing colorectal cancer as well as gastric cancer, so, *H. pylori* was represented as a risk factor (Ralsler et al.2023). Given the inflammatory nature of *H. pylori* infections, cytokines such as Interleukin 20 play a crucial role in immune responses and disease progression. Therefore, genetic variations in IL-20, such as the rs2981572 polymorphism, may influence susceptibility to kidney disorders. However, there are many reports showed the urinary tract infection caused by different pathogens such as *Pseudomonas aeruginosa* and *Proteus mirabilis* (Bassi, et al., 2024; Abdullah & Al-Rubaii, 2024; Ibrahim & Laftaah 2024; Jalil et al.2023). IL-20 is one of the most important members of the proinflammatory cytokines, besides other proinflammatory cytokines like IL-19, IL-22, IL-24, and IL-26. Each of these immunologically soluble proteins is related to a large family of soluble proteins called IL-10, which are grouped together as a subgroup under the name of IL-20 according to the subunits, receptors, biological functions, and common characteristics; The communication and interaction between epithelial and hematopoietic cells were also facilitated via IL-20 (Rutz et al.2014). IL-20 is also commonly referred to as the IL-20 receptor (IL-20R) due to its ability to communicate via the alpha and beta receptor complex of IL-20, and it can also express the ability to regulate distinct biological and immunological functions, as well as to carry out host defines and tissue homeostasis (Chen et al. 2018). In humans, gene polymorphisms among populations are the most prevalent form of genetic variation. More than 1% of humans show genetic polymorphisms, as opposed to DNA mutations, which appear at much lower rates in a few people. Genetic polymorphisms are considered important among humans because they contribute to differences between them, unlike mutations that can cause a hereditary disease (Chiarella et al. 2023). The general form of human genetic variation was referred to as single nucleotide polymorphisms (SNPs).

These SNPs are located in coding and non-coding proteins of RNA genes, which are classified as functional or neutral. The functional SNPs affect various biological processes, which may confer the risk of huge disorder, while the neutral SNPs have no effect (Ramírez-Bello et al. 2017). Many genetic polymorphisms have been linked as risk factors for disease development, such as renal cell carcinoma (Dhabaan et al. 2024). These studies may clarify the role of genetic polymorphisms in the immune interleukin genes in the development of diseases, especially kidney diseases and their complications, on the other hand, the role of the genetic polymorphism rs20541 in the interleukin 13 gene and its association with one of the most important kidney diseases, renal cell carcinoma (Dhabaan et al. 2024). Also there was an association between genetic polymorphism and urinary tract infections. Previous studies have not extensively focused on the association of the rs2981572 polymorphism in the IL-20 gene under study with health problems that specifically affect the kidney as an important part of the urinary system (Abbas & Al-Mathkhury 2020). Therefore, the aim of the study was carefully chosen to find the relationship and association between this polymorphism and kidney disorders in Iraqi patients infected with *H. pylori*.

Materials and methods

Declaration of ethics

Every participant agreed to give blood samples to the researchers. Per the Declaration of Helsinki, each subject gave their informed approval. The present work was approved by the Ethics Committee of the Baghdad health department, Iraq; the reference number was 485/11-8-2024.

Population samples

This study was approved by the Scientific Research Ethics Committee of Al-Iraqi University. All participants provided informed consent to donate blood samples and share personal information for research purposes. The present study was conducted among one hundred and fifty patients infected with *H. pylori* that represent a case group and one hundred and fifty healthy populations that represent a control group. All cases were diagnosed with kidney disorder in hospitals of the Baghdad governorate, and their ages were distributed between 30 and 45 years, as well as control.

Criteria of Population samples selection

Many criteria were taken into consideration to select the study sample, including age, comorbidities, and geographical area. Regarding age, the ages of the study participants ranged between 30 and 40 years. Moreover, the central geographical area in Iraq represented the study community, and all patient samples were men. The absence

of concomitant diseases was taken into consideration by checking their medical and family histories, as was the absence of any reports indicating that they had other chronic diseases.

Blood collection

A total of 8 ml of venous blood was collected from each participant. Of this, 4 ml was immediately transferred into EDTA tubes for DNA extraction and stored at -20°C until use. The remaining 4 ml was placed in a gel tube for serum isolation to estimate IL-20 levels

Identification of the rs2981572 T/G genetic polymorphism.

DNA extraction

According to the recommendation of Bioneer/Korean manufacturer, the kit of genomic DNA was used to extract the whole genome from peripheral whole blood. DNA quality was assessed using electrophoresis, while DNA concentration and purity were measured using a Nanodrop spectrophotometer. A 260/280 nm absorbance ratio between 1.7 and 1.9 was considered acceptable.

PCR assay

After DNA extraction, the IL-20 gene and rs2981572 polymorphism were explored by a tetra-primer ARMS-PCR assay. Tetra-primer ARMS-PCR was used for both IL-20 gene amplification and rs2981572 polymorphism detection. The two outer forward and reverse primers were used for IL-20 gene amplification, while two inner primers were designed for detecting the T and G alleles of rs2981572 and then forward and reverse primers were used for rs2981572 T/G polymorphism detection.

The gene amplification by PCR

The outer forward and reverse primers listed in Table 1 were used for detection the IL-20 gene. The PCR amplification for the IL-20 gene was achieved in a final volume of 25µl consisting of 10µl of Premix (Bioneer/Korean), 2µl of each primer forward and reverse, 7µl of DNA template, and the remainder of the volume is completed with nuclease-free water. Concerning the amplification conditions of IL-20 gene, the denaturation stage at 95 °C for 5 min represented the initiation stage. After the initiation stage, the second stage of amplification conditions was completed by 35 cycles which included three steps: denaturation, annealing and extension. According to the above stage, the reaction conditions were included 95°C for 30sec, 57°C for 30 sec and 72°C for 30 sec respectively. After these cycles, the extension step was completed, which is the last step at 72°C for 10 mins. The size of IL-20 gene product was 320bp for two outer primers. PCR products were analyzed using 1.5% agarose gel electrophoresis to confirm amplicon size and purity. However, the polymerase chain reaction (PCR) has been widely applied in many domains of Biology, including but not limited to (Al-saidi et al.2022; Jiad et al.2022; Sutan et al. 2023; Al-Dulimi et al. 2023; Bresam et al.2023; Al-Jumaily et al.2023; Mohammed et al. 2024).

rs2981572 polymorphism amplification

With regard to the rs2981572 polymorphism, two inner primers listed in Table 1 were used for the detection of T and G alleles, and the PCR amplification was the same as the IL-20 detection. In the present study, the primers are inserted in Table 1. The primers under study were used according to (Nakhzari Khodakheir et al. 2017).

Table 1 Primer sequences of the IL-20 gene (rs2981572 T/G) using TARMS-PCR

Gene/SNP	Primer sequences 5' → 3'		Size
IL-20 gene	Outer F	ACTCATCAATAATATTTTCATCATATGCT	320
	Outer R	AGTTTTAAGATAAAAATAAATGGGCTG	
rs2981572 T/G	T allele: Inner F	TTGTCATAAGCTTTTAATTCATTCTT	156
	G allele: Inner R	CAAGATAAAAATATTTTAGTGCAATGTC	219

IL-20 estimation

The Human IL-20 ELISA Kit (Biotech/Korea) was used for the estimation of the levels of IL-20 according to manufacturing recommendations. Only 4 ml of peripheral blood was let in a gel tube for a period in order to clot. At 5,000xg for 5 mins, all blood samples were applied in a centrifuge for serum separation. The serum was saved after separation at -20°C, until it was used for measuring the levels of IL-20.

Statistical analysis

Data were analyzed for homogeneity and normal distribution using IBM SPSS version 25.0. Mean ± standard error (SE) was reported for continuous variables. The association between rs2981572 polymorphism and kidney disorders was assessed using Fisher's exact test ($P < 0.05$). The odds ratio and confidence intervals were calculated via WinPepi software. The Hardy-Weinberg equilibrium was utilized to determine the results of preventive and

etioloical fractions. The Winpepi program online was used for genotype and allele frequency analysis.

Results

Gel electrophoresis and PCR results

For the rs2981572 polymorphism, the *T* and *G* allele fragments were amplified via two inner primers. The product sizes of *T* and *G* alleles fragments were 156 and 219 base pairs respectively. Fig 1 reflects the results of two specific bands in the rs2981572 polymorphisms for the control and case groups beside the IL-20 gene. In Table 2, the significant differences of genotypes and allele frequencies for the rs2981572 polymorphism in patients and controls are shown. The Hardy-Weinberg equilibrium (HWE) beside the frequencies of all forms of genotypes

heterozygote and homozygote were in good agreement. Statically, the genotypes distribution and alleles frequencies were analyzed using chi-square analysis. Furthermore, a statistical analysis of the odds ratio (OR) with 95% CI was conducted. Table 2 shows the reported percentages of rs2981572 genotype frequency in the IL-20 gene for both controls and patients in the current study. The findings showed that in the case group, TT genotype was higher in controls (58%) than cases (42%), acting as a protective factor (OR = 0.54, *P* = 0.01). TG genotype was significantly associated with disease risk (OR = 1.9, *P* = 0.025). GG genotype showed no statistical significance as a risk factor (*P* = 0.58). On the other hand, the results in Table 2 showed that the *T* allele was higher than *G* allele in case (58%) and control (67.3%) groups.

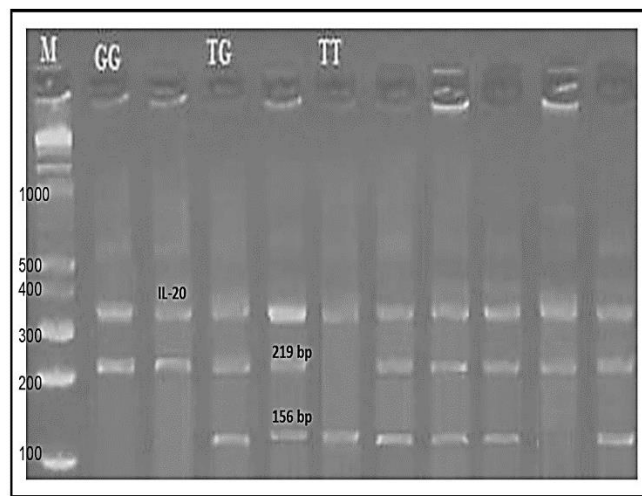


Fig1. The specific band of IL-20 rs2981572 polymorphisms that were found via TARMS-PCR amplification beside the IL-20 gene. 1.5% of gel agarose with 75 voltages for 70min was used in order to run the PCR products. A 100 bp molecular weight DNA marker is shown by the M lane. The fragment sizes of *T* and *G* alleles are shown in lane 1 and lane 4 at 156 bp and 219 bp, respectively.

Table 2 Genotypes frequencies of rs2981572 polymorphisms in both groups in the current study

Genotype	Cases (n=125)				Control (n=125)				OR (95%CI)	RF	<i>P</i>
	Observed No	Excepted %	Observed No	Excepted %	Observed no	Excepted %	Observed no	Excepted %			
TT	63	42%	16.82	33.64%	86	58%	23.12	46.24%	0.54 (0.34 – 0.85)	0.26	0.01
TG	48	32%	24.36	48.7%	30	20%	21.76	43.52%	1.9 (1.11 – 3.18)	0.15	0.025
GG	39	26%	8.82	17.66%	34	22%	5.12	10.24%	1.2 (0.50 - 3.10)	0.04	0.58
Total	150	100	125	100	150	100	50	100			

*Abbreviation: OR= Odds ratio, CI= Confidence Interval, RF=Risk factor, *P* value at 0.05

Table 3 The proportion of allele frequency for the rs2981572 polymorphism in the IL-20 gene

Target Gene	Allele	<i>H. pylori</i> infections Number (%)	Control Number (%)	OR (95%CI)	RF	<i>P</i>
IL-20 gene	<i>T</i>	174 (58%)	202 (67.3%)	0.67 (0.48- 0.93)	0.22	0.023
rs2234671 T/G	<i>G</i>	126 (42%)	98 (32.7%)	1.49 (1.07 - 2.08)	0.14	0.023

The findings of the current work in Table 3 scored the percentage of allele frequency for the rs2981572 polymorphism in the IL-20 gene. Table 3 shows the proportion of allele frequency for the rs2981572 polymorphism in the IL-20 gene, which is the result of the current study. The results of the current work reported a lower frequency proportion of the *G* allele in both cases (42%) and controls (32.7%). With a 95% CI = 1.07 – 2.08

and an OR (1.49) of the *G* allele, the risk factor (0.14) is indicated as significant etiological factor *P*= 0.023. Concerning the *T* allele, the results were reported OR (0.67) with 95% CI = 0.48-0.93, so the risk factor (0.22) has been shown to be a significantly protective factor *P*= 0.023. Based on these results, the development of kidney disorders and *H. pylori* infections is significantly linked to the TG genotype and *G* allele.

Table 4 The percentage of protective and etiological fractions in populations for genotypes and allele frequencies in IL-20 gene (rs2234671 T/G) polymorphism in controls and patients.

Target Gene	Genotypes and alleles	Prevented fraction %	Etiological fraction %
IL-20 gene	TT	26.4%	-
rs2234671 T/G	TG	-	15%
	GG	-	4.2%
	<i>T allele</i>	22.2%	-
	<i>G allele</i>	-	13.9%

Table 4 explains the proportion of prevented and etiological fractions among the population. About the TT genotype and *T* allele, the proportion of prevented fractions in the population was 26.4% and 22.2%, respectively, while the TG genotype and *G* allele showed an association with the development of the risk of *H. pylori* infections of the kidney infections in the Iraqi population. In addition to that, the proportions of the etiological fraction were 52.6% and 52.6% for the TG genotype and *G* allele frequency, respectively. For the GG genotype, the etiological fraction percentage was insignificant, 4.2% of populations.

Determining the IL-20 level

As shown in Fig. 2, the current study's results regarding the estimation of IL-20 levels were significantly higher in cases (1348.24 ± 29.09 pg/ml) than controls (812.91 ± 29.63 pg/ml, *P* = 4.7×10⁻²⁰). About 63% of patients exhibited elevated IL-20 levels. Asterisks are used to indicate the mean value. The upper and lower values are indicated in Fig2 by the ends extending up and down.

The IL-20 levels in patients according to genotypes.

The results in Table 5 explain the significant differences in IL-20 levels between cases and controls according to rs2981572 genotyping. According to the rs2981572 genetic variation genotypes in the IL-20 gene, the results in Table 5 indicated that there were highly significant variations between the IL-20 levels of patients and controls. TT genotype was associated with the highest IL-20 levels (*P* = 7.6×10⁻²⁰).TG and GG genotypes showed lower IL-20 levels but still significantly different from controls. Regarding Table 6, significant differences (*P*= 0.009) were noted in IL-20 levels between patients carrying the dominant TT genotype and the heterozygous TG genotype on the one hand and between the dominant TT homozygous genotype and the recessive GG genotype on the other hand (*P*= 0.02). Besides, the non-significant difference (*P* = 0.9) was noted among patients for the heterozygous TG genotype and recessive GG genotype. Such a result may be suggesting a possible link between the dominant genotype TT and the heterozygous genotype TG in bringing inflammatory cytokines like IL-20 to the site of infection caused by bacterial invasion of kidney tissue. However, much work is needed to prove this link unless there are contradictory studies.

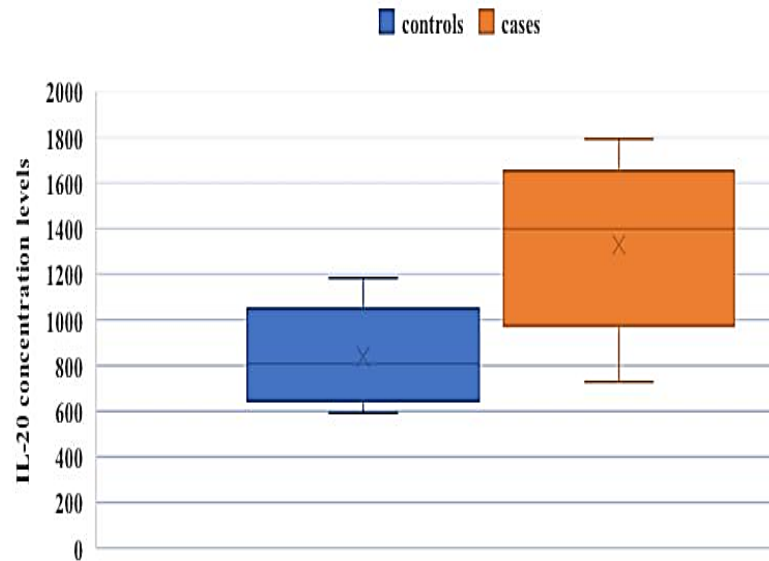


Fig 2. IL-20 concentration box plot for case and control groups. The values for controls and cases are shown by the blue and orange boxes, respectively.

Table 5 The distribution of IL-20 levels by the frequencies of the rs2981572 genotyping alleles in cases as opposed to controls.

Genotypes	IL-20 levels concentration (Mean ± SE)		p-value
	Cases	Control	
TT	(1449.31 ± 28.12)	(801.12 ± 44.66)	7.6×10 ⁻²⁰
TG	(1270.02 ± 58.83)	(817.38 ± 38.19)	1×10 ⁻⁶
GG	(1276.8 ± 64.69)	(841.48 ± 65.77)	0.004

Table 6 The distribution of IL-20 levels in the cases group based on the frequencies of the rs2981572 genotyping allele.

Genotypes	IL-20 levels concentration (Mean ± SE)		p-value
TT vs TG	(1449.31 ± 28.12)	(1270.02 ± 58.83)	0.009
TT vs GG	(1449.31 ± 28.12)	(1276.8 ± 64.69)	0.02
TG vs GG	(1276.8 ± 64.69)	(1276.8 ± 64.69)	0.9

Discussion

To the best of our knowledge, this is the first study in Iraq to investigate the association between rs2981572 polymorphism and *H. pylori* infections in patients with kidney disorders. Our findings align with (Wani et al.2018), who reported a higher frequency of the TT genotype and T allele in cases compared to controls. Similarly, (Nakhzari Khodakheir et al. 2017) found that the TG genotype was prevalent in patients with multiple sclerosis, which supports our findings regarding the TG genotype in kidney disorder patients infected with *H. pylori*. In general, several disorders are caused by *H. pylori*, such as adenocarcinoma, peptic ulcer, lymphoma,

and other problems (Ralsler et al.2023), as well as gastrointestinal diseases (Peek et al. 2002). Furthermore, (Aydogan et al.2012) study showed that infection caused by *H. pylori* bacteria is likely to cause many kidney problems. The infiltration of inflammatory cells with an increase number and proinflammatory cytokines into the site of infections is considered the main characteristic of infection via *H. pylori* (Bagheri et al.2018). The pressure exerted by immune cells such as neutrophils, macrophages, and lymphocytes can limit *H. pylori* infections and proliferation. This pressure naturally generates strong immunity against infection (Oertli et al. 2012). On the other hand, this bacterium has the ability to

modify the host's immunity by changing the functions of immune cells and inhibiting most immune responses that are adverse to its survival (Fan et al.2024). These contradictory mechanisms may be the reason for creating a diversity of immune responses, specifically regarding proinflammatory cytokines. Beside lipopolysaccharide, the other outer membrane proteins OipA, AlpA/B, SabA, and BabA were mediated in adherence of the gastric epithelial cells (Tshibangu-Kabamba et al.2021). The CagA virulence factor, encoded by the Cag pathogenicity island (PAI), manipulates NF- κ B signaling, leading to abnormal cell proliferation and adhesion. These effects may contribute to chronic inflammation, which is implicated in both gastric and extra-gastric diseases, including kidney disorders (Wang et al. 2023). The previous research indicates that a number of renal disorders are associated with *H. pylori*. The bacterial cytotoxin-associated gene *CagA* has the ability to increase serum IgA1 secretion and is considered one of the most important potential causes of kidney disease. The current study provided an explanation of its importance through the treatment of the bacteria that cause stomach ulcers, as continued infection with the bacteria may cause the transmission of infection to the kidneys and thus cause chronic kidney disease (Pan et al.2019). Moreover, fundamental investigations (Yang et al.2014) and clinical evidence (Lin et al.2015) suggest that *H. pylori* infection is likely linked to chronic damage to the renal system. The link between an *H. pylori* infection and subsequent risk of kidney failure in end stage was documented by (Lin et al.2015). Additionally, Gong et al. (2015) confirm that both acute and chronic *H. pylori* infections will change the serum levels of white blood cells, CD4+ T cells, low-density lipoprotein, and high-density lipoprotein, which are indicators of renal diseases. Chronic inflammation is maintained by *H. pylori* virulence factors, which not only contribute to the development of inflammatory reactions but also regulate and control them. The virulence factors of *H. pylori* allow the bacteria to colonize and survive, which further evades the immune system and eventually causes premalignant changes. An extended complex of mechanisms displayed by *H. pylori* modifies host cellular responses and signaling pathways (Baj et al.2020). In some cases, host factors like genetic polymorphisms and environmental influences may augment the colonization of *H. pylori*, which leads to susceptibility to related diseases (Miftahussurur & Yamaoka, 2015. According to a study by (Hussein et al.2010), the virulent *H. pylori* strains induce inflammation by activating mononuclear inflammatory cells and epithelial cells via encoded proteins. The spiral shape of the bacteria may also play a role in its penetration into epithelial cells and facilitate the colonization process (Constantino et al.2016). The

stimulation of the immune response resulting from bacterial infection is due to the nature of the bacterial cell wall structure, where the presence of lipopolysaccharide facilitates the process of bacterial attachment to the surface of the glycoprotein of macrophages that leads to the stimulation of NF- κ B, which seems to stimulate the activation of inflammatory cytokines (Ciesielska et al.2021). The stimulating of inflammatory cytokines is important in protecting against pathogens, such as IL-20, as it works to protect epithelial surfaces from pathogens (Logsdon et al.2012). According to reports, numerous cytokine functions of the IL-20 subfamily at epithelial location, aid in wound healing and having anti-inflammatory properties when bacteria are present (Gough et al.2017). The chronic inflammation may be caused by a long-term bacterial infection, which encourages the production of proinflammatory cytokines. One of these cytokines is IL-20. This is due to its ability to be produced by immune and epithelial cells as well, which enhances its role in inducing chronic inflammation despite its immune role (Chen, 2018). Usually, it is observed that *H. pylori* colonization results in a potent systemic immune response, generating an environment that is persistently inflammatory (kim et al.2009). There are many antigens that bacteria produce and express genetically, including Lewis (Le) antigens. These are antigens that are also expressed in the epithelial cells of the host stomach. Therefore, the molecular mimicry of bacteria for this type of antigens and its expression in bacteria may provide a molecular mimic to prevent the host immune simulation against bacteria. In addition, the expression of cytotoxic-associated gene *A* can also stimulate inflammatory cytokines and enhance bacterial motility. Moreover, the production of glycoproteins also protects bacteria from immunological products that are toxic to bacteria and also potentially through molecular mimicry (Lee et al.2006). This is one of the most important mechanisms to help in adhesion, colonization, and perhaps tissue invasion without being exposed to the host's immune defenses due to this simulation. Accordingly, treating bacteria early may prevent many related health problems, such as stomach problems, bacterial infections, and their negative impact on kidney function later on, in addition to other problems related to stomach ulcers that negatively affect the entire digestive system. Moreover, this study is not without a set of challenges, as it initially included a study community that was limited to one population, a limited number of patients, and a specific geographical area. Perhaps these circumstances are among the most important determinants that may not reflect many facts about the association of the disease with the genetic polymorphism under study. Genetic studies are useful in determining future risks, which can identify potential problems in the population.

Many diseases are linked to heredity, which may be affected by many factors, such as bacterial and viral infections and other related antigens on the one hand, and on the other hand, other stimuli through which genetic genes can be stimulated, which are linked to chronic, and autoimmune diseases, as well as the other disorders, and much literature have mentioned these facts in more detail. Accordingly, more future molecular studies related to this study may be helpful in proving the association of the rs2981572 genetic polymorphism with kidney disease patients. Notably, highlighting such studies could be crucial in the future, particularly for individuals with kidney failure, which may be a logical reason for kidney transplantation. It is known that kidney transplantation requires tissue compatibility, which determines the possible immune responses. So, tissue compatibility may not be the only problem that patients challenge during kidney transplantation. Their genetic factors may also be a problem, as they may either protect against or cause these disorders. This means that even if the kidney transplantation works, the patient may still experience possible disorders because of other genetic factors, not just the tissue compatibility complex (MHC).

Conclusion:

Our findings indicate that approximately 63% of patients exhibited significantly elevated IL-20 levels compared to the control group. Additionally, the data suggest a potential association between *H. pylori* infections and the TG genotype of the rs2981572 polymorphism in the IL-20 gene, particularly with the *G* allele. However, further studies with larger sample sizes are necessary to validate these findings.

Conflict of interest

All authors declare that they have no known financial interests.

References

Abbas HM, Al-Mathkhury HJ. (2020). Association between the rs2234671 polymorphism and the risk of recurrent urinary tract infections in Iraqi women. *Meta Gene*, 26:100763.

Abdullah MM, AL-Rubaii BA. (2024). Effect of *Lactobacillus supernatant* on swarming-related gene expression in *Proteus mirabilis* isolated from urinary tract infections. *Ukrainian Journal of Nephrology and Dialysis*, 84(4):39-48.

Al-Dulimi AG, Naema AF, Zedan ZK, Mohammed IH, Jabar AM, Abdulateef MH. RGD-coupled gold nanoparticles initiate apoptosis in human cancer cells.

InAIP Conference Proceedings 2023 Mar 31 (Vol. 2475, No. 1). AIP Publishing.

Alhoufie ST, Ibrahim NA, Alhhazmi AA, Makhdoom HM, Ali HM, Hemeg HA, Almutawif YA, Mahallawi WH, Alfarouk KO. (2022). Acute *Helicobacter pylori* Infection Prevalence Among Renal Failure Patients and Its Potential Roles with Other Chronic Diseases: A Retrospective Cohort Study. *Infection and Drug Resistance*, 15:6589–6599

Ali A, AlHussaini KI. (2024). *Helicobacter pylori*: A Contemporary Perspective on Pathogenesis, Diagnosis and Treatment Strategies. *Microorganisms*. 2024; 12(1):222.

Al-Jumaily RM, AL-Sheakli II, Muhammed HJ, Al-Rubaii BA. (2023). Gene expression of Interleukin-10 and Foxp3 as critical biomarkers in rheumatoid arthritis patients. *Biomedicine*, 43(4):1183-7.

Al-Marhoon MS. (2008). Is there a role for *Helicobacter pylori* infection in urological diseases? *Urology Journal*, 5(3):139-143.

Al-saidi M, Al-Bana RJ, Hassan E, Al-Rubaii BA. (2022). Extraction and characterization of nickel oxide nanoparticles from Hibiscus plant using green technology and study of its antibacterial activity. *Biomedicine*, 42(6):1290-1295.

Aydogan T, Ulas T, Selcoki Y, Alkan R, Yilmaz OC, Yalcin KS, Inan O, Dal MS, Turkay C. (2012). Effects of *Helicobacter pylori* eradication on proteinuria: a prospective study. *Wiener Klinische Wochenschrift*, 124(7-8):241-244.

Bagheri N, Salimzadeh L, Shirzad H. (2018). The role of T helper 1-cell response in *Helicobacter pylori*-infection. *Microbial pathogenesis*, 123:1-8.

Baj J, Forma A, Sitarz M, Portincasa P, Garruti G, Krasowska D, Maciejewski R. (2020). *Helicobacter pylori* Virulence Factors-Mechanisms of Bacterial Pathogenicity in the Gastric Microenvironment. *Cells*, 10(1):27.

Bassi AG, Al-Rubaii BA. (2024). Detection of pyocin S and the effects of *lactobacillus acidophilus* cell-free supernatants on multi-drug resistant *Pseudomonas aeruginosa* isolated from patients of Baghdad Hospitals. *Journal of Communicable Diseases*, 56(1):135-144

Bresam S, Alhumairi RM, Hade IM, Al-Rubaii BA. (2023). Genetic mutation rs972283 of the KLF14 gene and the incidence of gastric cancer. *Biomedicine*, 43(4):1256-60.

Chen J, Caspi RR, Chong WP. (2018). IL-20 receptor cytokines in autoimmune diseases. *Journal of leukocyte biology*, 104(5):953-959.

Chiarella P, Capone P, Sisto R. (2023). Contribution of Genetic Polymorphisms in Human

- Health. *International Journal of Environmental Research and Public Health*, 20(2):912.
- Ciesielska A, Matyjek M, Kwiatkowska K. (2021). TLR4 and CD14 trafficking and its influence on LPS-induced pro-inflammatory signaling. *Cellular and molecular life sciences*, 78:1233-1261.
- Constantino MA, Jabbarzadeh M, Fu HC, Bansil R. (2016). Helical and rod-shaped bacteria swim in helical trajectories with little additional propulsion from helical shape. *Science Advances*, 2(11):e1601661.
- Dhabaan AA, Abbas HM, Muhammed HJ, Saleh TH. (2024). Identification of the IL-13 gene rs20541 single nucleotide polymorphism and its association with renal cell carcinoma in Iraqi patients. *Ukrainian Journal of Nephrology and Dialysis*, 83(3):41-50.
- Fan J, Zhu J, Xu H. (2024). Strategies of *Helicobacter pylori* in evading host innate and adaptive immunity: insights and prospects for therapeutic targeting. *Frontiers in Cellular and Infection Microbiology*, 14:1342913.
- Gong Y, Wei W, Jingwei L, Nannan D, Yuan Y. (2015). *Helicobacter pylori* infection status correlates with serum parameter levels responding to multi-organ functions. *Digestive diseases and sciences*, 60:1748-1754.
- Gough P, Ganesan S, Datta SK. (2017). IL-20 signaling in activated human neutrophils inhibits neutrophil migration and function. *The Journal of Immunology*, 198(11):4373-82.
- Hussein NR, Argent RH, Marx CK, Patel SR, Robinson K, Atherton JC. (2010). *Helicobacter pylori* dupA is polymorphic, and its active form induces proinflammatory cytokine secretion by mononuclear cells. *The Journal of infectious diseases*, 202(2):261-269.
- Ibrahim GJ, Laftaah BA. (2024). The efficiency of certain amino acids in regulating chABC1 gene expression in *Proteus mirabilis*. *Iraqi Journal of Science*, 65(9):4983-4992.
- Jalil IS, Mohammad SQ, Mohsen AK, Al-Rubaii BA. (2023). Inhibitory activity of *Mentha spicata* oils on biofilms of *Proteus mirabilis* isolated from burns. *Biomedicine*, 43(02):748-52.
- Jiad AL, Ismael MK, Salih TA, Malik SN, Al-Rubaii BA. (2022). Genotyping and evaluation of interleukin-10 and soluble HLA-G in abortion due to toxoplasmosis and HSV-2 infections. *Annals of parasitology*. 2022; 68(2):385–390
- Kim KK, Kim HB. (2009). Protein interaction network related to *Helicobacter pylori* infection response. *World journal of gastroenterology: WJG*, 15(36):4518.
- Lee HS, Choe G, Kim WH, Kim HH, Song J, Park KU. (2006). Expression of Lewis antigens and their precursors in gastric mucosa: relationship with *Helicobacter pylori* infection and gastric carcinogenesis. *The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland*, 209(1):88-94.
- Lin SY, Lin CL, Liu JH, Yang YF, Huang CC, Kao CH. (2015). Association between *Helicobacter pylori* infection and the subsequent risk of end-stage renal disease: a nationwide population-based cohort study. *International Journal of Clinical Practice*, 69(5):604-610
- Logsdon NJ, Deshpande A, Harris BD, Rajashankar KR, Walter MR. (2012). Structural basis for receptor sharing and activation by interleukin-20 receptor-2 (IL-20R2) binding cytokines. *Proceedings of the National Academy of Sciences*, 109(31):12704-12709.
- Miftahussurur M, Yamaoka Y. (2015). *Helicobacter pylori* virulence genes and host genetic polymorphisms as risk factors for peptic ulcer disease. *Expert review of gastroenterology and hepatology*, 9(12):1535-1547.
- Mohammed RA, Al-Asady ZT, Frayyeh MJ, Alrubaii BA. (2024). The influence of radiotherapy exposure on anti-TPO Ab, anti-Tg Ab, anti-nuclear Ab, anti-DSA Ab and complete blood markers in hospital physician workers in Nuclear Baghdad Hospital. *Opera Medica et Physiologica*, 11(2):5-15.
- Nakhzari Khodakheir T, Pourtalebi-Firoozabadi A, Sangtarash MH, Nikraves A. (2017). Association between Interleukin-19 (IL-19) and Interleukin-20 (IL-20) Genes Polymorphisms with Multiple Sclerosis in an Iranian Population. *Gene Cell Tissue*, 4(2):e11957.
- Oertli M, Sundquist M, Hitzler I, Engler DB, Arnold IC, Reuter S, Maxeiner J, Hansson M, Taube C, Quiding-Järbrink M, Müller A. (2012). DC-derived IL-18 drives Treg differentiation, murine *Helicobacter pylori*-specific immune tolerance, and asthma protection. *The Journal of clinical investigation*, 122(3):1082-96.
- Pan W, Zhang H, Wang L, Zhu T, Chen B, Fan J. (2019). Association between *Helicobacter pylori* infection and kidney damage in patients with peptic ulcer. *Renal failure*, 41(1):1028-1034.
- Peek RM Jr, Blaser MJ. (2002). *Helicobacter pylori* and gastrointestinal tract adenocarcinomas. *Nature Reviews Cancer*, 2(1):28-37.
- Pellicano R, Mazzaferro V, Grigioni WF, Cutufia MA, Fagoonee S, Silengo L, Rizzetto M, Ponzetto A. (2004). *Helicobacter* species sequences in liver

samples from patients with and without hepatocellular carcinoma. *World Journal of Gastroenterology*. 10(4):598-601.

- Ralser A, Dietl A, Jarosch S, Engelsberger V, Wanisch A, Janssen KP, Middelhoff M, Vieth M, Quante M, Haller D, Busch DH, Deng L, Mejías-Luque R, Gerhard M. (2023). *Helicobacter pylori* promotes colorectal carcinogenesis by deregulating intestinal immunity and inducing a mucus-degrading microbiota signature. *Gut*, 72(7):1258-1270.
- Ramírez-Bello J, Jiménez-Morales M.(2017). Functional implications of single nucleotide polymorphisms (SNPs) in protein-coding and non-coding RNA genes in multifactorial diseases. *Gaceta medica de Mexico*, 153(2):238-250.
- Rutz S, Wang X, Ouyang W. (2014).The IL-20 subfamily of cytokines--from host defence to tissue homeostasis. *Nature Reviews Immunology*, 14(12):783-95.
- Sultan RS, Al Khayali BD, Abdulmajeed GM, Al-Rubaii BA. (2023). Exploring small nucleolar RNA host gene 3 as a therapeutic target in breast cancer through metabolic reprogramming. *Opera Medica et Physiologica*, 10(4):36-47.
- Sun Q, Yuan C, Zhou S, Lu J, Zeng M, Cai X and Song H. (2023). *Helicobacter pylori* infection: a dynamic process from diagnosis to treatment. *Frontiers in cellular and infection microbiology*, 13:1257817.
- Tshibangu-Kabamba E, Yamaoka Y. (2021). *Helicobacter pylori* infection and antibiotic resistance - from biology to clinical implications. *Nature Reviews Gastroenterology & Hepatology*, 18(9):613–629.
- Usui Y, Taniyama Y, Endo M, Koyanagi YN, Kasugai Y, Oze I, Ito H, Imoto I, Tanaka T, Tajika M, Niwa Y, Iwasaki Y, Aoi T, Hakozaiki N, Takata S, Suzuki K, Terao C, Hatakeyama M, Hirata M, Sugano K, Yoshida T, Kamatani Y, Nakagawa H, Matsuda K, Murakami Y, Spurdle AB, Matsuo K, Momozawa Y. (2023). *Helicobacter pylori*, Homologous-Recombination Genes, and Gastric Cancer. *New England Journal of Medicine*. *New England Journal of Medicine*, 388(13):1181-1190.
- Wang X, Gong Y, He L, Zhao L, Wang Y, Zhang J, Cui L. (2023). Clinical relevance and distribution of *Helicobacter pylori* virulence factors in isolates from Chinese patients. *Annals of Translational Medicine*, 11(8):301.
- Wani A, Ahmad BG, Akhtar T, Narang T, Kaur R. (2018). Association of proinflammatory cytokine IL-20 gene polymorphism with psoriasis in north Indian population. *Egyptian Journal of Medical Human Genetics*, 19(3):201-205.
- Yang M, Li FG, Xie XS, Wang SQ, Fan JM. (2014). CagA, a major virulence factor of *Helicobacter pylori*, promotes the production and under glycosylation of IgA1 in DAKIKI cells. *Biochemical and Biophysical Research Communications*, 444(2):276-281.