INTERNATIONAL JOURNAL OF
MEDICAL BIOCHEMISTRY

DOI: 10.14744/ijmb.2025.63308
Int J Med Biochem 2025;8(3):233–241

Research Article

The serum NF-κB and adiponectin levels in patients with acute pancreatitis

Naile Fevziye Mısırlıoglu[1], Gulbahar Guler Orucoglu[2], Solen Himmetoglu[3], Sumeyye Nur Aydın[4], Hafize Uzun[1]

[1]Department of Medical Biochemistry, Istanbul Atlas University Faculty of Medicine, Istanbul, Türkiye
[2]Department of Emergency, University of Health Sciences, Gaziosmanpasa Training and Research Hospital, Istanbul, Türkiye
[3]Department of Biochemistry, Biruni University Faculty of Medicine, Istanbul, Türkiye
[4]Department of Public Health, Istanbul Provincial Health Directorate, Istanbul, Türkiye

Abstract

Objectives: This study aimed to evaluate whether serum nuclear factor-kappa B (NF-κB) and adiponectin levels can provide insight into disease progression and serve as potential biomarkers for predicting disease severity in patients with acute pancreatitis (AP).

Methods: A total of 49 patients diagnosed with AP and admitted to the Emergency Department of Gaziosmanpaşa Training and Research Hospital were enrolled. An age-matched control group of 49 healthy individuals without AP was also included. Serum levels of NF-κB and adiponectin were measured and compared between groups.

Results: Patients with AP exhibited significantly elevated serum NF-κB levels and reduced adiponectin levels compared to the control group (both $p<0.001$). A strong negative correlation was observed between adiponectin and NF-κB levels in the AP group ($r=-0.865$, $p<0.05$). Receiver operating characteristic (ROC) analysis determined the optimal cut-off value for adiponectin as 3.4, with a sensitivity and specificity of 1.000. The optimal cut-off for NF-κB was 1.8, with a sensitivity of 1.000 and specificity of 0.96.

Conclusion: The findings suggest that serum NF-κB and adiponectin levels may be valuable biomarkers for assessing disease severity in AP. Their combined use or integration with existing scoring systems could enhance prognostic accuracy. Further experimental and clinical studies are necessary to evaluate the therapeutic potential of adiponectin and to validate these biomarkers for routine clinical use.

Keywords: Acute pancreatitis, adiponectin, disease severity, inflammation, nuclear factor kappa B

How to cite this article: Mısırlıoglu NF, Orucoglu GG, Himmetoglu S, Aydın SN, Uzun H. The serum NF-κB and adiponectin levels in patients with acute pancreatitis. Int J Med Biochem 2025;8(3):233–241.

Acute pancreatitis (AP) is a serious condition marked by sudden inflammation of the pancreas, which can result in significant complications and may necessitate intensive care. The disease is defined by an inflammatory response that causes swelling and bleeding in pancreatic tissue. In severe instances, it may lead to the necrosis of pancreatic tissue due to premature enzyme activation within the organ [1]. It is often associated with gallstones and excessive alcohol consumption. AP starts with the initiation of the process of autodigestion, which leads to the pancreas digesting itself, resulting in damage to tissues through activation of enzymes. Clinically, AP can present in both mild and severe forms; the severe form carries a risk of developing systemic inflammatory response syndrome (SIRS) and multiple organ failure [2].

Gallstones and chronic alcohol abuse account for approximately two-thirds of cases in the etiology of acute pancreatitis. Other common causes include the development of AP following endoscopic retrograde cholangiopancreatography

Address for correspondence: Naile Fevziye Mısırlıoglu, MD. Department of Medical Biochemistry, Istanbul Atlas University Faculty of Medicine, Istanbul, Türkiye
Phone: +90 532 573 77 13 **E-mail:** nailemisirlioglu@gmail.com **ORCID:** 0009-0007-4735-4091
Submitted: April 26, 2025 **Revised:** June 02, 2025 **Accepted:** June 03, 2025 **Available Online:** June 17, 2025

(ERCP) and hypertriglyceridemia [3]. Recent studies have demonstrated that metabolic abnormalities such as diabetes, hypertriglyceridemia, morbid obesity, and vitamin D deficiency are closely associated with the severity and prognosis of AP [4]. Since insulin resistance (IR) is a chronic, low-grade inflammatory state, it is hypothesized that IR plays a pathogenic role in other inflammatory diseases such as AP. This hypothesis is supported by evidence that pre-existing diabetes increases the risk of developing AP and progression to severe AP by increasing local and systemic complications in AP [5].

Nuclear Factor-B (NF-κB) is a modulator of cytokine receptors and adhesion biological activity. Recent research has shown that NF-κB is known as a transcription factor that controls cell apoptosis, adaptive immunity, cell proliferation and aging, as well as regulating gene expression of autoimmune molecules [6]. The kinase cascade mediates activation of NF-κB, a transcription factor commonly associated with activation of inflammation genes, and other signal transducers and activators of transcription that have been shown to lead to overexpression of inflammation genes [7] in pancreatic acinar cells [8]. Activation of NF-κB is increased in pancreatic cells during AP and exacerbates the inflammatory process. Especially in severe cases of AP, activation of NF-κB leads to excessive release of cytokines. This leads to SIRS and increases tissue damage. NF-κB plays is crucial in the pathogenesis of AP and is being investigated as an important biomarker for prediction in the course of the disease [9].

Adiponectin is a 30-kDa adipocyte-specific protein factor, and its primary function is to improve insulin sensitivity. Furthermore, this adipokine has anti-inflammatory properties through inhibition of macrophage differentiation resulting in protection of many organs [10]. In experimental studies have revealed the role of adiponectin in the pathogenesis and clinical course of AP [11–14].

Serum NF-κB and adiponectin levels are associated with the severity of acute pancreatitis and may serve as potential biomarkers for predicting disease progression. This hypothesis is based on the pro-inflammatory role of NF-κB and the anti-inflammatory, insulin-sensitizing properties of adiponectin. To our knowledge, no human study has evaluated these markers together in AP.

NF-κB was selected due to its central role in mediating inflammatory responses and its known activation in pancreatic acinar cells during AP, contributing to disease severity. Adiponectin was chosen for its anti-inflammatory and insulin-sensitizing effects, which may counteract the inflammatory cascade in AP. Together, these biomarkers represent opposing regulatory mechanisms that may influence the progression and outcome of the disease. However, in the literature review, no study was found that investigated serum NF-κB and serum adiponectin levels together in AP in humans. Therefore, this study aimed to investigate whether circulating NF-κB and adiponectin can offer insights into the progression of the disease and if these markers can be used to predict the severity of AP in patients.

Materials and Methods

Subject groups

This study was approved by the Biruni University Faculty of Medicine Ethics Committee (Date: 12/12/2024, Decision No: 2024-BİAEK/05-04), adhered to the principles outlined in the Declaration of Helsinki. All participants, including both patients and control subjects, were fully briefed about the study, and written informed consent was provided by the patients or their family members. Helsinki declaration in the main text.

A total of 49 patients permitted to the Emergency Department of Gaziosmanpaşa Training and Research Hospital and diagnosed with AP were enrolled in the study. Patients admitted to our emergency surgery outpatient clinic with abdominal pain and diagnosed with AP according to clinical and laboratory findings were prospectively evaluated.

AP is present: The sudden onset of intense upper abdominal pain that may radiate to the back, a marked increase in serum lipase or amylase levels (more than three times the normal range), and radiological evidence that suggests the presence of AP. Patients were diagnosed with AP according to the Revised Atlanta Criteria [15].

The control group consisted of age- and sex-matched healthy individuals who presented to the same institution for routine health check-ups during the same period and had no known chronic diseases or regular medication use.

Inclusion criteria

Patients aged 18 and above presented with abdominal pain, nausea, and vomiting, and met the criteria for acute pancreatitis (clinical signs of AP, amylase-lipase levels at least three times higher than normal, and the presence of at least two radiologic compatibility criteria) were included.

Exlusion criteria

Patients who did not consent to participate, those under 18 years old, and individuals with comorbidities (such as diabetes, renal failure, heart failure, advanced liver failure, recent myocardial infarction or stroke, major surgery within the last 6 months, or pregnancy) were excluded.

Patients' complaints, diseases, presence of exclusion criteria, duration/when complaints started, laboratory results and vital signs were documented on data collection forms before hospitalization. All patients diagnosed were admitted to hospital.

According to the post-hoc power analysis performed using G*Power 3.1.9.2, the statistical power of the independent samples t-test comparing the two groups (n_1=49, n_2=49) was calculated as 95% (1–β=0.95) at a significance level of α=0.05, assuming an effect size of Cohen's d=0.7.

Sample collection and measurements

For patients who presented to the emergency department and met the criteria for AP, antecubital venous access was established, and blood samples were collected for hemogram

and biochemistry. Imaging (hepatobiliary ultrasonography and abdominal computed tomography) was performed on patients with a more than three-fold increase in amylase/lipase levels. Blood samples were centrifuged at 4000 rpm for 10 minutes at 4°C. Biochemical tests were performed right away, and serum aliquots for additional parameters were stored at -80°C for later analysis.

Measurement of serum Nuclear Factor Kappa B (NF-κB) levels

Serum NF-κB levels sandwich human enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions (MyBioSource, Cat. No: MBS724341, MyBioSource, Inc., San Diego, CA, USA). Optical density was read with a microtitre plate photometer at 450 nm. The concentration was determined by interpolation from calibration curves prepared with standard samples provided by the manufacturer. The intra-assay and inter-assay coefficients of variation for NF-κB were <10% and <10%, respectively.

Measurement of serum Adiponectin levels

Serum adiponectin levels competitive-ELISA Kit according to the manufacturer's instructions (Quantikine® Human Adiponectin, R&D Systems, Inc., Minneapolis, MN). with detection limit of, respectively, 0.246 ng/mL. Optical density was read with a microtitre plate photometer at 450 nm. The concentration was determined by interpolation from calibration curves prepared with standard samples provided by the manufacturer. The intra-assay and inter-assay coefficients of variation for adiponectin were <10% and <10%, respectively.

The complete blood count (CBC) was recorded with an automatic hematology analyzer (Sysmex, Sysmex XN-1000, Norderstedt, Germany). Biochemical parameters were determined using the enzymatic methods (COBAS 8000, ROCHE-2007, Tokyo, Japan).

Statistical analysis

Statistical analyses were performed using SPSS v.26 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as counts (n) and percentages (%), while continuous variables were presented as mean±standard deviation. Data distribution normality was evaluated using the Kolmogorov-Smirnov test, Q-Q plots, and histograms. The Pearson chi-square test was used for comparing categorical variables, while the Mann-Whitney U test and Student's T-test were applied for comparisons between two independent groups. Spearman's correlation test assessed relationships among numerical variables. Laboratory parameters were categorized based on Receiver Operating Characteristic (ROC) curve analysis, with the optimal cutoff point determined by maximizing sensitivity and specificity. The Youden index was used to identify the best cutoff points, and the area under the curve (AUC) was reported. Confidence intervals were calculated using the Bootstrap method. (Bootstrap method performs multiple resampling (bootstrapping) to evaluate the performance of the model, calculates AUROC for each sample and then gives confidence intervals). Multivariate logistic regression (Enter and Forward: LR) analysis was performed to identify risk factors associated with AP. The goodness-of-fit of the model was evaluated using the Hosmer-Lemeshow test and highly correlated variables are not included in the model. The significance level for statistical tests was set at $p<0.05$.

Results

The sociodemographic and clinical characteristics of participants in both the patient and control groups are shown in Table 1. In this study, 49 age- and sex-matched patients with acute pancreatitis (AP) were compared with 49 healthy controls in terms of sociodemographic and clinical features. The BMI of patients in the AP group was significantly higher than that of the healthy controls ($p<0.001$). The health control group had no comorbidities, and none of the participants in either group were smokers or alcohol users. Amylase and lipase levels were both significantly higher in the AP group compared to the health controls ($p<0.001$ for both). Adiponectin levels were lower in the AP group, while NF-κB levels were significantly higher in the AP group ($p<0.001$ for both).

In the patient group, a strong negative correlation was observed between adiponectin and NF-κB levels ($r=-0.865$, $p<0.05$) (Table 2). No significant correlation was found between adiponectin and amylase levels, but a weak positive correlation was observed between NF-κB and amylase levels ($r=0.408$, $p<0.01$). Very weak correlations were found between lipase and adiponectin ($r=-0.290$) and between lipase and NF-κB ($r=0.280$), both of which were statistically significant ($p<0.05$).

Adiponectin and NF-KB levels were not significantly different between genders in the patient and healthy groups ($p>0.05$). Although Adiponectin levels were higher females in both groups, this difference was not statistically significant ($p=0.164$; p:0.440). In addition, no significant correlation was found between Adiponectin, NF-κB levels with age or BMI levels in both groups (Table 3 and Fig. 1).

Regression analysis was performed to evaluate the potential factors associated with the development of AP. The results indicated that none of the examined variables emerged as independent risk factors for the condition (Table 4). Although some parameters showed significant associations in univariate analysis, they did not retain their significance in the multivariate model.

In Figure 2 and Table 5, the performance of clinical parameters in the diagnosis of AP is shown in ROC curves. The Area Under the Curve (AUC) of adiponectin was 0.000 (95% CI:0.000–0.000), the AUC of NF-KB was 0.000 (95% CI:1.000–1.000), the AUC of amylase was 0.990 (95% CI:0.978–1.000), and the AUC of lipase was 1.000 (95% CI:1.000–1.000). The optimum cut-off point of adiponectin was 3.4 with a sensitivity of 1.000 and specificity of 1.000; the optimum cut-off point of NF-κB was 1.8 with a sensitivity of 1.000 and specificity of 0.96; the optimum cut-off point of amylase was 95.3 with a sensitivity of 0.96 and specificity of 1.000; the optimum cut-off point of lipase was 60.2 with a sensitivity of 0.96 and specificity of 1.000.

Table 1. Sociodemographic and clinical characteristics of patient and control groups

Characteristic	Healthy group (n=49)	Acute pancreatitis group (n=49)	p
Age	66.2±10.4	64.9±11.7	0.572
Gender, n (%)			1.000
Male	23 (46.9)	23 (46.9)	
Female	26 (53.1)	26 (53.1)	
BMI	24.0±2.1	27.1±4.1	**<0.001**
Comorbidity (+)	0(0.0)	25(51.0)	**<0.001**
Diabetes (+)	0(0.0)	34(69.4)	**<0.001**
Hypertension (+)	0(0.0)	25(51.0)	**<0.001**
Fasting blood glucose	80.0±10.2	136.3±46.9	**<0.001**
Amylase (U/L)	65.1±15.1	383.1±215.8	**<0.001**
Lipase (U/L)	34.3±13.4	119.8±55.2	**<0.001**
T. cholesterol (mg/dL)	169.3±13.9	214.7±16.8	**<0.001**
LDL (mg/dL)	101.8±11.0	149.1±10.3	**<0.001**
HDL (mg/dL)	45.9±6.8	39.3±9.4	**<0.001**
Triglyceride (mg/dL)	108.4±22.6	131.7±41.6	**0.003**
VLDL (mg/dL)	21.7±4.5	26.3±8.3	**0.003**
AST (U/L)	21.4±8.4	38.4±27.7	**0.003**
ALT (U/L)	26.2±8.5	35.2±18.8	0.052
LDH (U/L)	108.9±29.3	135.4±69.4	0.187
WBC (10^9/L)	7.9±1.1	10.0±2.6	**<0.001**
CRP (mg/L)	2.8±1.1	67.8±36.3	**<0.001**
Adinopectin (ug/L)	8.1±2.1	0.9±0.4	**<0.001**
NF-κB (ng/L)	0.9±0.4	6.1±0.9	**<0.001**

Student T test, Pearson chi-square Test, Mann-Whitney U test. BMI: Body mass index; T. cholesterol: Total cholesterol; LDL: Low density lipoprotein; HDL: High density lipoprotein; VLDL: Very low density; AST: Aspartate transaminase; ALT: Alanine transaminase; LDH: Lactate dehydrogenase; WBC: White blood cell; CRP: C-reactive protein; NF-κB: Nuclear factor kappa B.

Table 2. Correlation between adiponectin and NF-κB levels and other parameters in patient group (n=49)

	Adinopectin	NF-κB	CRP	Amylase	Lipase	WBC
Adinopectin (ug/L)	.	-0.865**	-0.876**	-0.263	-0.290*	-0.464**
NF-κB (ng/L)	-0.865**	.	0.960**	0.408**	0.282*	0.455**

Spearman Correlation Test; <0.25 very weak; 0.26–0.49 weak; 0.50–0.69 moderate; 0.70–0.89 high; 0.90–1.0 very high correlation. *: p<0.05; **: p<0.01. NF-κB, nuclear factor kappa B; CRP, C-reactive protein; WBC: White blood cell.

Table 3. Evaluation of adiponectin and NF-κB levels by gender

Group	Parameters	Gender		p
		Male	Female	
Acute pancreatitis group (n=49)	Adiponectin (ug/L)	0.8±0.4	1.0±0.4	0.164
	NF-KB (ng/L)	6.4±0.9	6.0±0.9	0.078
	Amylase (U/L)	413.3±200.1	356.3±229.3	0.200
	Lipase(U/L)	120.1±60.6	119.6±51.0	0.630
Healthy group (n=49)	Adiponectin (ug/L)	7.8±2.1	8.3±2.2	0.440
	NF-KB (ng/L)	0.9±0.4	0.9±0.3	0.976
	Amylase (U/L)	65.3±16.0	65.0±14.5	0.976
	Lipase(U/L)	34.1±15.9	34.5±11.1	0.801

Mann-Whitney U test. NF-κB: Nuclear factor kappa B.

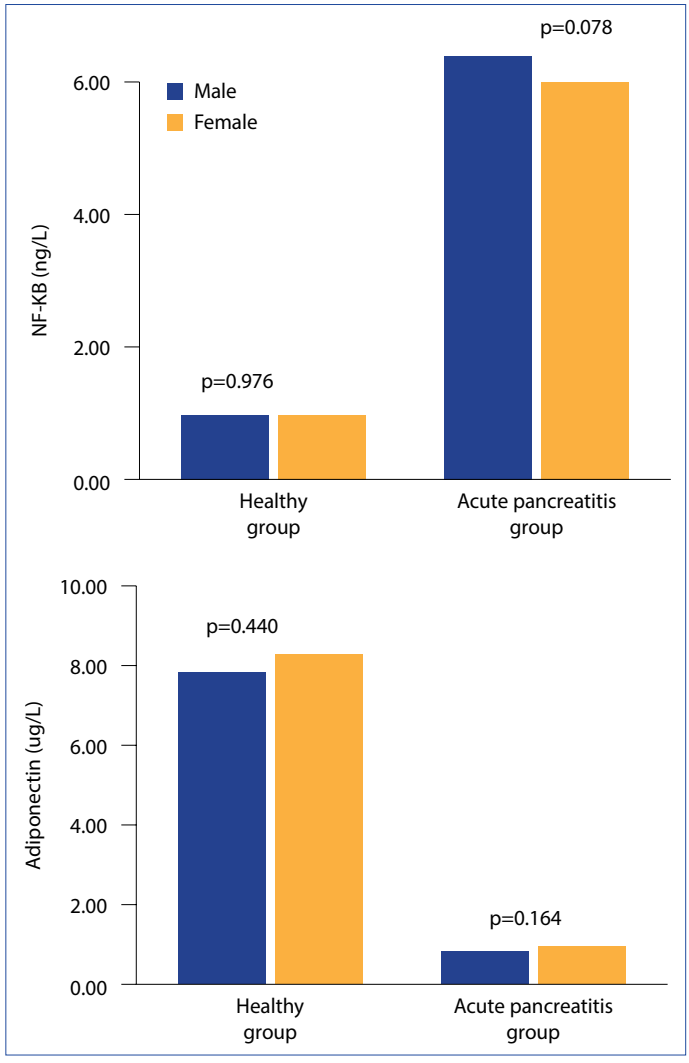

Figure 1. Evaluation of adiponectin and NF-κB levels by gender.
NF-κB: Nuclear factor kappa B.

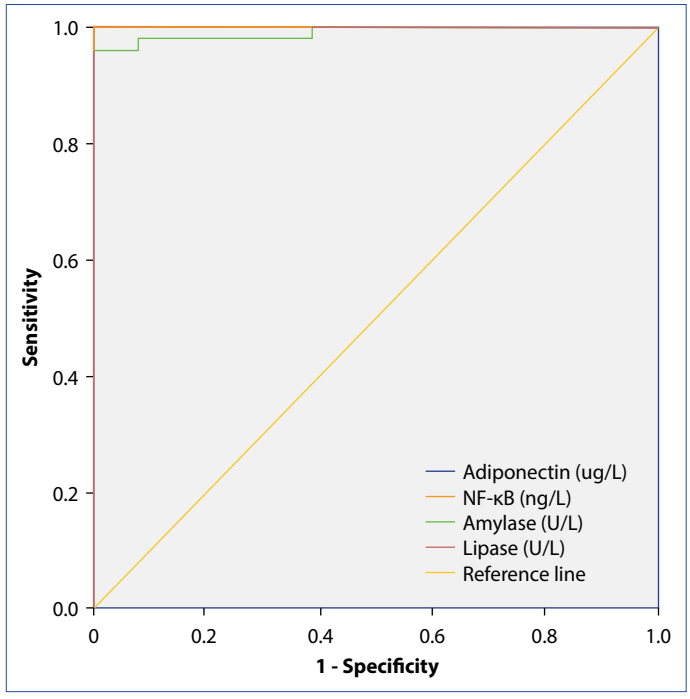

Figure 2. ROC curves evaluation of clinical parameters in the diagnosis of acute pancreatitis.
ROC: Receiver operating characteristic.

Discussion

AP is a gastrointestinal disorder associated with a relatively high mortality rate, ranging from 3% to 17%, and is a common reason for emergency department visits. The disease is frequently diagnosed in emergency settings due to its sudden onset, presenting symptoms such as nausea, vomiting, abdominal bloating, fever, shortness of breath, irritability, and changes in consciousness. Other signs may include fever, low oxygen levels, rapid breathing, elevated heart rate, low blood pressure, abdominal tenderness, bowel obstruction, and/or decreased urine output. Mortality and morbidity risk are influenced by factors like comorbid conditions and complications. Timely treatment initiation plays a crucial role in determining the prognosis. The growing use of rapid diagnostic tools has spurred research into new and faster diagnostic markers [16]. In present study, lower adiponectin levels and elevated NF-κB levels were observed in the AP group. A strong negative correlation between adiponectin and NF-κB was noted. While no significant correlation was found between adiponectin and amylase levels, a weak positive correlation was seen between NF-κB and amylase. We propose that high NF-κB levels and low adiponectin levels may serve as indicators of AP severity.

Although the precise pathogenesis of AP remains unclear, it has been suggested that the main mechanism involves a pathological process leading to autodigestion of pancreatic tissue. This occurs through the early activation of zymogens (digestive enzyme precursors) that are normally inactive within pancreatic acinar cells, ducts, and interstitial spaces [17]. Recent studies have also highlighted that severe pancreatic injury, and the systemic inflammatory response contribute to AP pathogenesis via NF-κB activation [18, 19]. The anti-inflammatory and protective effects of HTD4010 in HTG-AP are at least partially mediated through suppression of the TLR4/NF-κB axis, making this signaling pathway a promising therapeutic target for reducing disease severity in acute pancreatitis [20]. NF-κB signaling pathway as a key mechanism modulated by acinar cell-derived exosomes in the context of AP. NF-κB is well-established as a central mediator of inflammatory responses, and its activation plays a critical role in the progression of AP by promoting the expression of pro-inflammatory cytokines such as IL-6 and TNF-α [21]. Exosomes derived from healthy acinar cells were shown to have anti-inflammatory and cytoprotective effects, both *in vitro* and *in vivo*. Importantly, these exosomes suppressed NF-κB signaling activity, which corresponded with reduced apoptosis, lower ROS production, and decreased levels of systemic inflammatory markers in AP model rats. This suggests that exosomes exert their protective function by interfering with NF-κB-driven transcriptional responses that contribute to acinar cell damage and systemic

Table 4. Evaluation of risk factors associated with acute pancreatitis

Variables	Multivariate-enter method		Multivariate-forward: LR method	
	OR (95% CI)	p	OR (95% CI)	p
Amylase (U/L)	1.112 (0.951–1.299)	0.183	1.149 (0.996–1.324)	0.056
Body mass index	1.624 (0.919–2.870)	0.095	–	–
Hypertension	5.595 (0.000–12.460)	0.999	–	–
Triglyceride (mg/dL)	1.005 (0.958–1.054)	0.844	–	–

Forward LR and Enter methods were used for logistic regression analysis. Enter model: Hosmer Lemeshow test p=0.757, Cox & Snell R^2=0.714 Nagelkerke R^2=0.952, -2 Log Likelihood=13.173; forward LR model: Hosmer Lemeshow test p=0.803, Cox & Snell R^2=0.703 Nagelkerke R^2=0.937, -2 Log Likelihood=16.844. OR: Odds ratio; CI: Confidence interval.

Table 5. Evaluation of AUC and optimum cut-off point of clinical parameters

Parametre	AUC (%95 CI)	p	Cut-off	Sensitivity (%)	Specificity (%)
Adiponectin (ug/L)	0.000 (0.000–0.000)	<0.001	3.4	1.000	1.000
NF-KB (ng/L)	1.000 (1.000–1.000)	<0.001	1.8	1.000	0.960
Amylase (U/L)	0.990 (0.978–1.000)	<0.001	95.3	0.960	1.000
Lipase (U/L)	1.000 (1.000–1.000)	<0.001	60.2	0.960	1.000

AUC: Area under the curve; CI: Confidence interval.

inflammation. These findings support the idea that targeting NF-κB signaling via acinar cell-derived exosomes may offer a novel therapeutic strategy for reducing inflammation and tissue injury in AP. Moreover, this mechanism reinforces the role of intercellular communication—via exosomes—as a regulator of disease severity in pancreatitis [21]. The NF-κB pathway is among the most studied inflammatory signaling pathways in acinar cells and is associated with more severe forms of AP [22]. Results of Yu et al. [23] demonstrate that NF-κB is activated in response to cerulein via NADPH oxidase-derived reactive oxygen species and that this activation is essential for the induction of PAP-1 gene expression in pancreatic acinar cells. Furthermore, recombinant adiponectin has been shown to inhibit inflammation via the NF-κB pathway in AP [13]. Our findings align with the idea that adiponectin exerts protective effects by reducing NF-κB activity and pro-inflammatory cytokine responses in cerulein-induced AP, offering hope for the development of therapies targeting AP. As increasing adiponectin pharmacologically has shown promise in obesity treatment, it is possible that adiponectin may play a significant role in AP treatment in the future.

Recent studies have emphasized the role of adiponectin as an important regulator of inflammation, demonstrating its potential as a biomarker for assessing disease severity in inflammatory conditions such as AP [24]. Consistent with this, our study found higher serum NF-κB activity in the AP group, suggesting that inhibiting the NF-κB pathway could mitigate the early inflammatory response and offer potential new therapeutic approaches for AP. According to the results of this meta-analysis, adiponectin levels were not significantly different between patients with severe acute pancreatitis (SAP) and those with mild acute pancreatitis (MAP). Specifically, the standardized mean difference (SMD) was 0.11 (95% CI: -0.17 to 0.40, p=0.425), indicating no statistically significant association. Despite adiponectin's known anti-inflammatory properties, these findings suggest that it does not play a major role in the pathogenesis or severity differentiation of SAP. It also implies that adiponectin is unlikely to serve as a reliable biomarker for predicting or diagnosing severe forms of acute pancreatitis in clinical settings. While adiponectin is biologically active in inflammation regulation, its levels do not appear to be significantly altered in SAP, and thus it holds limited potential as a diagnostic or prognostic marker for this condition. Further research with larger, more homogenous patient populations may be necessary to clarify any potential role in specific subgroups [10]. Our study confirmed lower adiponectin levels in the AP group and observed a strong negative correlation between adiponectin and NF-κB levels. No significant correlation was found between adiponectin and amylase levels, reinforcing adiponectin's anti-inflammatory role. Adiponectin, an adipocyte-derived cytokine, is recognized for its anti-inflammatory and insulin-sensitizing effects, which are particularly important in inflammatory diseases such as AP [25]. Wos-Wroniewicz et al. [11] reported adiponectin in AP. Experimental studies have shown that adiponectin can inhibit NF-κB activation and downregulate pro-inflammatory cytokines like TNF-α and IL-6, thereby mitigating pancreatic inflammation [11, 13, 26]. These findings highlight adiponectin's modulatory role on the NF-κB pathway, a key mediator of inflammatory signaling in AP [27]. Adiponectin levels were significantly reduced in obese rats compared to the normal group, which is consistent with the known inverse relationship between adiponectin and obesity-related inflammation. Importantly, treatment with Sheng-jiang powder (SJP) re-

sulted in significantly increased serum adiponectin levels in the SJP-treated group (HSG) compared to the untreated obese group (HLG) [28]. This suggests that SJP may exert its protective effects against obesity-induced pancreatic inflammation partly by restoring or enhancing adiponectin levels. Given adiponectin's role in activating the AMPK signaling pathway, which is known to have anti-inflammatory and metabolic regulatory effects, this finding highlight adiponectin as a key mediator in the therapeutic mechanism of SJP. This supports the potential therapeutic significance of adiponectin in AP.

The NF-κB pathway as a central mediator in the inflammatory response associated with AP. NF-κB plays a pivotal role in the transcription of pro-inflammatory cytokines and chemokines, contributing to the development and progression of pancreatic injury and systemic complications. Natural plant-derived compounds can exert anti-inflammatory effects in AP by inhibiting the NF-κB signaling pathway. By blocking NF-κB activation, these phytochemicals reduce the production of inflammatory mediators, thus alleviating the severity of the disease. Targeting NF-κB with phytochemicals represents a promising therapeutic strategy for managing AP. These findings support continued research into natural compounds that can modulate this key inflammatory pathway and potentially lead to the development of effective treatments for AP [29]. Adiponectin is known to inhibit the ROS/NF-κB/NLRP3 inflammatory pathway, which may help differentiate pancreatic cancer (PC) from chronic pancreatitis (CP) in patients with elevated CA-19-9 levels, suggesting a potential diagnostic role for adiponectin in distinguishing CP from PC [30, 31].

Although adiponectin levels were numerically higher in females compared to males in both the acute pancreatitis and healthy control groups, the differences were not statistically significant. Similarly, NF-κB levels did not show a statistically significant difference between genders. These findings are consistent with previous studies suggesting that while adiponectin levels tend to be higher in females due to hormonal influences—particularly estrogen—this difference may not always reach statistical significance in small or moderate-sized study populations [32]. The lack of significance in our study may be attributed to the limited sample size and the cross-sectional design.

The ROC analysis demonstrated that NF-κB and lipase levels had perfect diagnostic performance in distinguishing patients from healthy individuals, with an AUC of 1.000, indicating excellent discriminatory ability. Similarly, amylase also showed near-perfect performance with an AUC of 0.990. These findings suggest that these biomarkers could serve as highly reliable indicators in the clinical differentiation between patient and control groups. In contrast, the adiponectin value, despite reporting 100% sensitivity and specificity, showed an AUC of 0.000, which is inconsistent and likely due to a data recording or analytical error. Overall, the high AUC values and corresponding sensitivity/specificity metrics support the potential diagnostic utility of these parameters, although external validation and larger sample sizes are necessary to confirm these preliminary results. Although weak correlations were observed between NF-κB and amylase, as well as between these biomarkers and lipase, these findings do not undermine the potential clinical relevance of NF-κB and adiponectin. Unlike amylase and lipase, which primarily reflect enzymatic activity, NF-κB and adiponectin provide insights into the inflammatory and metabolic dimensions of AP. Their combined evaluation with traditional markers may enhance disease characterization and should be further investigated in longitudinal studies. In this study, no variable was identified as an independent risk factor for AP in multivariate analysis. Although amylase and BMI showed borderline significance, they did not retain significance in the final models. Both regression models demonstrated good fit, but the lack of significant predictors may reflect sample size limitations. Although this study investigated the potential impact of various clinical and biochemical parameters on the development of AP, no statistically significant independent risk factor was identified. Larger-scale and prospective studies are needed to validate these findings. Additionally, exploring potential interactions and unmeasured confounders may contribute to a better understanding of the pathogenesis of AP.

Limitations of the study

This study has several limitations that should be acknowledged. First, the sample size was relatively limited, which may affect the generalizability of the findings. Larger, multicenter studies are needed to validate our results across more diverse patient populations. Second, insulin levels were not measured, which is a notable limitation given the known association between adiponectin, insulin sensitivity, and metabolic status. Inclusion of insulin and HOMA-IR values could have provided deeper insight into the relationship between metabolic regulation and inflammation in acute pancreatitis. Third, the study design was cross-sectional, preventing us from assessing changes in NF-κB and adiponectin levels over time or establishing causal relationships. Longitudinal studies would allow better evaluation of these markers throughout the disease course. Lastly, although NF-κB and adiponectin were evaluated as potential biomarkers, other relevant inflammatory and metabolic markers such as IL-6, TNF-α, CRP, or leptin were not included, which could have enriched the interpretation of the inflammatory pathways involved in disease severity. Despite these limitations, our findings contribute to the growing body of evidence supporting the role of inflammatory and metabolic biomarkers in acute pancreatitis and highlight areas for future investigation.

Conclusion

Our study aims to guide future research on the use of elevated serum NF-κB and decreased serum adiponectin levels—either alone or in combination with existing scoring systems—in evaluating disease severity in AP. Despite significant research, it remains unclear which scoring systems or laboratory parameters are most effective in assessing the severity of AP. Therefore, further clinical and experimental studies, particularly multicenter trials with larger patient populations, are necessary to identify reliable markers for disease assessment in AP.

Ethics Committee Approval: The study was approved by the Biruni University Faculty of Medicine Ethics Committee (no: 2024-BİAEK/05-04, date: 12/12/2024).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: No AI technologies utilized.

Authorship Contributions: Concept – N.F.M., H.U.; Design – N.F.M., G.G.O., S.H.; Supervision – N.F.M., H.U.; Funding – N.F.M., H.U.; Materials – S.H.; Data collection and/or processing – G.G.O.; Data analysis and/or interpretation – N.F.M., H.U., G.G.O., S.H.; Literature search – N.F.M., H.U., S.N.A.; Writing – N.F.M., H.U., G.G.O., S.H., S.N.A.; Critical review – N.F.M., H.U., G.G.O., S.H., S.N.A.

Peer-review: Externally peer-reviewed.

References

1. Rafaqat S, Radoman-Vujačić I, Patoulias D, Khurshid H, Klisić A. Adipokines and their role in acute pancreatitis. J Med Biochem 2024;43(4):512–27. [CrossRef]
2. Capurso G, Ponz de Leon Pisani R, Lauri G, Archibugi L, Hegyi P, Papachristou GI, et al. Clinical usefulness of scoring systems to predict severe acute pancreatitis: A systematic review and meta-analysis with pre and post-test probability assessment. United European Gastroenterol J 2023;11(9):825–36. [CrossRef]
3. Yu H, Lin L, Zhang Z, Zhang H, Hu H. Targeting NF-κB pathway for the therapy of diseases: Mechanism and clinical study. Signal Transduct Target Ther 2020;5(1):209. [CrossRef]
4. Kunnumakkara AB, Shabnam B, Girisa S, Harsha C, Banik K, Devi TB, et al. Inflammation, NF-κB, and Chronic Diseases: How are They Linked?. Crit Rev Immunol 2020;40(1):1–39. [CrossRef]
5. Bang E, Kim DH, Chung HY. Protease-activated receptor 2 induces ROS-mediated inflammation through Akt-mediated NF-κB and FoxO6 modulation during skin photoaging. Redox Biol 2021;44:102022. [CrossRef]
6. Chen S, Zhu J, Sun LQ, Liu S, Zhang T, Jin Y, et al. LincRNA-EPS alleviates severe acute pancreatitis by suppressing HMGB1-triggered inflammation in pancreatic macrophages. Immunology 2021;163(2):201–19. [CrossRef]
7. Li Q, Yang G, Feng M, Zheng S, Cao Z, Qiu J, et al. NF-κB in pancreatic cancer: Its key role in chemoresistance. Cancer Lett 2018;421:127–34. [CrossRef]
8. Zhang GX, Zhan C, Wang K, Han J, Shang D, Chen HI. Qingyi Decoction amerliorates acute biliary pancreatitis by targeting Gpbar1/NF-kb pathway. Front Biosci (Landmark Ed) 2019;24(5):833–48. [CrossRef]
9. Fang H, judd RL. Adiponectin regulation and function. Compr Physiol 2018;8:1031–63. [CrossRef]
10. Yu X, Zhang N, Wu J, Zhao Y, Liu C, Liu G. Predictive value of adipokines for the severity of acute pancreatitis: A meta-analysis. BMC Gastroenterol 2024;24(1):32. [CrossRef]
11. Wos-Wroniewicz E, Caban M, Malecka-Panas E. Role of adipokines in the assessment of severity and predicting the clinical course of acute pancreatitis. J Physiol Pharmacol 2020;71(5):605–14.
12. Mester P, Räth U, Schmid S, Müller M, Buechler C, Pavel V. Exploring the relationship between plasma adiponectin, gender, and underlying diseases in severe illness. Biomedicines 2023;11(12):3287. [CrossRef]
13. Dikmen K, Bostanci H, Gobut H, Yavuz A, Alper M, Kerem M. Recombinant adiponectin inhibits inflammation processes via NF-kB pathway in acute pancreatitis. Bratisl Lek Listy 2018;119:619–24. [CrossRef]
14. Hontsariuk DO, Ferfetska KV, Khrystych TM, Fediv OI, Temerivska TG, Jiguleva EO, et al. Incides of C-reactive protein, tumor necrosis factor-α, adiponectin, leptin and resistin in the blood of patients suffering from chronic pancreatitis and type 2 diabetes mellitus. J Med Life 2020;13(4):568–71. [CrossRef]
15. Toçoğlu AG, Köksal AŞ, Toka B, Mutlu F, Eminler AT, Uslan Mİ, et al. Validation of the revised Atlanta criteria in determining the severity of acute pancreatitis. Eur J Gastroenterol Hepatol 2023;35(10):1137–42. [CrossRef]
16. Szatmary P, Grammatikopoulos T, Cai W, Huang W, Mukherjee R, Halloran C, et al. Acute pancreatitis: Diagnosis and treatment. Drugs 2022;82(12):1251–76. [CrossRef]
17. Zheng Z, Ding YX, Qu YX, Cao F, Li F. A narrative review of acute pancreatitis and its diagnosis, pathogenetic mechanism, and management. Ann Transl Med 2021;9(1):69. [CrossRef]
18. Mayerle J, Sendler M, Hegyi E, Beyer G, Lerch MM, Sahin-Tóth M. Genetics, cell biology, and pathophysiology of pancreatitis. Gastroenterology 2019;156(7):1951–68.e1. [CrossRef]
19. Saluja A, Dudeja V, Dawra R, Sah RP. Early intra-acinar events in pathogenesis of 65 pancreatitis. Gastroenterology 2019;156(7):1979–93. [CrossRef]
20. Wu J, Liu X, Xiao H, Xu L, Tang Z, Wu Y, et al. Protective effects of HTD4010, a Reg3a/PAP-derived peptide, in a mouse model of hypertriglyceridemic acute pancreatitis: Involvement of TLR4/NF-kappa B. Biochem Biophys Res Commun 2022;630:118–24. [CrossRef]
21. Guo Y, Cao F, Ding Y, Lu J, Liu S, Li F. acinar cells derived exosomes alleviate the severity of acute pancreatitis. Discov Med 2021;31(163):95–105.
22. Yang J, Tang X, Li B, Shi J. Sphingosine 1-phosphate receptor 2 mediated early stages of pancreatic and systemic inflammatory responses via NF-kappa B activation in acute pancreatitis. Cell Commun Signal 2022;20(1):157. [CrossRef]
23. Yu JH, Lim JW, Kim H. Pancreatitis-associated protein-1 suppresses apoptosis in cerulein-stimulated pancreatic acinar cells in response to nuclear factor-kappa B activation. J Physiol Pharmacol 2019;70(6):849–57.
24. Gulumsek E, Yesildal F, Avci BS, Yigitdol I, Aktaş B, Kara B, et al. Monocyte to high-density lipoprotein and derived neutrophil to lymphocyte ratio in patients with acute pancreatitis are associated with the severity of the disease. Int J Med Biochem 2022;5:77–83.
25. Kishida K, Funahashi T, Shimomura I. Adiponectin as a routine clinical biomarker. Best Pract Res Clin Endocrinol Metab 2014;28(1):119–30. [CrossRef]

26. Maximus PS, Al Achkar Z, Hamid PF, Hasnain SS, Peralta CA. Adipocytokines: Are they the theory of everything? Cytokine 2020;133:155144. [CrossRef]
27. Araki H, Nishihara T, Matsuda M, Fukuhara A, Kihara S, Funahashi T, et al. Adiponectin plays a protective role in caerulein-induced acute pancreatitis in mice fed a high-fat diet. Gut 2008;57(10):1431–40. [CrossRef]
28. Miao YF, Li J, Zhang YM, Zhu L, Chen H, Yuan L, et al. Shengjiang powder ameliorates obesity-induced pancreatic inflammatory injury via stimulating activation of the AMPK signalling pathway in rats. World J Gastroenterol 2018;24(39):4448–61. [CrossRef]
29. Jiang W, Li X, Zhang Y, Zhou W. Natural compounds for the treatment of acute pancreatitis: Novel anti-inflammatory therapies. Biomolecules 2024;14(9):1101. [CrossRef]
30. Xu X, Huang X, Zhang L, Huang X, Qin Z, Hua F. Adiponectin protects obesity-related glomerulopathy by inhibiting ROS/NF-κB/NLRP3 inflammation pathway. BMC Nephrol 2021;22(1):218. [CrossRef]
31. Dranka-Bojarowska D, Lekstan A, Olakowski M, Jablonska B, Lewinski A, Musialski P, et al. The assessment of serum concentration of adiponectin, leptin and serum carbohydrate antigen-19.9 in patients with pancreatic cancer and chronic pancreatitis. J Physiol Pharmacol 2015;66(5):653–63.
32. Khoramipour K, Chamari K, Hekmatikar AA, Ziyaiyan A, Taherkhani S, Elguindy NM, et al. Adiponectin: Structure, physiological functions, role in diseases, and effects of nutrition. Nutrients 2021;13(4):1180. [CrossRef]