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Review Article

The Role of IL-6 in the Relationship Between Peptic Ulcer Disease and Depression: A Case-Control Study

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Abstract

Peptic Ulcer Disease (PUD) is a localized gastrointestinal inflammatory disorder characterized by mucosal damage and is increasingly recognized as being influenced by both physiological and psychological stressors. Interleukin-6 (IL-6), a pleiotropic pro-inflammatory cytokine, serves as an important mediator of inflammatory responses and may contribute to the interaction between gastrointestinal and psychological disorders. This study aimed to investigate the relationship between PUD and depression by evaluating the role of IL-6 as a potential underlying inflammatory mechanism. A case-control study was conducted involving 50 patients diagnosed with peptic ulcer disease by endoscopy and 50 healthy control subjects. Depression was diagnosed by a clinical psychologist, and its severity was assessed using the Patient Health Questionnaire-9 (PHQ-9). Serum IL-6 levels were measured using enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed using Student's t-test and one-way analysis of variance (ANOVA). The results showed that serum IL-6 levels were significantly higher in PUD patients than in healthy controls, increasing from 96.22 ± 16.16 pg/mL in the control group to 306.85 ± 39.28 pg/mL in the PUD group ($p < 0.001$). These findings indicate a strong association between PUD and systemic inflammation. Elevated serum IL-6 levels support its potential role as a key mediator in the gut–brain axis, linking gastrointestinal inflammation with psychological distress. Therefore, IL-6 may serve as a promising biomarker for understanding the inflammatory mechanisms underlying the association between peptic ulcer disease and depression.

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1. INTRODUCTION

Peptic ulcer disease (PUD) is a common gastrointestinal disorder driven by an imbalance between mucosal defensive factors and aggressive agents, primarily exacerbated by *Helicobacter pylori* infection and non-steroidal anti-inflammatory drug (NSAID) use [1][2]. Beyond local mucosal tissue damage, PUD is increasingly recognized for its systemic and psychological implications. Accumulating clinical evidence highlights a bidirectional psychophysiological relationship between gastrointestinal disorders and psychiatric conditions, particularly depression. Patients with PUD exhibit a significantly higher prevalence of major depressive disorder (MDD), while chronic psychological stress and depression can independently exacerbate gut mucosal ulceration [3][4]. This bidirectional crosstalk is largely mediated by the Gut–Brain axis, a complex neuroendocrine and immunologic network. Central to this Gut–Brain communication are inflammatory cytokines.

Interleukin-6 (IL-6) is a pleiotropic cytokine that plays a critical role in both mucosal inflammation and neuroinflammation [5]. In the gastrointestinal tract, persistent inflammation associated with PUD triggers continuous IL-6 elevation, impairing mucosal healing and driving a chronic inflammatory state [6][7]. Concurrently, elevated circulating IL-6 can cross the Blood–brain barrier, altering neurotransmitter metabolism and neuroendocrine function, thereby contributing to the pathogenesis of MDD [8][9]. Thus, IL-6 serves as a critical shared biologic mediator linking systemic inflammation in PUD with depressive symptoms. IL 6 was selected for this study over other inflammatory biomarkers because of its pleiotropic nature and well-documented ability to cross the blood–brain barrier (BBB). Unlike standard acute-phase reactants, IL-6 directly interacts with the Hypothalamic–Pituitary–Adrenal (HPA) axis, acting as a primary neuroendocrine switch that translates peripheral gastric inflammation into central depressive symptoms. While the existing literature extensively covers the independent roles of inflammation in PUD and depression, there remains a distinct scarcity of clinical data evaluating the simultaneous bidirectional crosstalk in patients with both conditions. Despite the established individual roles of IL-6 in PUD and MDD, clinical studies explicitly investigating its bridging role in patients suffering from concurrent PUD and depression remain limited.

Therefore, the main objective of this study was to estimate serum IL-6 levels in PUD patients with depression and to investigate the bidirectional psych-gastrointestinal interplay by evaluating IL-6 as an underlying inflammatory mechanism linking these two conditions.

2. METHOD

2.1. Subjects

Fifty cases and fifty controls comprised the 100 male participants in this case-control framework, with only males included to reduce biological diversity, since estrogen exhibits significant anti-inflammatory properties and directly suppresses interleukin-6 (IL-6) production. Furthermore, estrogen is gastroprotective (modulating gastric acid and mucus secretion) and is heavily involved in the pathophysiology of mood disorders [10]. Clinical confirmation of peptic ulcer relied on a gastroenterologist's assessment through the Fujifilm ELUXEO 700 endoscope. To control for confounding factors, strict filtering was required. People who do not meet the following criteria are not allowed to participate: 1) incomplete profiles, 2) women with PUD, or 3) anyone under 18 years old. 4) To be eligible, there should be no severe atypical hyperplasia or malignant tumors in the upper GIT. In addition, 5) recent surgical interventions, esophageal, gastric, or duodenal surgery within the past 3 months, were grounds for exclusion. Systemic or intestinal inflammatory disorders also precluded participation, indicating that no subjects had a history of autoimmune diseases, Crohn's disease, ulcerative colitis, or celiac disease.

2.2. Sample Size Determination

To determine a suitable, statistically valid sample size for this Case–control study, the finite population correction (FPC) method was used. This is appropriate given that the total population is under a few million in this case, about 800,000 from Karbala city. The sample size was calculated using the formula [11].With an estimated peptic ulcer prevalence of 6%, a 0.06% confidence level (Z = 1.96), a 5% margin of error, and a population size of 800,000:

$$n = N \times \frac{z^2 \times p\,(1-p)}{(e^2 \times (N-1)) + (z^2 \times p\,(1-p))}$$

Substituting the values into the formula:

$$n = 800{,}000 \times \frac{1.96^2 \times 0.06\,(1-0.06)}{(0.05^2 \times (800{,}000-1)) + (1.96^2 \times 0.06\,(1-0.06))} \rightarrow n = 800{,}000 \times \frac{3.8416 \times 0.06\,(0.94)}{(0.0025 \times 799{,}999) + (3.8416\,(0.94))}$$

$$n = 800{,}000 \times \frac{0.216732}{1{,}999.9975 + 0.216732} \rightarrow 800{,}000 \times \frac{0.216732}{2{,}000.2142} \rightarrow \frac{173{,}385.6}{2{,}000.2142} \approx 86.65$$

The final sample size was about 87 individuals, sufficient for a 95% confidence level and a 5% margin of error for the peptic ulcer prevalence estimate in Karbala. We collected 100 samples to boost significance.

2.3. Data Collection

Participants underwent a comprehensive evaluation that encompassed biological and social determinants. Behavioral history variables included factors such as smoking and address, in addition to standard measures such as age and BMI. Depression disorder was diagnosed by a psychologist who used the PHQ-9 to assess depressive symptoms over a 2-week period. Participants completed this 9-item survey on a 4-point Likert scale, where 0 means "not at all" and 3 means "almost every day." The total score (0–27) indicates the severity of depressive symptoms: none or very little (0–4), mild (5–9), moderate (10–14), moderately severe (15–19), or severe (20–27). A score of 10 or higher indicates clinical depression [12]. *H. pylori* was detected using the culturing technique for patients and stool antigen detection for controls.

2.4. Samples

From October to December 2025, data were collected from patients at the Kerbala center for Gastrointestinal and Liver Diseases in Kerbala, Iraq, and from controls outside the hospitals and private clinics. Fasting participants had 5-mL venous blood drawn in the morning using sterile syringes. Upon collection, samples were assigned unique group with ID by the laboratory information system. After clotting, samples were centrifuged at 4,000 rpm for 15 minutes and then stored in a deep freezer at -20°C until IL-6 measurement.

2.5. IL-6 Measurement

A sandwich enzyme-linked immunosorbent assay (ELISA) research kit (*Human IL6; ELK Biotechnology, USA*) was used to determine how much IL-6 there were. This kit was chosen because it was very specific and sensitive in human serum / plasma matrices.

2.6. Ethical Statement

The Medical Ethics Committee of the College of Applied Medical Sciences at Karbala University granted permission for this research. Their official clearance is recorded as Ref. No.: CLAMSKU/19. We ensured that every step was safe for people and followed both the Declaration of Helsinki and standard national frameworks to the letter.

2.7. Statistical Analysis

Statistical analysis was performed using SPSS 26.0 (SPSS Inc., Chicago, USA). After normality testing using the Shapiro-Wilk test, demographic data were compared using the chi-squared test and Fisher's exact test, while scaled data were compared using a student's t-test. Multiple comparisons were assessed using one-way ANOVA followed by Dunn's Bonferroni post hoc test. Correlation was assessed using the Pearson correlation test. Statistical significance was considered at $p < 0.05$.

3. RESULTS AND DISCUSSION

3.1. Demographic Results of the Study Groups

Results in Table 1 show significant differences between the two study groups in NSAID use ($p < 0.01$), with greater use in the patient group than in controls. There were significant differences between patients and controls in *H. pylori* infection ($p < 0.05$); patients showed only (12%) with *H. pylori* infection. There were no significant differences in address, smoking status, physical activity, or BMI between the two groups; however, age differed significantly, with PUD patients having a higher mean age than controls. PHQ-9 shows a significant difference ($p < 0.001$) between patient and control groups; patients have higher depression scores than controls. The distribution by depression severity shows a significantly ($p<0.001$) higher prevalence of depression in patients than controls, with no patients without depression.

Table 1. Demographic Results of the Study Groups

Parameter		Patients	Control	*P-value*
Adress	Urban	78.0%	78.0%	> 0.05
	Rural	22.0%	22.0%	
NSAIDs usage	Yes	64.0%	10.0%	< 0.01
	No	36.0%	90.0%	
H. pylori	Positive	12.0%	0.0%	<0.05
	Negative	88.0%	100%	
Smoking state	Never	36.0%	58.0%	> 0.05
	Former	18.0%	10.0%	
	Current	46.0%	32.0%	
Physical activity	Non activity	74.0%	88.0%	> 0.05
	Once per week	8.0%	4.0%	
	Twice per week	6.0%	2.0%	
	Three times per week	12.0%	6.0%	
Depression classes	No depression	0.0%	14.0%	<0.001
	Minimal depression	12.0%	38.0%	
	Mild depression	16.0%	30.0%	
	Moderate depression	38.0%	18.0%	
	Moderate-severe depression	30.0%	0.0%	
	Severe depression	4.0%	0.0%	
BMI (kg/m^2)		26.02 ± 5.16	26.58 ± 4.88	> 0.05
Age (year)		49.3 ± 17.26	32.32 ± 9.761	< 0.001
PHQ-9 (score)		12.1 ± 5.643	5.02 ± 3.889	< 0.001

Patients tend to use NSAIDs more than controls, making them a risk factor for developing PUD. NSAIDs induce peptic ulcers through several mechanisms. Some NSAIDs, known as non-selective NSAIDs, cause direct irritation of the mucosal layer and inhibit protective prostaglandins, resulting in open pores in the mucosal layer and damage to the inner layers by gastric acid. Some NSAIDs act through COX2 and cause direct inflammation [13]. GIT physiology and histology decline with age (ageing), and the mucosal protective layer becomes thinner due to reduced blood flow to the mucosa, leading to reduced mucus and bicarbonate secretion and diminished cell proliferation. These changes are intended to cause ulceration in the GIT canal without any other cause, but only as a response to tissue changes [14]. The bidirectional link between PUD and depression is attributed to the disease's burden and inflammatory response. These factors, along with genetic and environmental influences, contribute to long-term stress, pain, sleep disturbances, and anxiety, which can lead to depression in peptic ulcer patients. A study indicates that these patients have a 1.47-fold higher likelihood (47%) of developing depression compared to individuals without ulcers [15].

3.2. IL-6 Levels Comparison Between Peptic Ulcer Disease Patients and Controls

There was a highly significant increase in serum IL-6 levels in patients compared with controls ($p < 0.01$). As explained in Table 2.

Table 2. IL-6 Levels Comparison Between Peptic Ulcer Disease Patients and Controls

Biomarkers	Groups	Mean ± S. D	*P-value*
IL-6 *(pg/mL)*	Patient	306.85 ± 39.28	< 0.001
	Control	96.22 ± 16.16	

The simultaneous increase of interleukin-6 (IL-6) in peptic ulcer disease and depression results from a two-way feedback loop along the gut-brain axis. Chronic stress and depression enhance the activity of the hypothalamic-pituitary-adrenal (HPA) axis and cause gut dysbiosis. These changes lead to systemic elevation of IL-6 and directly hamper gastric mucosal healing. Conversely, localised gastric inflammation and *H. pylori* infection weaken the intestinal barrier, allowing endotoxins to enter the bloodstream. This process causes persistent peripheral IL-6 overproduction, which can cross the blood-brain barrier, trigger neuroinflammation, and worsen depressive symptoms [16][17].

3.3. IL-6 Levels Comparison Between Peptic Ulcer Disease Patients and Controls Based on Demographic Criteria

A highly significant ($p < 0.01$) increase in IL-6 parameters was observed across all patient age groups compared to controls, with a significant difference ($p < 0.05$) in IL-6 levels between patients aged 18-29 years and those aged 30 years or older. For BMI, address, and smoking factors, IL-6 shows a significant increase ($p < 0.01$) in peptic ulcer patients compared to controls, with no significant differences observed among patients classified by BMI, address, or smoking status ($p > 0.05$), as shown in Table 3.

Table 3. IL-6 Comparison Between Study Groups Based on Demographic Criteria

Indicators	Groups	Patients	Control	P-value
		Mean *(pg/mL)* ± S. D	Mean *(pg/mL)* ± S. D	
Age (year)	18 - 29	343.59 ± 37.33 a	97.05 ± 17.05	< 0.001
	30 – 44	294.63 ± 28.42 b	96.68 ± 14.61	< 0.001
	≥ 45	302.20 ± 39.09 b	96.29 ± 18.24	< 0.001
	p-value	0.020	0.997	
BMI (kg/m^2)	Normal weight	311.33 ± 35.95	96.83 ± 18.88	< 0.001
	Over weight	300.19 ± 37.15	96.33 ± 15.87	< 0.001
	Obese	310.65 ± 44.65	97.33 ± 15.88	< 0.001
	p-value	0.610	0.988	
Address	Urban	308.39 ± 39.91	94.97 ± 16.04	< 0.001
	Rural	301.40 ± 38.29	103.32 ± 15.56	< 0.001
	p-value	0.682	0.156	
Smoking state	Never	297.97 ± 35.2	92.64 ± 15.28	< 0.001
	Former	304.8 ± 37.11	98.45 ± 17.88	< 0.001
	Current	314.61 ± 43	103.85 ± 15.65	< 0.001
	p-value	0.540	0.074	

IL-6 levels increase with age due to the loss of important immune tolerance and changes in normal physiological functions, leading to macrophage activation and increased cytokine secretion [18][19]. But [20] and this study showed that immune responses in younger patients with peptic ulcer mediated by IL-6 were better than in elderly patients. Increasing BMI is linked to higher food intake, which increases the risk of peptic ulcer disease (PUD), especially from causative agents like *H. pylori* infection due to fast food or heavy NSAID use. Chronic or high-dose NSAID use is related to adverse effects such as sodium and water retention. This damage the mucosal layer and triggers a local inflammatory response mediated by proinflammatory cytokines such as TNF, IL-6, and IL-8 [21][22]. A person's location or habitat, whether urban or rural, influences their risk of developing GI tract diseases, such as PUD. Urban dwellers are more likely to be exposed to the inhalation of toxins and infectious agents than those in rural areas, which affects the distribution of gut microbiomes, causes mucosal damage, and triggers inflammatory responses (IL-6) that damage the gut mucosa [23]. Smoking is regarded as a key adverse factor contributing to PUD by increasing the permeability of the mucosal layer of the upper gut (stomach and duodenum), increasing oxidative stress, and promoting lipid peroxidation, which can cause cell death or necrosis in PUD. These processes trigger a protective immune response, such as IL-6, which promotes systemic inflammation [24][25].

3.4. Correlation Between IL-6 and PHQ-9

Pearson correlation showed a highly significant ($p<0.001$) positive correlation between IL-6 and the depression severity scale (PHQ-9), as demonstrated in Table 4.

Table 4. Correlation Between IL-6 and PHQ-9 in Patients Group

Biomarkers	PHQ-9 *(score)*	*P-value*
IL-6 *(pg/mL)*	0.556	< 0.001

In peptic ulcer disease (PUD), IL-6 explains the bidirectional psychophysiological link between PUD and depression as follows:

PUD is characterized by an inflammatory response mediated by some cytokines like IL-6; these cytokines activate the indolamine 2,3-dioxygenase (IDO) enzyme, an enzyme responsible for serotonin catabolism through the kynurenine pathway, which results in the initiation of depressive symptoms and the development of low mood [26]. On the other hand, if depression occurs first, chronic or mild depression causes systemic stress that triggers the secretion of inflammatory cytokines like IL-6. These inflammatory responses disrupt the gut immune barrier, such as the mucosal layer, and make it more vulnerable to ulcerative agents (like excessive use of NSAIDs) or acidic ulceration due to the thinning of the mucosal layer [8] [27]. This agrees with a study by [28] who found that long, stressful events correlated with chronic inflammation, characterized by elevated IL-6, which increases gut permeability by weakening mucosal tight junctions.

4. LIMITATIONS

It is important to acknowledge certain limitations of this study. First, the cross-sectional and case-control designs allow us to establish associations but do not permit definitive causal conclusions about the IL-6 pathway in the relationship between PUD and depression. Second, to eliminate the confounding effects of hormonal fluctuations, the study cohort was restricted to male participants. While this increased the internal validity of our biochemical assessments, it significantly limits the generalizability of our findings to females. Future longitudinal studies including both genders are warranted to validate these mechanisms.

5. CONCLUSION

IL-6 is a key inflammatory mediator within the gut-brain axis, linking peptic ulcer disease (PUD) and depression. Our findings show that serum IL-6 levels are markedly elevated in PUD patients with comorbid depression. These results support IL-6 as a shared biological mediator linking gastrointestinal mucosal damage and psychological disorders, highlighting its potential as a biomarker for this bidirectional relationship.

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REFERENCES

[1] Shukar Singh, Gursewak Singh, Tawqeer Shafi, and Shafkat Hussain Malik, "Overview of Peptic Ulcer Disease: Epidemiology, Causes, Pathophysiology, and Clinical Importance," *Curr. Pharm. Res.*, vol. 1, no. 2, pp. 222–230, Jun. 2025, doi: 10.63785/cpr.2025.1.2.184192.

[2] K. Singh, R. Kumar, A. P. Singh, M. Malhotra, A. P. Singh, and R. Rani, "Peptic Ulcer Disease: A Review," *Int. J. Medical, Pharm. Drug Res.*, vol. 8, no. 2, pp. 38–46, 2024, doi: 10.1001/jama.2024.19094.

[3] K. Yousaf and H. H. Pasha, "Correlation of Depression and Nightmares in Young Medical Students," *Pakistan J. Heal. Sci.*, vol. 6, no. 6, pp. 207–211, 2025, doi: 10.54393/pjhs.v6i6.3042.

[4] K. J. Fleetwood *et al.*, "Depression and physical multimorbidity: A cohort study of physical health condition accrual in UK Biobank," *PLoS Med.*, vol. 22, no. 2, pp. 1–17, 2025, doi: 10.1371/journal.pmed.1004532.

[5] N. Katkenov, Z. Mukhatayev, S. Kozhakhmetov, A. Sailybayeva, M. Bekbossynova, and A. Kushugulova, "Systematic Review on the Role of IL-6 and IL-1β in Cardiovascular Diseases," 2024. doi: 10.3390/jcdd11070206.

[6] E. I. Obeagu and G. U. Obeagu, "Exploring the intricate relationship between peptic ulcers and immunohematological responses A narrative review," *Med. (United States)*, vol. 104, no. 15, p. e42187, 2025, doi: 10.1097/MD.0000000000042187.

[7] A. C. Y. Al-Fatlawi, H. R. Hasan, and Q. M. Al-Obaidy, "Evaluation of the levels of kidney injury molecule-1 and cystatin C as early biomarkers for prediction of acute kidney injury complications in paediatric male patients – a case-control study," *Pediatr. Pol.*, vol. 100, no. 1, pp. 38–51, 2025, doi: 10.5114/polp.2025.149167.

[8] E. Roohi, N. Jaafari, and F. Hashemian, "On inflammatory hypothesis of depression: what is the role of IL-6 in the middle of the chaos?," *J. Neuroinflammation*, vol. 18, no. 1, pp. 1–15, 2021, doi: 10.1186/s12974-021-02100-7.

[9] S. Zhang *et al.*, "Bidirectional Crosstalk between Stress-Induced Gastric Ulcer and Depression under Chronic Stress," *PLoS One*, vol. 7, no. 12, 2012, doi: 10.1371/journal.pone.0051148.

[10] A. C. Y. Al-Fatlawi, Z. H. Khudair, and A. Q. Alhaideri, "Endothelin-1 and endothelial nitric oxide (eNOs) synthase as predictive biomarkers of clinical-subclinical atherosclerosis related to diabetes mellitus: a cross-sectional study," *Polish J. Cardio-Thoracic Surg.*, vol. 22, no. 4, pp. 285–293, 2025, doi: 10.5114/kitp.2025.158073.

[11] A. C. Y. Al-Fatlawi, Z. H. Khudair, and A. Q. Jaafar, "Midkine (MK) as a novel biomarker of clinical-subclinical coronary atherosclerosis and related to diabetes mellitus: clinical applications," *Anaesthesia, Pain Intensive Care*, vol. 29, no. 6, pp. 559–566, Jun. 2025, doi: 10.35975/apic.v29i6.2915.

[12] K. Kroenke, R. L. Spitzer, and J. B. W. Williams, "The PHQ-9: Validity of a brief depression severity measure," *J. Gen. Intern. Med.*, vol. 16, no. 9, pp. 606–613, 2001, doi: 10.1046/j.1525-1497.2001.016009606.x.

[13] E. Nesiama, L. Mirembe, K. Weber, S. Isaac, D. Trammell, and I. Obokhare, "Massive Gastrointestinal Bleeding Related to NSAID Use in a Patient with Ileorectal Anastomosis," *Case Rep. Surg.*, vol. 2024, no. 1, pp. 1–7, 2024, doi: 10.1155/2024/4619458.

[14] A. Gallo *et al.*, "Main Disorders of Gastrointestinal Tract in Older People: An Overview," *Gastrointest. Disord.*, vol. 6, no. 1, pp. 313–336, 2024, doi: 10.3390/gidisord6010022.

[15] S. Y. Kim, C. Min, D. J. Oh, and H. G. Choi, "Reciprocal association between depression and peptic ulcers: Two longitudinal follow-up studies using a national sample cohort," *Sci. Rep.*, vol. 10, no. 1, pp. 1–8, 2020, doi: 10.1038/s41598-020-58783-0.
[16] K. A. Abdel-Sater, "Stress, neurotransmitters, and the microbiota–gut–brain axis: mechanisms of mucosal injury," *Res. Results Pharmacol.*, vol. 11, no. 4, pp. 162–174, 2025, doi: 10.18413/rrpharmacology.11.587.
[17] K. A. Abdel-Sater and H. A. Hassan, "Gut microbiota and stress ulcers: unraveling the neurotransmitter connection," 2025. doi: 10.3389/fnins.2025.1594179.
[18] A. Bleve, F. Motta, B. Durante, C. Pandolfo, C. Selmi, and A. Sica, "Immunosenescence, Inflammaging, and Frailty: Role of Myeloid Cells in Age-Related Diseases," *Clin. Rev. Allergy Immunol.*, vol. 64, no. 2, pp. 123–144, 2023, doi: 10.1007/s12016-021-08909-7.
[19] S. Leonardo and F. Fregni, "Association of inflammation and cognition in the elderly: A systematic review and meta-analysis," *Front. Aging Neurosci.*, vol. 15, no. February, 2023, doi: 10.3389/fnagi.2023.1069439.
[20] R. A. Ali, "Immunological Assessment of Interleukin-6 in Patients with Gastric (Stomach) Ulceration of Acute and Chronic Types in Babylon Province," *SAR J. Pathol. Microbiol.*, vol. 5, no. 02, pp. 39–42, 2024, doi: 10.36346/sarjpm.2024.v05i02.003.
[21] W. A. Nasif, M. Hasan Mukhtar, A. S. El-Moursy Ali, M. M. Nour Eldein, R. A. Almaimani, and S. S. Ashgar, "Body mass index is associated with Helicobacter pylori infection and increased oxidative DNA damage in an obese population," *J. Int. Med. Res.*, vol. 50, no. 2, 2022, doi: 10.1177/03000605221076975.
[22] S. Jin, N. Nepal, and Y. Gao, "The role of toll-like receptors in peptic ulcer disease," *Immunol. Med.*, vol. 45, no. 2, pp. 69–78, 2022, doi: 10.1080/25785826.2021.1963190.
[23] S. Chen, W. Yu, Y. Shen, L. Lu, X. Meng, and J. Liu, "Unraveling the mechanisms underlying air pollution-induced dysfunction of the oral-gut-brain axis: Implications for human health and well-being," *Asian Biomed.*, vol. 19, no. 1, pp. 21–35, 2025, doi: 10.2478/abm-2025-0002.
[24] X. Gui, Z. Yang, and M. D. Li, "Effect of Cigarette Smoke on Gut Microbiota: State of Knowledge," *Front. Physiol.*, vol. 12, no. June, pp. 1–14, 2021, doi: 10.3389/fphys.2021.673341.
[25] K. Kumboyono *et al.*, "Detection of Vascular Inflammation and Oxidative Stress by Cotinine in Smokers: Measured Through Interleukin-6 and Superoxide Dismutase," *Int. J. Gen. Med.*, vol. 15, no. September, pp. 7319–7328, 2022, doi: 10.2147/IJGM.S367125.
[26] C. Yilmaz and G. Ikizer, "Psychoneuroimmunological Processes in Mood and Anxiety Disorders and Their Relation with Psychotherapy," *Psikiyatr. Güncel Yaklaşımlar-Current Approaches Psychiatry*, vol. 14, no. 1, pp. 86–97, 2022, doi: 10.18863/pgy.943148.
[27] Y. Mou *et al.*, "Gut Microbiota Interact With the Brain Through Systemic Chronic Inflammation: Implications on Neuroinflammation, Neurodegeneration, and Aging," *Front. Immunol.*, vol. 13, no. April, pp. 1–25, 2022, doi: 10.3389/fimmu.2022.796288.
[28] A. Shahini and A. Shahini, "Role of interleukin-6-mediated inflammation in the pathogenesis of inflammatory bowel disease: focus on the available therapeutic approaches and gut microbiome," Mar. 16, 2023. doi: 10.1007/s12079-022-00695-x.

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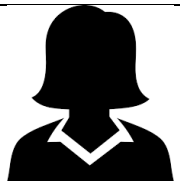

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