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A role of some immunological markers for diabetic Type2 patients in Diyala province

A Thesis

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By

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CHAPTER ONE…… INTRODUCTION

1. Introduction

Diabetes mellitus (DM) is a metabolic condition characterized by increased blood glucose levels. The hormone insulin moves glucose from the blood into the cells to be stored or used for energy, untreated high blood glucose can damage the nerves, eyes, kidneys and others organs. There are several types of diabetes mellitus include: Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) are the two primary types of DM, and both are typically brought on by defects in insulin secretion (T1DM) or action (T2DM) (Eizirik *et al*., 2020). T1DM presents in children or adolescents, while T2DM is thought to affect middle-aged and older adults who have prolonged hyperglycemia due to poor lifestyle and dietary choices (Herath *et al*., 2018).

Prediabetes and type 2 diabetes are prevalent, affecting, respectively, roughly 34% and 13% of all US people in 2018 (Davidson *et al*., 2021). According to the most recent data, diabetes mellitus (DM) is still a serious worldwide health concern and is expected to increase significantly over the next few decades. This will have a considerable impact on healthcare spending, especially in emerging nations (Cuadros *et a*l., 2021). Unfortunately, in diabetes, the host's immune response is disrupted. In addition to the risk of natural barrier damage due to neuropathy, T2D can also affect cellular immunity. This is caused by insulin deficiency and hyperglycemia (Tessaro *et al*., 2017).

IL-15 therapy has been shown to delay the onset of diabetes in mice, possibly due to the cytokine's stimulation of NK cells, indicating a protective role for this substance in type 1 diabetes (Siewko *et al*., 2019). Plasma IL-15 in humans is markedly reduced in obesity and adversely correlated with fat mass (Shi *et al*., 2019).

The findings of the study demonstrate that IL-33 inhibits the progression of disease in prediabetic non-obese diabetes mice and identify IL-33/ST2 as a possible therapeutic target to avert type I diabetes (Lu *et al*., 2019) Data results mentioned the release of IL-33 from necrotic cells might induce autophagy, which can further balance the effects of increased apoptosis secondary to contrast-induced nephropathy (CN) in diabetic kidney disease (DKD) (Demirtas *et* al., 2016).

Another study suggests that IL-33 and/or IL-33/ST2 dynamics and biological functions may contribute to total glycemia in people and may constitute a new target for the therapeutic effects of glucose-lowering treatments (Hasan *et al*., 2019).

There are few reports on the role of IL-36 cytokines in type 2 diabetes, despite several studies demonstrating their effects on psoriasis, arthritis, and systemic lupus erythematosus (Boutet *et al*., 2020). The inflammatory cytokines IL-36 and IL-36 showed elevated expression in T2DM patients, while the anti-inflammatory cytokine IL-36Ra showed lower expression. Inflammation and blood lipid levels were inversely correlated with the levels of inflammatory cytokines. According to the findings, IL-36 cytokines may one day serve as a new T2DM diagnostic marker or therapeutic target (Li *et al*.,2021).

Less research has been done on complement C4 in metabolic diseases. Nevertheless, accumulating evidence indicated that C4 may contribute to T1DM (Zhang *et al*., 2021). Another important relationship between inflammation and thrombosis in diabetes is provided by complement C3. According to a paper, complement C3 interacts with fibrin, causing patients with T1DM and T2DM to experience extended fibrinolysis (Shim *et al*., 2020). Complement C4 has been less studied in metabolic disorders. Nevertheless, accumulated data suggested that C4

Abstract

Diabetes Mellitus (DM) is a metabolic disease, involving inappropriately elevated blood glucose levels . DM has several categories, including type 1, type 2, maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary causes due to endocrinopathies, steroid use, etc. This study was conducted in the Baquba Teaching Hospital - Diyala Health Department, in the period from the beginning of October 2021 to the end of January 2022.Which aimed to evaluate some immunological indicators for patients infected with diabetes type 2 which included assessment levels of interleukins IL-15, IL-33, and IL-36 in DM patients and healthy population and assessment levels of complements proteins C3 and C4 in DM patients and healthy population. A total of 90 blood samples were obtained for the current study and classified into groups as follow:The first group: - Approval of (60) blood samples from diabetes mellitus type2 and medically diagnosed by specialized doctors in the Baquba Teaching Hospital Consultation and after diagnosed by laboratory test. Where the number of males was (28) and the number of females (32) within age range between (21-70) years and they were divided into age groups.The second group: (30) samples of apparently healthy people of both sexes were adopted and used as a control group, where the number of males was (15) and the number of females (15) within the age range between (21-70) years and they did not suffer from any Chronic or acute illness at the time of sample collection.

Results of our study show non-significant different ($p>0.05$) among patients according to gender and disorders. In contrast, our study revealed significant different among age groups, where the 41-50 years and 51-60 years scored highest percentage (25.60% and 28.90%) than 21-30 years and 31-40 years that scored least percentage (11.10% and 15.60%). Additionally results of current study mentioned the decreased median levels of C4 complement, IL-15, IL-33,

plays a role in T1DM (Zhang *et al*., 2021). Recent study demonstrated that C3a can increase insulin secretion (Flyvbjerg, 2017). Another study showed there is possible link between C3 and diabetes could be due to C3adesArg or ASP, the proteolytic fragment of C3, which is a paracrine metabolic factor that can stimulate glucose uptake and lipid storage in adipose tissue (Ajjan and Schroeder, 2019).

Aims of study

The current study aims to know the role of some immunological markers in immunopathognsis of diabetes by:

- Assessment levels of Complements proteins C3,C4 and levels of interleukins IL-15, IL-33, and IL-36 in DM patients