

Original article

Association Between Some Inflammatory Markers and HbA1c in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background and aims. Patients with type 2 diabetes exhibit subclinical inflammation and nearly all signs of systemic inflammation, which characterized by high circulating levels of inflammatory parameters. The current study aimed to assess the levels of the inflammatory markers such as, C-reactive protein (CRP), Erythrocyte sedimentation rate (ESR) and leukocyte counts (WBC) count in patients with T2DM and to correlate their values with the HbA1c levels. **Methods.** This cross-sectional study was conducted on 41 consecutive patients with type 2 diabetes attending the outpatient department of Tajoura-Heart Hospital. All patients were had laboratory investigations including; Hemoglobin A1c (HbA1C), C-reactive protein(CRP), Complete blood count(CBC) and Erythrocyte sedimentation rate (ESR). Patients were assessed according to glycemic status, patients with under control of diabetics (HbA1C level was equal to or less than 7.5%), and patients with poorly controlled diabetics (HbA1c level was greater than 7.5%). **Results.** Statistically significant association was observed between ESR, CRP levels and level of HbA1c. The ESR and CRP level were significantly higher in poorly-controlled diabetic patient than who with well controlled diabetics (p value= 0.037 and 0.017 respectively). WBC levels were higher in patients with poorly controlled than well controlled patients but the difference was not statistically significant (p value= 0.771). **Conclusion.** Inflammation and glycemic control have a strong association in patients with type 2 diabetes, suggesting that inflammation plays a role in diabetes pathogenesis.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a serious global health issue. Currently affecting 415 million individuals, it is predicted that this figure will rise to 642 million by 2040 [1]. Type 2 diabetic mellitus can lead to significant consequences as neuropathy, retinopathy, nephropathy, and cardiovascular disorders [2,3]. Impaired insulin production, insulin resistance, and systemic inflammation were the key contributors to the pathogenesis of this complex disease [3]. Inflammation may be crucial to this disease's development, according to recent research [4]. Subclinical inflammation and nearly all signs of systemic inflammation have been observed in T2DM patients [1]. High levels of inflammatory cytokines and C-reactive protein (CRP), are present in the blood during this systemic and subclinical inflammatory process [1]. A sensitive measure of enhanced inflammatory activity in the artery wall is provided by high-sensitivity CRP (hs-CRP) as well [5].

In routine clinical practice serum or plasma C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) are the most commonly used laboratory tests for detecting the acute phase response and thus diagnosis and monitoring of inflammatory conditions [6]. Both tests provide identical results in patients with chronic inflammatory conditions. Although CRP values rise more quickly than ESR (rising within 2 hours and peaking at 48 hours) therefore it tends to be more reliable for disease monitoring and is less impacted by patient age, anemia, pregnancy, and high protein levels [7].

In 1930, CRP was identified in a patient who had pneumococcal pneumonia [9]. It is produced by hepatocytes in reaction to cytokines, particularly interleukin-6, that are released during an infection and tissue inflammation [8]. CRP has both pro-inflammatory and anti-inflammatory properties, contributing to the host defense [7]. Numerous viral and noninfectious inflammatory diseases, as well as several malignancies, are associated with elevated serum CRP levels [9].

The ESR was initially described more over a century ago, however it is still widely used as a nonspecific indicator of inflammation to help diagnose conditions and follow disease activity [3,10]. The ESR is an inexpensive, easily measured, and it is the rate (in mm/h) at which red blood cells develop aggregates [9]. Furthermore, ESR influenced by the concentration of circulating acute-phase proteins, particularly fibrinogen and it is like CRP, can rise in a range of inflammatory and cancerous conditions [9].

In the pathogenesis of T2DM, both insulin resistance and beta cell insufficiency are linked to elevated levels of numerous inflammatory markers [11]. The accumulation of glycation adducts in tissue proteins is linked to the development of complications [1]. Plasma glucose measures (fasting (FBS) and postprandial blood sugar (PPBS) as well as measurements of glycated hemoglobin (HbA1c) levels are required for optimal glycemic control monitoring. The HbA1c level reflects the average glycemic control over the past three months, whereas the patient's glucose tests provide a picture of short-term glycemic control [1].

To our knowledge, no enough studies have been done in Libyan T2DM patients for estimation of inflammatory markers. Therefore, the present study was done to evaluate not only the levels of some inflammatory markers such as ESR, CRP and leukocyte count but also to correlate their values with the parameters of glycemic regulation, such as HbA1c levels

METHODS

Study design and setting

A descriptive cross-sectional study was conducted at Tajoura- Heart Hospital between the period of April to June 2021.

Participant enrollment and data collection

A total of 41 consecutive adult patients with T2DM were included in this study. History of liver disease, inflammatory disease, chronic kidney disease, acute and chronic infection, parathyroid disease, hypercortisolism, cancer, anemia, hematological diseases, malabsorption, alcoholism, recent use of vitamin D or calcium preparations, and pregnancy or breastfeeding were all considered as exclusion criteria. Patients who were on heparin or oral contraceptives, both of which might raise the ESR, were also excluded. T2DM was defined according to World Health Organization criteria [12].

Laboratory analysis

All demographic information (age, gender, and weight) of subjects was gathered from medical records after they had given written informed consent. All patients underwent venous blood sampling following an overnight fast lasting at least 8 hours. Ethylenediaminetetraacetic acid (EDTA)-containing vacutainer tubes were used to measure the HbA1c level and for routine CBC analysis (using quantitative colorimetric kits). The remaining 5 ml of blood were centrifuged to create serum, which was utilized to calculate the CRP values. The Westergren technique was used to calculate ESR (mm/h) [3].

Statistical analysis

All data were collected, tabulated and statistically analyzed using Statistical Package for the Social Sciences (SPSS) software, version 20. The age and weight were presented as the means \pm standard deviations. Whereas gender and levels of HbA1c, ESR, CRP, and WBC were presented as percentages. The Chi-Square test was run to determine the association between two variables. The probability value (p) was considered significant if it was less than 0.05 and highly significant if was (<0.001).

Ethical considerations

The study was approved by the Department of Medical Laboratories Sciences at University of Tripoli. All participants

provided consent before participating in the study.

RESULTS

A total of 41 patients were included in the study, of whom 19 (46.3%) were males and 22 (53.7%) were females. The mean age was 56.8 ± 10.3 years and the mean weight was 85.80 ± 15.90 kg. The demographic characteristics of the study population are shown in (Table 1).

Table 1. Characteristics of 41 patients with Type II diabetes enrolled in the study

Variables	Values
Total patients, n (%)	41(100%)
Age (years)	59.12 ± 12.39
Weight	85.80 ± 15.90
Gender	
Male, n (%)	19 (46.3%)
Females, n (%)	22 (53.7%)

When the patients were assessed according to HbA1C, of these 41 patients, 8 (19.5%) had their diabetes under control (HbA1C level was equal to or less than 7.5%), whereas 33 (80.5%) patients were poorly controlled diabetics (HbA1c level was greater than 7.5%).

As outlined in Table (2). There was a statistically significant association between ESR level and level of HbA1c. The ESR level was significantly higher in poorly-controlled diabetic group (patient with HbA1C greater than 7.5%) than who with well controlled diabetics (patient with HbA1C equal to or less than 7.5%) (p value=0.037).

Table 2. Correlation between HBA1C with Erythrocyte sedimentation rat (ESR)

HBA1C		ESR			Chi-Square Tests		
		Total	Normal ESR level	High ESR level	Value	df	P value
Total	N(%)	41(100%)	13(31.7%)	28(68.3%)	4.352	1	0.037
Well controlled group	N(%)	8 (100%)	5 (62.5%)	3(37.5%)			
Poorly controlled group	N(%)	33(100%)	8(24.2%)	25(75.8%)			

A significant association was also noted between the level of CRP and HbA1C. The patients who have HbA1C level greater than 7.5% are more likely to have higher CRP level than others with controlled HbA1C (P < 0.05) (Table 3).

Table 3. Correlation between HBA1C with C-Reactive protein (C.R.P)

Hba1c		C.R.P			Chi-Square Tests		
		Total	Normal CRP level	High CRP level	Value	df	P value
Total	N(%)	41(100%)	26(63.4%)	15(36.6%)	5.734 ^a	1	0.017
Well controlled group	N(%)	8(100%)	8(100%)	0			
Poorly controlled group	N(%)	33(100%)	18(54.5%)	15(45.5%)			

On the other hand, the chi-square test did not show a significant correlation in the levels of both WBC and HbA1C between the two groups p value > 0.05 (Table 4).

Table 4. Correlation between HbA1c with leukocyte counts (WBC)

HbA1c		WBC			Chi-Square Tests		
		Total	Normal WBC count	High WBC count	Value	df	P value
Total	N(%)	41(100%)	37(90.2%)	4(9.8%)	0.085	1	0.771
Well controlled group	N(%)	8(100%)	7(87.5%)	1(12.5%)			
Poorly controlled group	N(%)	33(100%)	30(90.9%)	3(9.1%)			

DISCUSSION

This study was conducted at the outpatient department (OPD) of Tajoura- heart Hospital between the period of April to June 2021, and aimed to analyze the levels of the inflammatory markers such as, C-reactive protein (CRP), Erythrocyte sedimentation rate (ESR) and leukocyte counts (WBC) in patients with type 2 diabetes mellitus. Also, to associate their values with the parameters of glycemic regulation, such as HbA1c levels.

Our results showed that there was a statistically significant association between ESR level and HbA1c levels in patients with type 2 diabetes mellitus. The ESR was significantly elevated in (75.8%) of patients with poorly controlled diabetics group. These findings are consistent with the findings from a study published by Nadeem and her colleagues who found higher ESRs in patients with diabetes than in healthy subjects, indicating a role for inflammation in the pathogenesis of the disease [13].

Furthermore, in the present study a significant correlation was found between the levels of CRP and HbA1c. The level of CRP was high in nearly half of patients (45.5%) in poorly controlled diabetics group. This result was similar to the study performed by Elimam et al, and was also consistent with the findings of Malenica et al, where the significantly higher CRP levels observed in patients with T2DM compared to the healthy population [1,14]. In contrast, a study performed by Lima and colleagues found no significant difference in level of CRP between patients with T2DM and healthy controls [15].

On the other hand, Leukocyte count and HbA1c level were not found to significantly correlate in the current study. Although the WBC levels in the poorly controlled group were greater than those in the well-controlled group, the difference was not statistically significant (p value= 0.771). Despite earlier research suggesting otherwise, in a large Chinese population, patients with and without diabetes, HbA1c was independently linked with WBC count within the normal range [16]. Our findings also contradict with a study on UK adults in which a high leukocyte count was found to be strongly linked with the occurrence of diabetes [10].

The current study has some limitations. First, the study was included a relatively small sample size and the participant were only from one city. Second, the study was across-sectional design, therefore, it was not possible to determine the direct association and consequently the causations.

CONCLUSION

Our study reported correlations between elevated glycosylated hemoglobin levels, which reflect poor glycemic control, and both CRP and ESR levels, which are inflammatory markers that reflect the role of glycemic control and subclinical inflammation in patients with T2DM.

Funding

None.

Declaration of competing interest

None.

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