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The Use of Mannose-Binding Lectin as a Predictive Signal for Renal Decline in Non-Hypertensive Type 1 Diabetes Mellitus Males

Israa H. Ibrahim*

Abstract

Introduction: Mannose-binding lectin is a macromolecule of the innate immune system that provides a third pathway of complement system activation from the protein subfamily called the collectins, it can primarily respond to pathogens that have sugar receptors on cell membranes to mediate phagocytic activity. **Methods:** 82 type 1 male patients were enrolled in this study as well as 21 healthy control persons, information collected from patients by questionnaire age, body mass index (BMI), duration of disease, chronic diseases, and blood collected for fasting blood sugar (FBS), hemoglobin A1C (HbA1c), serum creatinine, and mannan-binding lectin (MBL) measurements, and glomerular filtration rate was calculated using equation dependent on serum creatinine. **Results:** It shows a significant decrease in BMI in patients' group as compared with control group; also, there was an increase in FBS, HbA1c, and MBL in patients' groups as compared with control group. There was a positive correlation between MBL and BMI. **Conclusion:** We conclude that MBL was increased in patients with type 1 diabetes and may be an early sign of renal disease; also, there was an effect of obesity on the increase of MBL in those patients. **Conclusion**: The mannose-binding lectin may be used as an early diagnostic index for renal decline and the elevation of this protein is related to an increase in body weight.

Keywords: Glomerular filtration rate, Mannose-binding lectin, Mannan-binding lectin, Renal disease

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Introduction

Mannose-binding lectin is a hepatic macromolecule protein that is considered an important molecule in the innate immune system, it provides a third pathway of complement system activation and it is considered as the first line of defense against invading pathogens. This protein is from the protein subfamily called the collections which have collagenous regions and lectin domains.[1,2] The ability of MBL to activate the complement system comes from its ability to bind to a wide range of neutral sugars that are found on the surface of microorganisms such as N-acetyl-D-glucosamine, mannose, fucose, N-acetyl-mannosamine, as well as glucose. It makes this protein important in primary response within hours to days to a pathogen with sugar receptors on the cell membrane to mediate effectors that have killing or phagocytosis activity.[3,4] In patients with type 1 diabetes mellitus (DM), significant proportion of them develops diabetic renal disease from different causes such as low-grade inflammation and activation of the complement system.[5] This association with renal disease accounts for 30–50% of diabetic patients with an increased proportion rapidly.[6]

At the genetic level, the study on MBL2 knockout mice revealed that the activation of the MBL pathway is impaired and thus the MBL secretion was not found, and this led to these mice being protected from developing nephropathy caused by diabetes.[7] In humans, the gene for the expression of mannose-binding lectin (MBL2 gene) was located on chromosome 10 with polymorphism in exon 1 and the promotor region and this caused the levels of MBL to vary from person to person significantly.[2,8]

Departmet of Basic Sciences, College of Dentistry, University of Karbala, Karbala, Iraq

Corresponding Author: Israa H. Ibrahim, College of Dentistry, University of Karbala, Karbala, Iraq. E-mail: almosawy2014@gmail.com

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Methods

Patients

We enrolled 82 type 1 DM male patients (age 25–50 years) who were admitted into the diabetes and endocrine disease center in Karbala province in Iraq from December 2023 to March 2024 and healthy persons from the same average age (No = 21) as a control group. The information collected from patients by questionnaire was age, body mass index (BMI), duration of disease, and chronic diseases. We eliminate the patients who have hypertension and renal diseases.

Samples

We collect blood from patients in fasting state and the whole blood in ethylenediaminetetraacetic acid tubes used for hemoglobin A1C (HbA1c) measurement, and serum in plane tubes used for fasting blood sugar (FBS), serum creatinine, and MBL measurements.

Procedures

The glomerular filtration rate (GFR) was calculated using the equation dependent on serum creatinine eGFR (mL/min) = ([140–age) × Wt/(0.814 × S. Cr in μmoL/L]) × (0.85 if female) (Mula-Abed *et al*., 2012).

FBS, HbA1c, and serum creatinine were done by Abbott System in Al-DAQAH medical laboratory, and MBL was measured by using the enzyme-linked immunosorbent assay (ELISA) technique (BT LAB human mannose-binding lectin ELISA kit) in the laboratory at the College of Medicine/University of Karbala using device (BioTek 800 TS).

Statistical Analysis

The statistical analysis for this study was made using Microsoft Excel 2024 and we calculated mean, standard deviation, independent unequal sample *t*-test, and correlation regression.

Results

Table 1 shows the comparison between the control and patient groups in age, BMI, FBS, HbA1c, serum creatinine, eGFR, and MBL. This table reveals a significant decrease in BMI at $P < 0.01$ in the patients' group as comparison with the control group [Figure 1], while there were significant increases at *P*- $P < 0.05$ in FBS [Figure 2] and HbA1c [Figure 3] and at $P < 0.01$ in MBL [Figure 4] in patients' group as comparison with control group.

Figure 5 shows significant positive correlation regression (r = 0.47%) between mannose-binding lectin concentration and the BMI [Figure 5].

Discussion

The results show a significant decrease in BMI in patients as compared with the control group and this result was compatible with another study that revealed the reason for the lower BMI in patients may be because of the lower insulin secretory response as compared with healthy individuals.[9] However, those patients appear like lean individuals.[10] The mortality rate in underweight type 1 diabetic patients increases by 3.4 times more than in normal-weight or even obese patients.[11] The mouse model study reveals that the mannose-binding lectin increases in diabetic patients within a specific genotype, this result may indicate the correlation between complement system activation and the onset of diabetic nephropathy.[12]

In this study, there was a significant increase in mannose-binding lectin in patients as compared with the control group, and these results were agreed with another study that found a rise in mannose-binding lectin in patients at early onset independent of genetic predisposition.[13] Another study reveals that MBL increased

Table 1: The comparison between the control and patients group in all parameters taken

Parameters	*Control, n=21 (Mean±SD)*	*Patients, n=82 (Mean±SD)*
Age (years)	41.714±4.326	43.854±6.5755
BMI (kg/m^2)	32.563±5.622	26.564±2.260**
FBS (mg/dL)	111.118±6.556	204.995±88.494*
HbA1c (mg/dL)	5.605±0.284	8.859±1.851*
Serum creatinine (mg/dL)	0.920±0.150	0.910±0.300
eGFR (mL/min/1.73 m^2)	75.345±15.225	82.862±31.792
MBL (ng/mL)	436.684±287.597	817.333±370.379**

*Significant differences at $P<0.05$, **Significant differences at $P<0.01$

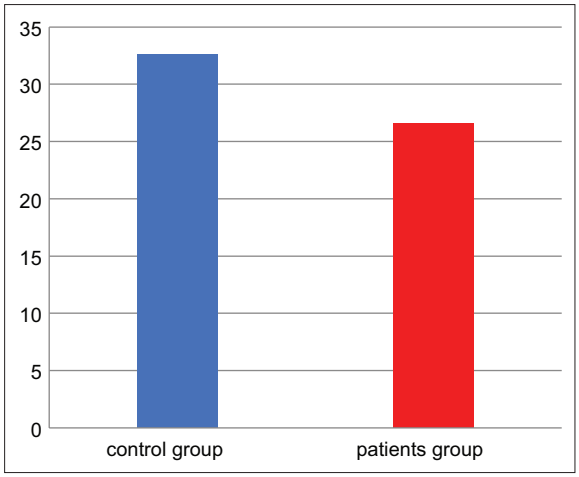

Figure 1: Mean of body mass index in control and patient groups show significant differences at $P < 0.01$

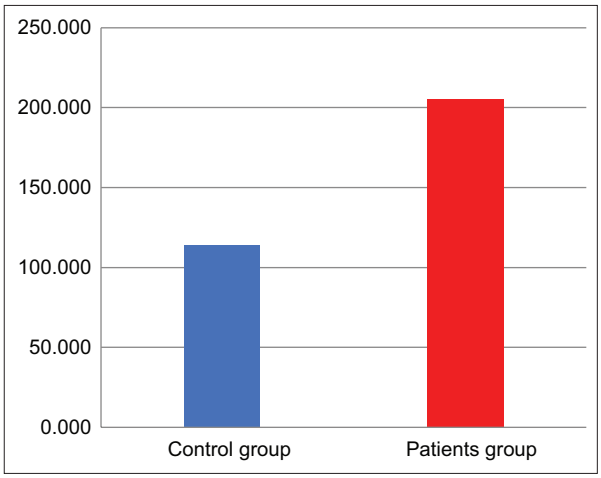

Figure 2: Mean of fasting blood sugar in control and patient groups show significant differences at $P < 0.05$

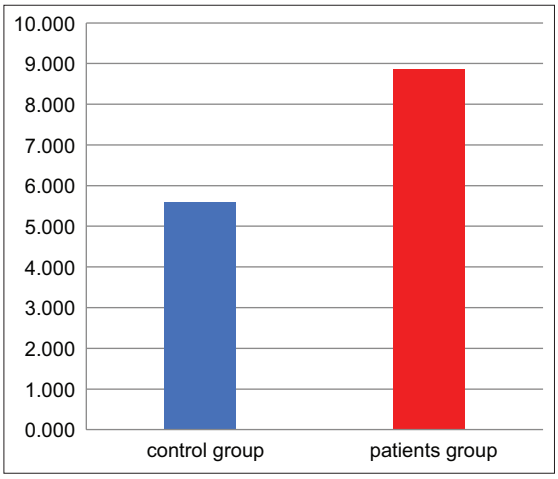

Figure 3: Mean of hemoglobin A1C in control and patient groups show significant differences at $P < 0.05$

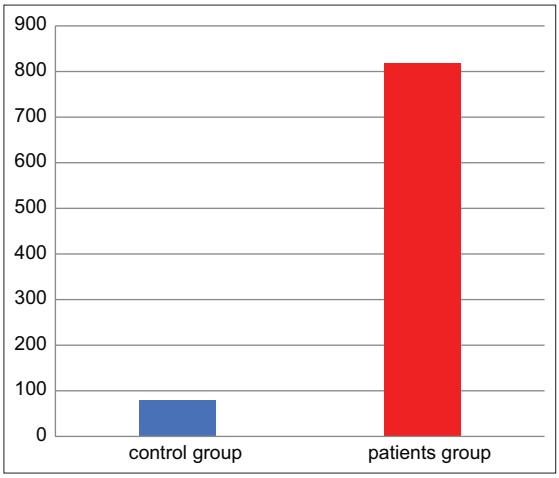

Figure 4: Mean of mannan-binding lectin in control and patient groups show significant differences at $P < 0.01$

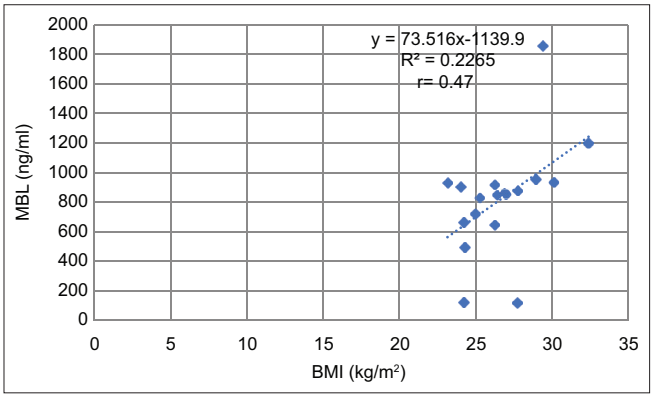

Figure 5: The correlation between body mass index and mannan-binding lectin

in patients with diabetic nephropathy without its association with low-grade inflammatory markers.[14] The progression of diabetic nephropathy in type 1 diabetes was associated with the elevation of mannose-binding lectin.[5] Insulin resistance may be cause an increase in mannose-binding lectin, and insulin resistance is the cause of many complications of diabetes.[15]

The study shows a significant correlation between mannose-binding lection and BMI and it may be the effect of obesity on general health and inflammatory response, but these results disagree with another study that shows there was no association between MBL and BMI and insulin resistance because the MBL is not synthesis in the adipose tissue.[16] Others show that the mannose-binding lectin does not differ between normal-weight and obese individuals.[12] The other study agreed with our study with the combined elevation of mannose-binding lectin with the elevation of BMI.[17] Previous studies on mice reveal that excessive production of complement proteins like mannose-binding lectin occurs in obese animals, suggesting a correlation between adipose tissue inflammation and insulin resistance.[18-20]

Conclusion

We conclude that mannose-binding lectin was elevated in type 1 diabetic patients despite normal eGFR and serum creatinine, which indicates that the elevation of this protein may be used as an early diagnostic index for renal injury. The correlation between mannose-binding lectin and BMI may indicate the effect of obesity on the increase in the concentration of that protein and thus renal decline.

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