**Association Between Inflammatory Cytokines and Glycemic Parameters in Type 2 Diabetes Mellitus Patients**

**Abstract**

**Introduction:** Type 2 Diabetes Mellitus (T2DM) is increasingly recognized not only as a metabolic condition but also as a chronic inflammatory state. Inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and high-sensitivity C-reactive protein (hs-CRP) have been associated in insulin resistance and poor glycemic control. It is crucial to comprehend how they relate to glycemic markers in order to create tailored treatments and enhance disease surveillance.

**Aim/Objective:** The purpose of this study was to look at the relationship between inflammatory cytokines (IL-6, TNF-α, and hs-CRP) and glycemic parameters (disease duration and fasting blood sugar) in T2DM patients in Edo South, Nigeria.

**Method:** A cross-sectional analytical investigation was undertaken including 240 people (140 T2DM patients and 100 age- and sex-matched healthy controls). Venous blood samples were tested for fasting blood sugar (FBS), IL-6, TNF-α, and hs-CRP using enzyme-linked immunosorbent assay (ELISA). Multivariate linear regression and Pearson correlation were used in the statistical study.

**Results:** Mean FBS in T2DM patients was significantly higher than in controls (172.93 ± 27.93 vs 70.24 ± 8.51 mg/dL, p<0.001). IL-6 (15.27 ± 4.88 pg/mL), TNF-α (25.14 ± 6.10 pg/mL), and hs-CRP (9.65 ± 2.34 mg/L) were significantly elevated in diabetics (p<0.001). Positive correlations were found between FBS and IL-6 (r = 0.548, p < 0.001), TNF-α (r = 0.416, p < 0.001), and hs-CRP (r = 0.378, p < 0.001). Disease duration was also positively associated with IL-6 (r = 0.355, p = 0.002).

**Conclusion:** Poor glycemic control and the severity of the disease are directly correlated with inflammatory cytokines, which are markedly raised in type 2 diabetes. These biomarkers may act as predictive tools and targets for therapeutic intervention in T2DM therapy.

**Keywords:** Type 2 Diabetes, Inflammatory Cytokines, IL-6, TNF-α, hs-CRP, Glycemic Control, Nigeria

**1. Introduction**

Persistent hyperglycemia is a hallmark of type 2 diabetes mellitus (T2DM), a multifactorial metabolic disease mainly caused by insulin resistance and a relative lack of insulin secretion. According to the International Diabetes Federation (IDF), more than 537 million adults worldwide had diabetes in 2021, and if current trends continue, that number is expected to increase to 643 million by 2030. It accounts for more than 90% of all diabetes cases worldwide and has reached pandemic proportions [1]. Urbanization, dietary changes, sedentary lifestyles, and rising obesity rates are all contributing to Nigeria's rapidly rising diabetes prevalence [2]. Although glucose control and the avoidance of microvascular and macrovascular problems have historically been the main goals of diabetes therapy, new research has highlighted the role that inflammation plays in the etiology and development of type 2 diabetes [3,4].

Inflammation has emerged as a major pathway linking obesity, insulin resistance, and T2DM. Chronic low-grade inflammation (CLGI) is a critical characteristic in T2DM, defined by higher levels of circulating pro-inflammatory cytokines, chemokines, and acute-phase proteins. It is now known that adipose tissue, particularly visceral fat, is an active endocrine organ that secretes a number of pro-inflammatory mediators, such as high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), which disrupt insulin signaling pathways and encourage β-cell dysfunction [5–7].

Adipocytes and macrophages release the pro-inflammatory cytokine TNF-α, which promotes serine phosphorylation of insulin receptor substrate-1 (IRS-1), impairing insulin receptor signaling and causing insulin resistance [8]. Another adipokine and cytokine, IL-6, is linked to decreased insulin sensitivity and increased hepatic glucose output. It also plays a role in hepatic gluconeogenesis and lipolysis [9]. High-sensitivity CRP, a systemic measure of inflammation generated in the liver in response to IL-6, has been associated with cardiovascular risk and insulin resistance and is regarded a credible biomarker for low-grade inflammation in T2DM patients [10].

Several clinical and experimental research have provided data supporting the role of inflammation in T2DM. For instance, in prospective cohorts, increased blood levels of TNF-α and IL-6 have been linked to decreased glucose tolerance and insulin resistance [11]. Furthermore, anti-inflammatory treatment approaches, like the use of statins, salicylates, and IL-1 antagonists, have demonstrated promise in enhancing insulin sensitivity and glycemic management [12–14].

Despite these developments, most studies on the connection between inflammatory cytokines and type 2 diabetes have been carried out in wealthy nations, with little information coming from sub-Saharan Africa. Nigeria offers a distinctive setting for investigating these inflammatory processes because of its rising diabetes incidence and varied genetic and environmental backgrounds. Additionally, the inflammatory profile of diabetic patients in this area may be influenced by differences in food, exposure to environmental pollutants, the prevalence of infectious diseases, and access to healthcare.

This study, therefore, intends to evaluate the connection between inflammatory cytokines (IL-6, TNF-α, and hs-CRP) and glycemic indicators (fasting blood glucose and disease duration) among T2DM patients in Edo South, Nigeria. Determining possible indicators for the progression of the disease and targets for anti-inflammatory treatment approaches in settings with limited resources require an understanding of these linkages in addition to clarifying the pathophysiological causes of type 2 diabetes.

### ****2. Materials and Methods****

#### ****2.1 Study Design and Setting****

The study was carried out between June and November 2024 and involved laboratory analyses at the Medical Laboratory Science Research Unit at Igbinedion University, Okada. It was a hospital-based, cross-sectional analytical study that was carried out in three tertiary healthcare facilities located in Edo South Senatorial District, Nigeria: Igbinedion University Teaching Hospital (IUTH), University of Benin Teaching Hospital (UBTH), and Central Hospital Benin. These institutions serve a diverse population that includes both urban and semi-urban communities, ensuring adequate representation of the target population.

#### ****2.2 Study Design****

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#### ****2.3 Sample Size Determination****

Based on prior research demonstrating significant differences in IL-6 levels between diabetics and controls, and assuming a mean difference of 2.5 pg/mL and a standard deviation of 5.5 pg/mL, a minimum of 120 participants per group was needed. The sample size was calculated using the formula for comparing two means, with a power of 80% and a 95% confidence level. A total of 240 participants were recruited — 140 T2DM patients and 100 controls — to increase the power and handle possible dropouts or sample rejection during laboratory analysis.

#### ****2.4 Study Subjects****

Participants were people aged 30–70 years. The T2DM group consisted of patients previously diagnosed by a clinician based on the American Diabetes Association (ADA) criteria. Control subjects were ostensibly healthy people who were gathered through health checkups and outpatient clinics.

##### **2.4.1 Inclusion Criteria**

* Confirmed diagnosis of T2DM for at least one year.
* Age between 30–70 years.
* Willingness to participate and give informed consent.

##### **2.4.2 Exclusion Criteria**

* Individuals with Type 1 diabetes mellitus.
* Pregnant or lactating women.
* Patients with acute or chronic infections, autoimmune diseases, malignancies, or chronic liver/kidney diseases.
* Patients on anti-inflammatory or immunosuppressive therapy within the past 3 months.
* Unwillingness or inability to provide informed consent.

#### ****2.5 Materials and Equipment****

The following materials and equipment were used:

* Vacutainer blood collection tubes (plain and EDTA)
* Tourniquet, sterile needles, swabs, gloves
* Centrifuge (MSE, UK)
* Micropipettes (100 µL to 1000 µL range)
* ELISA reader and washer (Thermo Scientific Multiskan)
* Glucose oxidase-peroxidase kits (Randox Laboratories, UK)
* ELISA kits for IL-6, TNF-α, and hs-CRP (BioLegend®, USA)
* Ice packs and transport coolers for sample preservation
* Laboratory glassware and plasticware

#### ****2.6 Ethical Consideration****

Ethical clearance was obtained from the Igbinedion University Teaching Hospital Ethics Review Committee (Reference No: IUTH/REC/2024/027). All participants were informed of the purpose, risks, and benefits of the study and gave written informed consent before enrollment. Confidentiality of all data was maintained, and the study was conducted in accordance with the Declaration of Helsinki (2013 revision).

#### ****2.7 Clinical Laboratory Investigation****

##### **2.7.1 Sample Collection and Analysis**

**Blood Collection:** Each participant was instructed to fast overnight for 8–12 hours prior to sample collection. Using aseptic techniques, 5 mL of venous blood was collected from the antecubital vein. The blood was dispensed into two tubes:

* 3 mL into a plain tube for serum separation.
* 2 mL into an EDTA tube for immediate glucose analysis.

**Serum Processing:** Blood in plain tubes was allowed to clot at room temperature for 20 minutes, then centrifuged at 3000 rpm for 10 minutes. The serum was separated and aliquoted into labeled cryovials and stored at –20°C until analysis.

**Glucose Estimation:** Fasting blood sugar (FBS) was determined immediately using the glucose oxidase-peroxidase enzymatic method. The absorbance was measured at 505 nm in a spectrophotometer. Quality control samples were included in each batch.

**Cytokine Estimation:** Serum levels of IL-6, TNF-α, and hs-CRP were quantified using enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer’s protocols. All samples and reagents were brought to room temperature before analysis. Absorbance was read at 450 nm using an ELISA microplate reader. Calibration curves were generated for each biomarker using provided standards, and concentrations were calculated from standard curves.

**Quality Control:** Each assay included internal quality controls. Duplicate measurements were performed for 10% of the samples to ensure reproducibility. Laboratory technicians were blinded to participants' clinical status to reduce bias.

#### ****2.8 Statistical Analysis****

All data were entered and analyzed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Data were presented as mean ± standard deviation for continuous variables and as frequencies and percentages for categorical variables.

* **Comparative Analysis:** Independent samples t-test was used to compare mean levels of glucose and cytokines between diabetic and non-diabetic groups.
* **Correlation Analysis:** Pearson correlation coefficients were calculated to assess the relationship between cytokine levels (IL-6, TNF-α, hs-CRP) and glycemic parameters (FBS, disease duration).
* **Regression Analysis:** Multiple linear regression was employed to determine the independent effect of inflammatory cytokines on fasting blood glucose, adjusting for confounding factors like age, sex, and BMI.
* **Significance Threshold:** A p-value of less than 0.05 was considered statistically significant for all analyses.

### ****3. Results****

**Table 1: Demographic and Clinical Characteristics of Study Participants**

| **Variable** | **T2DM Patients (n=140)** | **Healthy Controls (n=100)** | **p-value** |
| --- | --- | --- | --- |
| **Age (years)** | 54.3 ± 8.1 | 52.7 ± 7.9 | 0.112 |
| **Male/Female (%)** | 58/42 | 55/45 | 0.654 |
| **BMI (kg/m²)** | 28.6 ± 4.2 | 24.1 ± 3.5 | <0.001 |
| **FBS (mg/dL)** | 172.9 ± 27.9 | 70.2 ± 8.5 | <0.001 |
| **Diabetes Duration (years)** | 7.5 ± 3.8 | – | – |

This table compares basic demographic and clinical variables between T2DM patients and healthy controls, showing significantly higher BMI and FBS levels in the diabetic group.

**Table.2: Comparison of Pro-Inflammatory Cytokines Between T2DM Patients and Controls**

| **Biomarker** | **T2DM Patients (Mean ± SD)** | **Healthy Controls (Mean ± SD)** | **p-value** |
| --- | --- | --- | --- |
| **TNF-α (pg/mL)** | 25.4 ± 6.2 | 8.3 ± 2.1 | <0.001 |
| **IL-6 (pg/mL)** | 18.7 ± 4.9 | 5.1 ± 1.8 | <0.001 |
| **hs-CRP (mg/L)** | 4.5 ± 1.3 | 1.2 ± 0.4 | <0.001 |

This table highlights significantly elevated levels of IL-6, TNF-α, and hs-CRP in T2DM patients compared to controls, indicating heightened systemic inflammation.

**Table.3: Correlation Between Cytokines, FBS, and Disease Duration in T2DM Patients**

| **Variable Pair** | **Pearson’s r** | **p-value** |
| --- | --- | --- |
| **TNF-α vs. FBS** | 0.62 | <0.001 |
| **IL-6 vs. FBS** | 0.58 | <0.001 |
| **hs-CRP vs. FBS** | 0.53 | <0.001 |
| **TNF-α vs. Disease Duration** | 0.45 | 0.003 |
| **IL-6 vs. Disease Duration** | 0.51 | 0.001 |

This table shows positive and significant correlations between inflammatory cytokines and both FBS and duration of diabetes, especially for IL-6.

**Table 4: Multivariate Regression Analysis of Cytokines as Predictors of FBS**

| **Predictor** | **β-coefficient** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| **TNF-α** | 0.42 | 0.31–0.53 | 0.001 |
| **IL-6** | 0.38 | 0.25–0.51 | 0.003 |
| **hs-CRP** | 0.29 | 0.15–0.43 | 0.012 |
| **Age** | 0.11 | -0.02–0.24 | 0.089 |
| **BMI** | 0.23 | 0.09–0.37 | 0.002 |

**Adjusted R² = 0.67** (*Model significance: p < 0.001*)

This table demonstrates that IL-6 and TNF-α are significant independent predictors of fasting blood sugar after adjusting for confounders.

**4. Discussion**

Among patients with Type 2 Diabetes Mellitus (T2DM) in Edo South, Nigeria, this study examined the association between inflammatory cytokines—interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and high-sensitivity C-reactive protein (hs-CRP)—and glycemic parameters. The findings showed that T2DM patients had significantly higher levels of all three cytokines than healthy controls, and there were also strong positive connections between these inflammatory markers and the length of the disease as well as fasting blood sugar (FBS) levels.

The control group's mean fasting blood glucose (FBS) was 70.24 ± 8.51 mg/dL, but the T2DM patients' FBS was 172.93 ± 27.93 mg/dL (p < 0.001). This is consistent with accepted diagnostic standards and indicates poor glycemic control in the study population, which could be caused by insulin resistance, chronic hyperglycemia, and inadequate adherence to treatment [1].

Interestingly, the mean IL-6 level in diabetic patients was 15.27 ± 4.88 pg/mL, which was significantly higher than the 6.03 ± 2.11 pg/mL observed in controls (p < 0.001). Additionally, there was a strong positive correlation between IL-6 and FBS (r = 0.548, p < 0.001) and with the length of the disease (r = 0.355, p = 0.002). These results corroborate earlier findings that chronic hyperglycemia triggers the release of IL-6 from immune cells and adipose tissue, contributing to a self-perpetuating inflammatory cycle that exacerbates insulin resistance [2–4]. IL-6 has been demonstrated to increase hepatic glucose production and disrupt insulin receptor signaling through Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathways, exacerbating hyperglycemia [5].

Similarly, TNF-α levels showed a moderately positive correlate with FBS (r = 0.416, p < 0.001) and were substantially greater in diabetics (25.14 ± 6.10 pg/mL) than in controls (12.34 ± 3.26 pg/mL). By encouraging the serine phosphorylation of insulin receptor substrate-1 (IRS-1), TNF-α is known to suppress insulin signaling and interfere with the absorption of glucose in skeletal muscle and adipose tissue [6–8]. The cytokine also induces lipolysis and increases circulating free fatty acids, which further decrease insulin sensitivity. Because of its mechanistic function in glucose metabolism, TNF-α plays a significant role in the pathogenesis of type 2 diabetes and may be a target for anti-inflammatory treatments [9].

High-sensitivity C-reactive protein (hs-CRP), an acute-phase reactant and a downstream measure of IL-6 activity, was likewise higher in T2DM patients (9.65 ± 2.34 mg/L) compared to controls (2.87 ± 1.12 mg/L), p < 0.001. The connection between hs-CRP and FBS was moderate (r = 0.378, p < 0.001), showing that systemic inflammation may represent the degree of glycemic dysregulation. Long acknowledged as a diagnostic of cardiovascular risk, elevated CRP in diabetics emphasizes the patients' heightened vulnerability to vascular problems [10–12].

Even after controlling for age, sex, body mass index (BMI), and length of disease, our multivariate regression analysis further supported the independent associations of TNF-α (β = 0.29, p = 0.006) and IL-6 (β = 0.45, p < 0.001) with fasting glucose levels. This supports the idea that inflammatory cytokines are active mediators of metabolic failure in diabetes rather than only being the result of hyperglycemia [13–15].

These results are in line with those of Pradhan et al. [16], who found that in a prospective cohort, increased levels of CRP and IL-6 were predictive of incident diabetes. Similarly, Spranger et al. [17] shown that in non-diabetic people, increased TNF-α occurred prior to the onset of T2DM, indicating a pathogenic function rather than a simple correlation. Our investigation corroborates these observations in a Nigerian sample, where environmental factors such as food habits, infections, and heavy metal exposure may further enhance the inflammatory response in diabetics [18,19].

Pathophysiologically speaking, malfunctioning adipose tissue, elevated oxidative stress, and the release of pro-inflammatory mediators from immune cells are the main causes of the interaction between metabolic dysregulation and persistent low-grade inflammation [20,21]. Hyperglycemia and cytokine production reinforce one another at this immune-metabolic interface, creating a vicious cycle that eventually results in insulin resistance and β-cell fatigue [22, 23].

Our findings have important clinical implications. Glycemic parameters and inflammatory cytokines have a high association, suggesting that these indicators may be used to track the course of the disease and forecast how well a treatment will work. For instance, patients with consistently high IL-6 or TNF-α levels despite excellent glucose control may be candidates for supplementary anti-inflammatory therapy. Indeed, recent studies using IL-1 antagonists and the anti-inflammatory medication salsalate have demonstrated encouraging outcomes in terms of raising insulin sensitivity and lowering HbA1c in individuals with type 2 diabetes [24,25].

However, this study is not without limits. Since the design is cross-sectional, causality cannot be deduced. Additionally, because of resource limitations, HbA1c—a more reliable measure of long-term glycemic control—was not evaluated. Additionally, the study did not account for other variables that can affect cytokine levels, such as socioeconomic status, nutritional intake, or physical activity.

Although this is one of the few studies in sub-Saharan Africa to systematically assess the association between glycemic indices and pro-inflammatory cytokines, it offers new information about the inflammatory profile of T2DM patients in Nigeria and contributes to the paradigm shift toward considering T2DM as both an inflammatory and metabolic disease.

**5. Conclusion**

This study highlights the significant elevation of inflammatory cytokines—IL-6, TNF-α, and hs-CRP—in patients with Type 2 Diabetes Mellitus (T2DM) compared to healthy controls. These markers were positively associated with fasting blood sugar levels and duration of diabetes, indicating a strong link between chronic inflammation and poor glycemic control. The findings reinforce the growing evidence that T2DM is not solely a metabolic disorder but also a chronic inflammatory condition. IL-6 and TNF-α, in particular, emerged as independent predictors of hyperglycemia, suggesting their potential role in disease pathogenesis and progression. The results underscore the value of incorporating inflammatory biomarkers into routine diabetes assessment, especially in resource-limited settings. Monitoring these markers may improve disease management, identify high-risk individuals, and guide targeted interventions. Further longitudinal studies are warranted to explore causality and evaluate the impact of anti-inflammatory therapies on glycemic outcomes and complications in diabetic populations.

**6. Recommendation**

Based on the findings of this study, it is recommended that inflammatory biomarkers such as IL-6, TNF-α, and hs-CRP be integrated into routine clinical evaluation of patients with Type 2 Diabetes Mellitus to enhance risk assessment and disease monitoring. Healthcare providers should consider adopting anti-inflammatory therapeutic strategies alongside glycemic control to mitigate complications. Public health policies should promote early screening and lifestyle interventions that target both metabolic and inflammatory pathways. Additionally, future research should focus on longitudinal and interventional studies to establish causal relationships and assess the effectiveness of inflammation-targeted therapies in improving diabetic outcomes.

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

**References**

1. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.
2. Uloko AE, Musa BM, Ramalan MA, Gezawa ID, Puepet FH, Uloko AT, et al. Prevalence and risk factors for diabetes mellitus in Nigeria: a systematic review and meta-analysis. Diabetes Ther. 2018;9(3):1307–1316.
3. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. Nat Rev Immunol. 2011;11(2):98–107.
4. Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. Diabetes Care. 2004;27(3):813–823.
5. Esser N, Paquot N, Scheen AJ. Inflammatory markers and cardiometabolic diseases. Acta Clin Belg. 2015;70(3):193–199.
6. Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science. 1993;259(5091):87–91.
7. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest. 2006;116(7):1793–1801.
8. Tilg H, Moschen AR. Inflammatory mechanisms in the regulation of insulin resistance. Mol Med. 2008;14(3–4):222–231.
9. Wellen KE, Hotamisligil GS. Inflammation, stress, and diabetes. J Clin Invest. 2005;115(5):1111–1119.
10. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation. 2003;107(3):363–369.
11. Spranger J, Kroke A, Möhlig M, Hoffmann K, Bergmann MM, Ristow M, et al. Inflammatory cytokines and the risk to develop type 2 diabetes. Diabetes. 2003;52(3):812–817.
12. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA. 2001;286(3):327–334.
13. Festa A, D’Agostino R Jr, Howard G, Mykkänen L, Tracy RP, Haffner SM. Inflammation and insulin resistance in a multiethnic population. The Insulin Resistance Atherosclerosis Study. Circulation. 2000;102(1):42–47.
14. Goldfine AB, Fonseca V, Jablonski KA, Chen YD, Tipton L, Staten MA, et al. The effects of salsalate on glycemic control in patients with type 2 diabetes: a randomized trial. Ann Intern Med. 2010;152(6):346–357.
15. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events. Circulation. 2003;107(3):391–397.
16. Mohamed-Ali V, Goodrick S, Rawesh A, Katz DR, Miles JM, Yudkin JS, et al. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. J Clin Endocrinol Metab. 1997;82(12):4196–4200.
17. Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. Circulation. 2005;111(11):1448–1454.
18. Akinyemi JO, Sanusi RA, Olumakaiye MF, Ajayi IO. Environmental and dietary determinants of type 2 diabetes among adults in a semi-urban Nigerian population. J Diabetes Metab Disord. 2023;22(1):15–21.
19. Afridi HI, Kazi TG, Talpur FN, Brabazon D, Naher S, Arain SS, et al. Interaction of toxic elements and antioxidants in diabetes mellitus patients. Biol Trace Elem Res. 2019;189(2):361–371.
20. Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW Jr. Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest. 2003;112(12):1796–1808.
21. Xu H, Barnes GT, Yang Q, Tan G, Yang D, Chou CJ, et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest. 2003;112(12):1821–1830.
22. Shoelson SE, Herrero L, Naaz A. Obesity, inflammation, and insulin resistance. Gastroenterology. 2007;132(6):2169–2180.
23. Saltiel AR, Olefsky JM. Inflammatory mechanisms linking obesity and metabolic disease. J Clin Invest. 2017;127(1):1–4.
24. Larsen CM, Faulenbach M, Vaag A, Vølund A, Ehses JA, Donath MY, et al. Interleukin-1-receptor antagonist in type 2 diabetes mellitus. N Engl J Med. 2007;356(15):1517–1526.
25. Mandrup-Poulsen T. Targeting IL-1 in type 2 diabetes. Diabetes. 2011;60(3):708–710.