


C-Reactive Protein in Uncomplicated T2DM: Associations with Disease Duration and Lifestyle

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Article Info	ABSTRACT
<p>Keywords: C-Reactive Protein, Inflammation, Lifestyle, Type 2 Diabetes Mellitus,</p>	<p>Type 2 Diabetes Mellitus (T2DM) is a silent killer that may progress to severe complications without overt early symptoms. It arises from insulin secretion defects, insulin resistance, or both, resulting in chronic hyperglycemia. Prolonged hyperglycemia induces metabolic stress and systemic inflammation, exacerbated by modifiable lifestyle factors. Detecting subclinical inflammation (even in uncomplicated T2DM) is critical for timely intervention. We evaluated serum C-Reactive Protein (CRP), a hepatic inflammatory marker, in uncomplicated T2DM patients, assessing its links to disease duration and lifestyle. This cross-sectional analytical study enrolled 37 uncomplicated T2DM patients under routine care. CRP was quantified via latex agglutination; demographic/behavioral data were collected via questionnaires. CRP positivity occurred in 29.7% of patients (n=11), predominantly women (59.5%), aged 41-50 (62.2%), with T2DM duration <5 years (64.9%). CRP levels correlated significantly with disease duration (p = <0.001) and smoking (p = 0.016) but not diet (p = 0.580) or physical activity (p = 0.163). Nearly one-third of uncomplicated T2DM patients exhibited elevated CRP, strongly associated with disease duration and tobacco exposure (active or passive). CRP may serve as an early warning biomarker, urging tighter control of modifiable environmental and behavioral risks.</p>
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INTRODUCTION

Diabetes Mellitus (DM) remains a growing global health challenge, with its prevalence escalating annually. Insulin plays a pivotal role in facilitating glucose uptake into cells for energy production or storage, as well as regulating protein and lipid metabolism. Impaired insulin secretion, insulin resistance, or both lead to elevated blood glucose levels (hyperglycemia) (IDF, 2025). Chronic hyperglycemia induces organ damage and dysfunction, particularly in the eyes, kidneys, nerves, heart, and blood vessels (Widodo, 2014).

Type 2 Diabetes Mellitus (T2DM) accounts for 90-95% of all DM cases worldwide (ADA, 2024). Often termed a silent killer, T2DM progresses insidiously without overt symptoms yet carries a high risk of severe complications. These complications are broadly categorized into microangiopathy (retinopathy, nephropathy, neuropathy) and

macroangiopathy (coronary artery disease, stroke, peripheral vascular disease) (Wani et al., 2016). Evidence shows that individuals with longer disease duration experience significant functional decline, such as impaired balance and reduced quality of life, even in the absence of clinically manifest complications, reflecting an ongoing subclinical pathological burden (Dyah et al., 2014; Komalasari et al., 2023).

A key driver of T2DM progression is chronic low-grade inflammation, mediated by metabolic stress and immune dysregulation, which promotes proinflammatory cytokine release (González et al., 2023). C-Reactive Protein (CRP), an acute-phase reactant synthesized by the liver in response to inflammation, rises within 6-10 hours post-inflammatory stimulus, peaking at 24-48 hours. While healthy individuals typically exhibit serum CRP levels <5 mg/L, concentrations escalate markedly during acute or chronic inflammation (Nurisani et al., 2022; Tsamarah et al., 2021).

Lifestyle factors further exacerbate inflammatory responses in T2DM. Physical inactivity, tobacco exposure (active or passive), and diets high in fat and sugar amplify systemic inflammation, accelerating complications. Thus, effective T2DM management—through regular exercise, tobacco avoidance, and balanced nutrition—is critical to stabilizing blood glucose and mitigating inflammation (Rini et al., 2022).

Although CRP's role in T2DM-related inflammation is well-documented, data on CRP levels in uncomplicated T2DM patients remain scarce. Importantly, inflammation may precede overt complications. Disease duration and lifestyle factors (e.g., physical activity, tobacco exposure, diet) are hypothesized to elevate CRP levels. This study evaluates CRP levels in outpatient uncomplicated T2DM patients and their associations with disease duration and lifestyle, aiming to assess CRP's potential as a clinical monitoring tool for subclinical inflammation. The findings are expected to contribute not only to theoretical and scientific advancement in metabolic and inflammatory research but also offer practical implications in clinical diabetes care. This study may serve as a reference for clinicians and health policymakers in developing early monitoring strategies and preventive interventions to mitigate inflammation-driven complications in T2DM.

METHODS

This analytical cross-sectional study enrolled participants from the outpatient clinic of a regional healthcare facility. A cross-sectional design was selected as it allows for the concurrent assessment of exposures and outcomes within a defined population, making it efficient for identifying potential associations. While this design cannot establish causality, it is appropriate for hypothesis generation and provides a current overview of the conditions in uncomplicated T2DM patients (Kesmodel, 2018).

Samples were collected via accidental sampling over six months. This method was chosen due to the limited accessibility of respondents within a clinical setting and the feasibility of recruiting patients during routine visits. To minimize bias, only eligible patients attending routine check-ups were approached. Eligible respondents provided informed consent and met the following criteria: confirmed diagnosis of T2DM, regular follow-up visits at the healthcare facility and had no documented complications of diabetes.

Collected variables included sex, age, duration of T2DM (<5 years versus ≥ 5 years) (Rahmi et al., 2022), and lifestyle factors. Dietary habits were categorized as balanced (consistent consumption of nutritious meals) or unbalanced (frequent intake of high-sugar/fat foods) (Cao et al., 2025). Physical activity was classified as regular (≥ 2 sessions per week of brisk walking, cycling, or equivalent exercise) or irregular (<2 sessions per week) (Piotrowska et al., 2023). Tobacco exposure was assessed as frequent (near-daily exposure to active or passive smoking) or minimal (rare or no exposure) (Erikardo et al., 2024).

Venous blood samples were collected under aseptic conditions. Serum was separated by centrifugation at 3,000 rpm for 15 minutes. CRP levels were determined using latex agglutination method with Fortress CRP Latex Reagent, where agglutination indicated a positive result (CRP >6 mg/L). Positive and negative controls were processed simultaneously using identical protocols.

Data were analyzed using IBM SPSS Statistics 25. The Shapiro-Wilk normality test was conducted to determine the appropriate statistical procedure, and the results indicated non-normal distribution ($p = <0.05$); therefore, non-parametric tests were employed. Fisher's exact test was used to examine associations between CRP levels and T2DM duration, dietary habits, and physical activity, due to the presence of expected cell counts less than 5 in $\geq 20\%$ of the cells, while Chi-square test assessed relationships with tobacco exposure, as all cells met the minimum count assumptions for this variable. Statistical significance was set at $p < 0.05$ with 95% confidence intervals.

RESULTS AND DISCUSSION

The study included 37 eligible participants who provided written informed consent. Participants completed questionnaires with researcher guidance to ensure accurate responses, followed by venous blood collection for CRP analysis. As shown in Table 1, the majority of respondents were female (59.5%, $n=22$), aligning with previous studies reporting higher T2DM prevalence in women (62%) (Lariwu et al., 2024). This gender disparity may be attributed to women's greater susceptibility to increased body mass index and hormonal influences. Estrogen, through Estrogen Receptor alpha ($ER\alpha$) activation in hepatic, skeletal muscle, and adipose tissues, enhances glucose uptake and lipid oxidation, improving insulin sensitivity. However, hormonal fluctuations during menstrual cycles and postmenopause can significantly reduce estrogen levels, impairing insulin sensitivity and promoting visceral fat accumulation, thereby exacerbating metabolic dysfunction (Mauvais-Jarvis, 2015; Tramunt et al., 2020).

Table 1. Characteristics of Uncomplicated T2DM Patients

Characteristic	Frequency	Prevalence (%)
Sex		
Female	22	59.5
Male	15	40.5
Total	37	100.0
Age (Years)		
30-40	4	10.8

Characteristic	Frequency	Prevalence (%)
41-50	23	62.2
51-60	9	24.3
61-70	1	2.7
Total	37	100.0
Mean±SD	48.08±5.43	
T2DM Duration		
<5 Years	24	64.9
≥5 Years	13	35.1
Total	37	100.0
CRP Results		
Positive (≥6 mg/L)	11	29.7
Negative (<6 mg/L)	26	70.3
Total	37	100.0

Table 1 reveals relatively few T2DM cases in the 30-40 age group, likely due to optimal physiological function during this period and frequent underdiagnosis of early T2DM symptoms in younger individuals (Kianoush & Osei, 2019; Pataky et al., 2021). The highest prevalence occurred in the 41-50 age group, consistent with RISKESDAS 2018 data showing age-related increases in T2DM incidence, attributable to declining insulin sensitivity and reduced physical activity (Chia et al., 2018; Kemenkes RI, 2019). The lower representation of 51-60 year-olds may reflect this study's exclusion of patients with complications, as older individuals more frequently develop advanced disease (Tenchov et al., 2024).

Most participants had a T2DM duration <5 years (64.9%, n=24), suggesting improved early detection through health education and screening accessibility (Salsabila et al., 2024). The smaller proportion with ≥5 years duration (35.1%, n=13) may reflect higher complication rates and reduced healthcare engagement in this group (Komalasari et al., 2023; Rahmi et al., 2022). The results of this study are consistent with previous findings reporting that 40% of 1,765 T2DM respondents in China had a disease duration of less than 5 years. Similar research in Indonesia also showed that 84.16% of individuals with T2DM had been diagnosed for less than 5 years. These data indicate that the majority of T2DM patients tend to be identified at an early stage of the disease (Dyah et al., 2014; Yao et al., 2023).

CRP positivity was detected in 29.7% (n=11) of participants, indicating the presence of subclinical inflammation. The elevation of CRP in T2DM conditions is attributed to excessive Reactive Oxygen Species (ROS) production resulting from hyperglycemia. Over time, this condition leads to vascular lipid accumulation due to AMP-activated Protein Kinase (AMPK) activation, thereby increasing the risk of atherosclerosis and complications in T2DM patients (Galicia-Garcia et al., 2020; Purbasari et al., 2022). These inflammatory processes often precede overt clinical symptoms, highlighting the importance of early biomarker detection. Previous studies have reported that CRP levels in healthy individuals are typically less than 5 mg/L, making them undetectable when tested using the latex agglutination method (Yekti et al., 2014).

Table 2. Association Between T2DM Duration, Dietary Habits, Physical Activity, and Tobacco Exposure with CRP Levels

Variable	Category	CRP Results		Statistical Analysis Results
		Positive	Negative	
T2DM Duration	<5 years	2	22	Fisher's exact test $p = <0.001$ ($p <0.05$)
	≥ 5 years	9	4	
	Total	11	26	
Dietary Habits	Balanced	3	8	Fisher's exact test $p = 0.580$ ($p >0.05$)
	Unbalanced	8	18	
	Total	11	26	
Physical Activity	Regular ($\geq 2x/\text{week}$)	7	22	Fisher's exact test $p = 0.163$ ($p >0.05$)
	Irregular ($< 2x/\text{week}$)	4	4	
	Total	11	26	
Tobacco Exposure	Frequent	9	10	Chi-square test $p = 0.016$ ($p <0.05$)
	Minimal	2	16	
	Total	11	26	

Bivariate analysis (Table 2) revealed significant associations between elevated CRP levels and both T2DM duration ($p = <0.001$) and tobacco exposure ($p = 0.016$). These findings support the hypothesis that chronic hyperglycemia, sustained over time, intensifies oxidative stress and endothelial dysfunction, thereby promoting systemic low-grade inflammation in T2DM. The strong correlation with disease duration aligns with the progressive nature of T2DM, in which prolonged metabolic dysregulation activates multiple proinflammatory pathways (Irwanto et al., 2021; Slaghuis, 2023). Tobacco exposure demonstrated particular concern, with 51.4% of participants reporting daily contact, consistent with known inflammatory effects of smoke constituents like nicotine and polycyclic aromatic hydrocarbons that stimulate CRP production (Erikardo et al., 2024; Purbasari, et al., 2022). This high prevalence underscores the importance of addressing modifiable risk factors, such as smoking, in T2DM management.

Interestingly, neither dietary habits ($p = 0.580$) nor physical activity ($p = 0.163$) showed significant relationships with CRP levels in this cohort. This condition may be attributed to the fact that dietary patterns do not exert an immediate effect on the inflammatory response but rather influence it gradually and depend on the progression of the individual's T2DM. Furthermore, this study only assessed current dietary habits of T2DM patients and did not capture their historical dietary behavior. Consequently, if participants had previously modified their eating patterns, this could have influenced the results. This is supported by previous studies indicating that the longer a person lives with T2DM, the lower their dietary adherence tends to become—although the opposite trend may also occur in some cases. (Dahlia et al., 2025; Yannakoulia, 2006). Although previous studies have reported that physical activity contributes to reducing inflammation and protecting body tissues from oxidative stress (Piotrowska et al., 2023; Venkatasamy et al., 2013), the differing findings in this study may be attributed to the absence of a specifically designed approach to assess the impact of

physical activity on inflammation, thereby allowing the influence of other, potentially stronger, proinflammatory factors such as T2DM duration and tobacco exposure.

CONCLUSION

This study demonstrates that 29.7% of patients with uncomplicated T2DM exhibited elevated CRP levels, suggesting the presence of subclinical inflammation despite the absence of overt complications. A significant association was found between elevated CRP levels and both disease duration ($p = <0.001$) and tobacco exposure ($p = 0.016$), highlighting their roles as key inflammatory drivers in uncomplicated T2DM. In contrast, dietary patterns and physical activity showed no statistically significant correlation with CRP elevation in this cohort. These results underscore the importance of monitoring inflammatory markers like CRP in uncomplicated T2DM patients, particularly for those with longer disease duration or tobacco exposure, to facilitate early intervention and potentially mitigate progression toward complications. Further studies employing quantitative hs-CRP assays, cohort designs, and multivariate analyses are recommended to strengthen the findings of this study.

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