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Evaluation of Serum Level of Galectin-3 in Prediabetic and Type-2 Diabetic Patients With and Without Vascular Complications

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Abstract

Background: Diabetes mellitus is the most prevalent metabolic condition. Increased galectin-3 plasma concentrations have been linked to micro- and macro-vascular problems of Type-2 diabetes mellitus (T2DM).

Aim and objectives: To study the correlation between serum concentrations of galectin 3 in prediabetic and type 2 diabetic individuals with macro and microvascular complications.

Patients and Methods: This case-control research was performed on 160 cases and 40 healthy controls. Cases are separated into five groups: Group (A): 40 prediabetic patients, Group (B): 40 individuals with T2DM without complications, Group (C): 40 individuals with T2DM with microvascular complications, Group (D): 40 individuals with T2DM with macrovascular complications and control Group: 40 healthy controlled attended in outpatient's clinics at AL- Azhar university hospitals from July 2022 to April 2023.

Results: Our finding indicated that there was a significant increase in plasma level of galectin -3 in group A, group B, group C, and group D when contrasted with healthy control group. There was a significant distinction between group A and group B concerning Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), hemoglobin A1c (HbA1C), Triglycerides, low-density lipoprotein cholesterol (LDL-C), High-density lipoprotein cholesterol (HDL-C), galectin-3 and between group C and group D concerning HbA1C, HDL-C & Galectin-3.

Conclusion: One potential biomarker for the early detection of diabetes and prediabetes is galectin-3. Additionally, it can measure how diabetic microvascular and macrovascular problems are developing. Galectin-3 levels were higher in instances with type 2 diabetes compared to non-diabetic individuals, according to our findings.

Keywords: Hemoglobin A1c, Galectin-3, Type-2 diabetes mellitus

1. Introduction

D iabetes mellitus, the most prevalent metabolic disorder, seems to be increasing in prevalence on a global scale. Some authors have linked elevated plasma concentrations of galectin-3 to micro and macrovascular complications of T2DM.¹

People with both pre-diabetes and type 2 diabetes are at a higher risk of cardiovascular disease and death. This is likely because pre-

diabetes is linked to the start of microvascular dysfunction. Type 2 diabetes is characterized by vascular damage, and pre-diabetes is characterized by generalized microvascular dysfunction.²

In contrast to healthy controls, several studies have shown that people with impaired glucose tolerance, microvascular and macrovascular consequences of type 2 diabetes mellitus, and high plasma Galectin-3 levels are associated with these conditions.³

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One of the many important ways in which inflammation is regulated is via a class of lectins called galectins that bind soluble beta-galactosides. It is present in several visceral adipose tissues, including those of the lungs, heart, brain, and blood vessels. Endothelium and mesangium-related tissues that are prone to diabetic vascular problems.⁴

Galectin-3 controls cell-cell cooperation, promotes migration, differentiation, and proliferation, and modulates extracellular connections during cellular activation and self-antigen recognition.⁵

Advanced glycation end products (AGEs) are free radicals that cause endothelial dysfunction, organ damage (such as diabetic retinopathy, nephropathy, and vasculopathy), and interactions with cell adhesion molecules. Galectin-3 has a great affinity for these compounds.⁶

This research aimed to study the correlation among serum concentrations of galectin 3 in prediabetic and T2DM cases with macro and microvascular complications.

2. Patients and methods

This Case-Control trial was performed on 160 individuals and 40 healthy controls. Patients were divided into five groups: Group (A): 40 prediabetic cases, Group (B): 40 individuals with T2DM without complications, Group (C): 40 individuals with T2DM with microvascular complications ((DKD, DR, or DN), Group (D): 40 cases with T2DM with macrovascular complications (CVD) and control Group: 40 healthy control. This research was performed in outpatient clinics at AL-Azhar University hospitals from July 2022 to April 2023.

Inclusion criteria: Age 30-60 years with diabetes mellitus

Exclusion criteria: Patients with autoimmune diseases, patients with chronic kidney diseases (Nondiabetic), patients with T1DM or cancer, inflammatory diseases (e-g, gout, eczema, thyroiditis, bronchial asthma, hepatitis, allergic reaction), and patients treated with

corticosteroids.

Operational design: From each patient, the following data was collected upon admission:

Complete entire history taking included: (Personal history: age, sex, occupation and marital state and history of previous surgeries); clinical examination comprised vital signs (temperature, heart rate, blood pressure, respiratory rate) and pallor, jaundice, cyanosis, and lymph node enlargement. Calculate BMI, the abdominal inspection or abdominal palpation, laboratory study: CBC, and arterial duplex on the leg were performed.

Serum Galectin 3 level: Serum Galectin 3 levels were determined by storing fasting serum samples at -80 degrees Celsius until the analysis day. The serum galectin three concentration was determined using human galectin three reagents (Ray Bio-tech Inc., Norcross, GA, USA) in conjunction with an enzyme-linked immunosorbent assay. A Synergy HT Multi-Mode Microplate Reader (Bio-Tek, Winooski, VT, USA) was employed to conduct the absorbance measurements.

Administrative and Ethical Design: Ethical Committee and Al-Azhar University Hospitals provided official approval. The ethical committee of the faculty of medicine supplied approval.

Results were analyzed using IBM Corp.'s (Armonk, NY, USA) statistical package for the social sciences (SPSS), version 22. The mean and standard deviation were the components of descriptive statistics for continuous data, whereas the percentage was used for categorical variables. In order to compare the three groups, the researchers used a one-way analysis of variance (ANOVA) tool. We used the least significant distinction test on continuous data. The amounts of intracellular adhesion molecules were correlated with various variables using Pearson's bivariate correlation coefficient. Significant p-values were defined as those below the 0.05 level.

3. Results

Table 1. Comparison among control group and group (A)

	CONTROL GROUP (N=40)		GROUP (A) (N=40)		P VALUE
AGE					
MEAN± S.D	52.1 ± 4.12		52.58 ± 4.47		0.618
GENDER	No.	%	No.	%	
MALE	16	40	20	50	0.368
FEMALE	24	60	20	50	
BMI					

MEAN± S.D	27.92±1.298	28.61±1.094	0.012*
HOMA-IR			
MEAN± S.D	2.04±0.403	5.15±0.423	<0.001*
HbA1C			
MEAN± S.D	4.86±0.324	5.96±0.379	<0.001*
TRIGLYCERIDES (MG/DL)			
MEAN± S.D	146.50±13.399	163.10±6.994	<0.001*
HDL-C (MG/DL)			
MEAN± S.D	39.50±1.519	38.30±0.911	<0.001*
LDL-C (MG/DL)			
MEAN± S.D	56.52±5.362	85.10±4.243	<0.001*
CRP (MG/DL)			
MEAN± S.D	2.00±0.641	5.61±0.656	<0.001*
GALECTIN-3 (NG/ML)			
MEAN± S.D	0.32±0.04	0.68±0.07	<0.0001*

BMI: Body Mass Index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HbA1C: hemoglobin A1C, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, CRP: C-reactive protein.

P: p value for comparing between the studied groups, *: Statistically significant at P <0.05

Table 1 showed that there was significant variation among control group and group A as regard HOMA-IR, HbA1C, Triglycerides, HDL-C, LDL-C, CRP, Galectin-3 and BMI and no statistically significant difference as regard age and gender.

Table 2. Comparison among control group & group (B)

	CONTROL GROUP (N=40)		GROUP (B) (N=40)		P VALUE	MEAN± S.D	MEAN± S.D	P VALUE
AGE						2.04±0.403	5.57±0.222	<0.001*
MEAN± S.D	52.1 ± 4.12		52.45 ± 4.81		0.727			
GENDER	No.	%	No.	%		4.86±0.324	7.26±0.628	<0.001*
MALE	16	40	24	60	0.073			
FEMALE	24	60	16	40				
BMI						146.50±13.399	180.39±8.068	<0.001*
MEAN± S.D	27.92±1.298		28.75±1.175		0.004*			
HOMA-IR						39.50±1.519	36.10±1.945	<0.001*
						56.52±5.362	94.79±4.362	<0.001*
						56.52±5.362	94.79±4.362	<0.001*
						2.00±0.641	5.75±0.540	<0.001*
						0.32±0.04	1.67±0.18	<0.001*

BMI: Body Mass Index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HbA1C: hemoglobin A1C, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein

cholesterol, CRP: C-reactive protein.

P: p value for comparing between the studied groups, *: Statistically significant at P <0.05

Table 2 showed that there a significant disparity among control group and group B as regard HOMA-IR, HbA1C, Triglycerides, HDL-C, LDL-C, CRP, Galectin-3 and BMI and no statistically significant difference as regard age and gender.

Table 3. Comparison among control group & group (C)

	CONTROL GROUP (N=40)		GROUP (C) (N=40)		P VALUE
AGE					
MEAN± S.D	52.1 ± 4.12		50.7 ± 6.15		0.235
GENDER	No. %		No. %		
MALE	16	40	25	62.5	0.044*
FEMALE	24	60	15	37.5	
BMI					
MEAN± S.D	27.92±1.298		29.12±1.515		<0.0003*
HOMA-IR					
MEAN± S.D	2.04±0.403		5.79±0.194		<0.0001*
HBA1C					
MEAN± S.D	4.86±0.324		7.54±0.446		<0.0001*
TRIGLYCERIDES (MG/DL)					
MEAN± S.D	146.50±13.399		192.60±4.378		<0.0001*
HDL-C (MG/DL)					
MEAN± S.D	39.50±1.519		37.48±5.588		0.03*
LDL-C (MG/DL)					
MEAN± S.D	56.52±5.362		112.65±5.199		<0.001*
CRP (MG/DL)					
MEAN± S.D	2.00±0.641		6.64±0.613		<0.0001*
GALECTIN-3 (NG/ML)					
MEAN± S.D	0.32±0.04		1.97±0.1		<0.0001*

Calorie Mass Index (BMI), Insulin Resistance Evaluation Using the Homeostatic Model (HOMA-IR), Hemoglobin A1C, High-density lipoprotein cholesterol, and low-density lipoprotein cholesterol are abbreviations for the same thing. acronym for "C-reactive protein".

There is a statistically significant difference between the groups that were analyzed (*) when the p-value is less than 0.05

Table 3 revealed that there a significant variation among control group & group C as regard HOMA-IR, HbA1C, Triglycerides, HDL-C, LDL-C, CRP Galectin-3 and BMI and no statistically significant difference as regard age and gender.

Table 4. Comparison between control group and group (D)

	CONTROL GROUP (N=40)		GROUP (D) (N=40)		P VALUE
AGE					
MEAN± S.D	52.1 ± 4.12		50.88 ± 6.06		0.295
GENDER	No. %		No. %		
MALE	16	40	21	52.5	0.26
FEMALE	24	60	19	47.5	
BMI					
MEAN± S.D	27.92±1.298		29.00±1.600		<0.001*
HOMA-IR					
MEAN± S.D	2.04±0.403		5.66±0.259		<0.0001*
HBA1C					
MEAN± S.D	4.86±0.324		8.23±0.530		<0.001*
TRIGLYCERIDES (MG/DL)					
MEAN± S.D	146.50±13.399		194.80±3.930		<0.001*
HDL-C (MG/DL)					
MEAN± S.D	39.50±1.519		38.92±2.693		0.395
LDL-C (MG/DL)					
MEAN± S.D	56.52±5.362		114.80±5.235		<0.001*
CRP (MG/DL)					
MEAN± S.D	2.00±0.641		6.90±0.556		<0.001*
GALECTIN-3 (NG/ML)					
MEAN± S.D	0.32±0.04		2.26±0.13		<0.001*

BMI: Body Mass Index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HbA1C: hemoglobin A1C, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, CRP: C-reactive protein.

*Statistically significant at P <0.05, denoted as P, is the p-value for the comparison between the groups that were analyzed

Table 4 showed that there was significant distinction among control group and group D concerning HOMA-IR, HbA1C, Triglycerides, LDL-C, CRP, Galectin-3 & BMI and no statistically significant difference as regard age, gender and HDL-C.

Table 5. Comparison between group (A) and group (B)

	GROUP (A) (N=40)		GROUP (B) (N=40)		P VALUE
AGE					
MEAN± S.D	52.58 ± 4.47		52.45 ± 4.81		0.915
GENDER	No.	%	No.	%	
MALE	20	50.0	24	60.0	0.500
FEMALE	20	50.0	16	40.0	
BMI					
MEAN± S.D	28.61±1.094		28.75±1.175		0.582
HOMA-IR					
MEAN± S.D	5.15±0.423		5.57±0.222		<0.001
HbA1C					
MEAN± S.D	5.96±0.379		7.26±0.628		<0.001
TRIGLYCERIDES (MG/DL)					
MEAN± S.D	163.10±6.994		180.39±8.068		<0.001*
HDL-C (MG/DL)					
MEAN± S.D	38.30±0.911		36.10±1.945		0.001*
LDL-C (MG/DL)					
MEAN± S.D	85.10±4.243		94.79±4.362		<0.001*
CRP (MG/DL)					
MEAN± S.D	5.61±0.656		5.75±0.540		0.30
GALECTIN-3 (NG/ML)					
MEAN± S.D	0.68±0.07		1.67± 0.18		<0.001*

BMI: Body Mass Index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HbA1C: hemoglobin A1C, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, CRP: C-reactive protein.

P: p value for comparing between the studied groups, *: Statistically significant at P <0.05

Table 5 showed that there was significant distinction among group A & group B regarding HOMA-IR, HbA1C, Triglycerides, LDL-C, HDL-C, Galectin-3 and no statistically significant variance regarding age, gender, CRP & BMI.

Table 6. Comparison between group (C) and group (D)

	GROUP (C) (N=40)		GROUP (D) (N=40)		P VALUE
AGE					
MEAN± S.D	50.7 ± 6.15		50.88 ± 6.06		0.983
GENDER	No.	%	No.	%	
MALE	25	62.5	21	52.5	0.498
FEMALE	15	37.5	19	47.5	
BMI					
MEAN± S.D	29.12±1.515		29.00±1.600		0.701
HOMA-IR					
MEAN± S.D	5.79±0.194		5.66±0.259		0.013*
HbA1C					
MEAN± S.D	7.54±0.446		8.23±0.530		<0.001*
TRIGLYCERIDES (MG/DL)					
MEAN± S.D	192.60±4.378		194.80±3.930		0.021*
HDL-C (MG/DL)					
MEAN± S.D	37.48±5.588		38.92±2.693		0.146
LDL-C (MG/DL)					
MEAN± S.D	112.65±5.199		114.80±5.235		0.06
CRP (MG/DL)					
MEAN± S.D	6.64±0.613		6.90±0.556		0.058
GALECTIN-3 (NG/ML)					
MEAN± S.D	1.97±0.1		2.26±0.13		<0.001*

BMI: Body Mass Index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HbA1C: hemoglobin A1C, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, CRP: C-reactive protein.

P: p value for comparing between the studied groups, *: Statistically significant at P <0.05

Table 6 illustrated that there was a significant variation among group C & group D as regard HbA1C, HDL-C and Galectin-3 and no statistically significant difference as regard age, gender, BMI, HOMA-IR, Triglycerides, LDL-C and CRP.

Table 7. Association between Galectin-3 and various group (A, B, C, D) parameters

	GALECTIN-3	
	r	P VALUE
GROUP (A)		
CRP	-0.190	0.241
HbA1C	-0.228	0.157
GROUP (B)		
CRP	-0.493	0.001*
HbA1C	0.148	0.361
GROUP (C)		
CRP	0.570	<0.001*
HbA1C	0.028	0.865
GROUP (D)		
CRP	-0.565	<0.001*
HbA1C	0.622	<0.001*

C-reactive protein, hemoglobin A1C, and the p-value for the comparison between the groups under study,

*: Statistically significant at $P < 0.05$

Table 7 showed that there was no significant distinction in group A between CRP, HbA1C and Galectin-3, in group B there was a statistically significant difference among CRP and Galectin-3 and no statistically significant difference between HbA1C and galectin-3, in group C, there was a significant variance among CRP and Galectin-3 and no statistically significant disparity among HbA1C and galectin-3 and in group D there was a statistically significant distinction among CRP, HbA1C and Galectin-3.

4. Discussion

In group A (prediabetic cases), when contrasted with the healthy control group, results showed that a statistically significant increase in the plasma level of galectin -3 in the prediabetic group ($0.32 + 0.04$ vs $0.67 + 0.1$).

In cross-sectional research performed by Atalar et al.,⁷ According to a study that included healthy controls, people with prediabetes, and people with type 2 diabetes, serum Galectin-3 increases in type 2 diabetes but not in prediabetes or healthy controls. There was a positive link between serum Galectin-3 and fasting plasma glucose (FPG), HbA1c, and hs-CRP. This biomarker is helpful for an early estimate of the chronic inflammatory process in diabetes.

In the research by Holmager et al.,⁸ compared to healthy controls, this research observed elevated concentrations of Galectin-3 among individuals diagnosed with diabetes and those with reduced glucose tolerance.

Also, group B (non-complicated diabetic patients), compared to the control healthy group, showed a statistically significant increase in plasma level of galectin-3 in non-complicated diabetic group B ($0.32 + 0.04$ vs $1.7 + 0.2$ with $P = < 0.001$).

In addition, compared results between group A

(prediabetics) and group B (non-complicated diabetics) results also showed a statistically significant increase plasma level of galectin-3 in non-complicated diabetic group B ($0.67 + 0.1$ vs $1.7 + 0.2$ with $P = < 0.001$), no variations among both groups as concerning age, sex, BMI and hs CRP but there were statistically significant distinctions in HOMA -IR, and HbA1c among group B (non-complicated diabetics).

Yilmaz et al.,⁹ found that Diabetic individuals' galectin-3 levels were significantly greater than those of the prediabetic and nondiabetic groups, and the prediabetic group's levels were higher than those of the nondiabetic group.

Again, when comparing results in the control healthy group with people with diabetes with microvascular complications in group C, our results showed a more statistically significant increase in plasma level galectin-3 ($0.32 + 0.04$ vs $1.97 + 0.01$ with $P = < 0.0001$). Also, when comparing the control healthy group with people with diabetes with macrovascular complications as in group D, our results showed a more and more statistically significant increase in plasma level of galectin-3 in people with diabetes with macrovascular complications ($0.32 + 0.04$ vs $2.3 + 0.1$ with $P = < 0.0001$).

Diabetic patients exhibited elevated levels of galectin-3, particularly in those who had recently developed cardiovascular disease and complications (Berezin AE.). Furthermore, elevated concentrations of galectin-3 were found to be correlated with prediabetes, T2DM, and vascular complications in the latter.¹⁰

When comparing diabetic patients with microvascular complications vs. patients with macrovascular complications, results in this study found that galectin-3 plasma levels were more and more with a statistically significant increase in plasma level of galectin-3 in people with diabetes with macrovascular complications ($1.97 + 0.01$ vs. $2.3 + 0.1$ with $P = < 0.001$) and these patients had also statistically significant increase in HOMA-IR, HbA1c, and hs CRP.

Hodeib et al.,¹¹ found that in cases with macroalbuminuria, galectin-3 was significantly higher than in those with microalbuminuria and was more in microalbuminuric than in normoalbuminuric patients, demonstrating that elevated galectin-3 in the circulation is essential for diabetic nephropathy development and progression. Also, Weigert et al.¹² concluded that galectin-3 is elevated and negatively correlates with HbA1c in cases with type 2 diabetes, pointing to a modifying function galectin-3 in human metabolic diseases.

In this study, we studied the correlation between levels of plasma galectin-3 and hs-CRP or HbA1c. In group A (prediabetics), there was no significant correlation between galectin -3 and hs-CRP ($r = -$

0.190, $P=0.241$) nor with HbA1c ($r= -0.228$, $P=0.157$). Still, in group B (non-complicated diabetes), there were highly significant negative correlations between galectin-3 and hs-CRP ($r= -0.493$, $P= 0.001$) and no correlation with HbA1c ($r= 0.148$, $P= 0.361$). Both microvascular and macrovascular diabetic complications showed that there was statistically highly significant negative correlation between galectin-3 and hs-CRP ($r= -0.570$, $p = <0.001$) but no correlation with HbA1c ($r= 0.028$, $P= 0.865$) in people with diabetes with microvascular complications while group with macrovascular complications had statistically highly significant negative correlations with hs-CRP ($r= -0.565$, $P= < 0.001$) and statistically highly significant positive correlations with HbA1c. ($r=0.622$, $P= < 0.001$).

In the analyses performed by Holmager et al.,⁸ Individuals diagnosed with diabetes mellitus type 1 and heart failure showed an increase in plasma galectin-3 levels, which was correlated positively with HbA1c. However, in the group of people with type 2 diabetes, Berezin et al.¹³ discovered no such correlation among hs-CRP, HbA1c, & Galectin-3 levels.

Elevated levels of galectin-3 were thus detected in diabetic individuals, especially those who had recently developed cardiovascular disease and complications.¹⁴

Also, the plasma level of galectin-3 was increased more than fivefold or more in people with diabetes with complications when in contrast to the control healthy group. The diabetic group with macrovascular complications had the most significant increase in galectin-3 level compared to microvascular complications. Further data suggests that higher levels of circulating Galectin-3 are related to diabetes and the difficulties that come along with it. This indicates that Galectin-3 is intimately tied to the disease states being discussed. A link between the circulating amount of Galectin-3 and diabetes and its complications has been demonstrated through clinical research. As a result, the utilization of Galectin-3 as a biomarker and predictor for these illnesses holds great potential.¹⁵

5. Conclusion

One potential biomarker for diabetes and prediabetes detection is galectin-3. It can also be used to monitor the progression of macro and microvascular complications related to diabetes. Galectin-3 levels were shown to be higher in persons with type 2 diabetes compared to those without the disease. In type 2 diabetes mellitus (T2DM) patients, galectin-3 levels are consistently higher across the board, and they were associated with an increased risk

of the main outcome. To determine if galectin-3 is merely an indication of disease or a factor in the onset and development of diabetes complications, more mechanistic studies are required.

Disclosure

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Authorship

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Conflicts of interest

There are no conflicts of interest.

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