Journal for Research in Applied Sciences and Biotechnology

www.jrasb.com

ISSN: 2583-4053

Volume-2 Issue-5 || October 2023 || PP. 210-214

https://doi.org/10.55544/jrasb.2.5.31

Role of Retinol Binding Protein -4(RBP-4) and some Biochemical Parameters in Type II Diabetes Mellitus Patients

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www.jrasb.com || Vol. 2 No. 5 (2023): October Issue

Received: 28-10-2023	**Revised:** 15-11-2023	**Accepted:** 20-11-2023

ABSTRACT

Diabetes is an important public health issue that adversely affects the lives of millions of individuals worldwide. RBP4 involvement in the pathogenesis of insulin resistance and type 2 diabetes. The aimof this study to assessment of role retinol binding protein -4 and other biochemical parameters in T2DM. Eighty eight participated in this study. Forty four T2DM, age between (40-60) years and forty four healthy control age between (40-55). there was a highly significant increase of FBS, HbA1C, TC, TG, LDL-C and VLDL-C, while a significant decreased of HDL-C between control and T2DM patients. There was a highly significant increase of RBP-4 level between different group (control and T2DM patients). Conclusion: Elevation of retinol in diabetic patients is considered a riskindicator for them with the early onset of cardiovascular disease, and this is a result of the continuous increase in the concentrations of sugar levels in the blood, and thus a defect in the metabolism of fats occurs, which leads to its rise, and this is an indicator of the entry of a diabetic patient with one of thecomplications, which is heart disease.

Keywords- T2DM, Retinol Binding Protein-4, HbA1c, Lipid profile, FBS.

I. INTRODUCTION

Diabetes is a serious public health problem that has a negative impact on millions of people's lives globally. The number of people who havediabetes has been rising globally (1).On a global scale, it is predicted that the number of diabetics would rise from 416 million in 2015 to 643 million in 2040.A recent study found that people as a whole had a prevalence of diabetes of 10.5%(2, 3).About 90% of all instances of diabetes are type 2 diabetes mellitus. Insulin resistance is the term used todescribe the reduced insulin response in T2DM (4). Because insulin is useless in this circumstance, the body first produces more insulin to maintain glucose homeostasis; but, over time, this production decreases, leading to T2DM.Diabetes is a condition that can completely destroy the body. It affects people of all ages and health statuses, including both rich and poor peoples, both gender, as well as, adult and children (5). Additionally, insulin and glucagon, the hormones in charge of controlling blood glucose levels in order to regulate blood glucose levels, are imbalanced in diabetes and contribute to the disease(6). Initiallyidentified as a hormone released by the liver that transports vitamin A (retinol) from the liver to peripheral tissues, retinol binding protein 4 (RBP4) was later found to be a receptor for vitamin A. Adipocytes have been discovered as an additional source of RBP4 in recent investigations, and evidence from both animal and human studies has implicated RBP4in the etiology of insulin resistance and type 2 diabetes (7). RBP4 levels were linked to metabolic syndrome, obesity, insulin resistance, and type 2diabetes, according to recent clinical trials in adults (8). Furthermore, there is some evidence that patients with advanced renal impairment fromT2DM had higher serum or plasma RBP4 levels. This study's objective is to evaluate the involvement of retinol binding protein-4 and other biochemical factors in type 2 diabetes (9).

Journal for Research in Applied Sciences and Biotechnology

www.jrasb.com

ISSN: 2583-4053

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II. MATERIAL AND METHODS

Eighty eight people took part in the study. 44 T2DM patients, agedbetween 40 and 60, and 44 healthy controls, aged between 40 and 55. All participants' demographic information, including their age, height, and weight, was recorded. Fasting serum glucose (FSG), glycated hemoglobin (HbA1c), and lipid profile (total cholesterol, triglyceride, high density lipoprotein, and low density lipoprotein) were all measured in the blood samples used for the laboratory examination. An ELISA kit was used to measure the level of retinal binding protein -4.

To conduct the statistical analysis, Excel was employed. Data are reported as averages and standard deviations (SD). P-values under 0.05 were considered significant, and p-values under 0.01 were considered extremely significant.

III. RESULTS

There was a highly significant increase of weight, high and BMI betweendifferent group. while no significant of age between different group.

Table (1): Anthropometric measurements between different group.

Parameter	Mean±SD		p-value
	Control (n=43)	T2DM Patients (n=39)	
Age (year)	43.90±3.92	45.38±5.34	0.101
Weigh (kg)	70.72±9.46	82.96±12.39	0.001
Height(cm)	165.53±7.90	170.30±9.47	0.01
BMI (kg/m2)	25.90±3.63	28.78±4.75	0.003

As shown in table (2) there was a highly significant increase of FBS, HbA1C, TC, TG, LDL-C and VLDL-C, while a significant decreased of HDL-C between control and T2DM patients.

Table (2): Biochemical parameters between different group (control andT2DM patients).

Parameter	Mean±SD		p-value
	Control (n=44)	T2DM Patients (n=44)	
FBS (mg/dl)	79.72±5.84	164.48±66.11	0.0001
HbA1c (%)	5.04±0.45	8.64±1.95	0.0001
TC (mg/dl)	151.79±31.49	230.2±50.88	0.0001
TG (mg/dl)	99.18±19.9	193.8±57.89	0.0001
HDL-C (mg/dl)	50.74±6.87	42.66±6.53	0.0001
LDL-C (mg/dl)	86..40±30.64	148.7±47.43	0.0001
VLDL-C (mg/dl)	19.83±3.98	38.76±11.57	0.000

There was a highly significant increase of RBP-4 level between different group (control and T2DM patients).

Parameter	Mean±SD		p-value
	Control (n=43)	T2DM patients (n=39)	
RBP-4 level(ng/ml)	1.186±0.76	3.42±0.93	0.0001

Table (3): RBP-4 level between group (control and T2DM patients).

Parameter	Mean±SD		p-value
	Control (n=44)	T2DM Patients (n=44)	
FBS (mg/dl)	79.72±5.84	164.48±66.11	0.0001
HbA1c (%)	5.04±0.45	8.64±1.95	0.0001
TC (mg/dl)	151.79±31.49	230.2±50.88	0.0001
TG (mg/dl)	99.18±19.9	193.8±57.89	0.0001
HDL-C (mg/dl)	50.74±6.87	42.66±6.53	0.0001
LDL-C (mg/dl)	86..40±30.64	148.7±47.43	0.0001

ISSN: 2583-4053
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VLDL-C (mg/dl)	**19.83±3.98**	**38.76±11.57**	**0.000**

As shown in table (4): there was a highly positive correlation between RBP-4 level and weight, BMI, FBS, HbA1c, TC, TG, LDL-C and, VLDL-C, while negative correlation coefficient between RBP-4 and HDL-C in T2DM patients.

Table (4): Correlation coefficient between RBP-4 level and different parameters in T2DM.

parameters	**RBP-4 level in T2DM**	
	r	**p-value**
Age	0.293	0.113
High	-0.015	0.926
Weight	**0.540	0.000
BMI	0.478**	0.002
FBS	0.601**	0.000
HBA1c	0.464**	0.003
TC	0.567**	0.000
TG	0.506**	0.001
HDL-C	-0.476**	0.002
LDL-C	0.550**	0.000
VLDL-C	0.506**	0.001

IV. DISCUSSION

RBP (retinol binding protein) is connected to the metabolism of glucose. A surplus of free fatty acids causes hyperinsulinemia by reducing the ability of hepatocyte receptors to bind insulin. Hepatocytes and adipocytes are the sites of RBP transport protein synthesis. Patients with obesity, diabetes, and non-alcoholic fatty liver disease (NAFLD) had higher RBP levels in type 2 diabetes, metabolic syndrome, and obesity all cause insulin resistance. Down-regulation of the insulin-responsive glucose transporter GLUT4 was discovered to go along with it. RBP4, a serum retinol-binding protein, was secreted by adipocytes in response to decreased adipocyte GLUT4. All experimental animals and in humans, elevated blood levels of RBP-4 proved to be the precursor to the onset of systemic insulin resistance. Reduced serum RBP4 levels significantly improved insulin sensitivity in mice, whereas elevated serum RBP4 levels decreased glucose absorption into skeletal muscle and increased glucose synthesis by liver (10, 11). Increased serum retinol-binding protein (RBP) levels have been linked to the emergence of type 2 diabetes and insulin resistance. Transthyretin-RBP complex secretion from the liver has been decreased, and RBP clearance via the kidney has been improved, using two series of small molecules (12). Apolipoprotein plasm in plasma requires binding to dyslipidemia, which includes both of hypercholesterolemia, hypertriglyceridemia and due to its lipid-soluble physical properties. in atherosclerosis the the majority danger is Apolipoprotein plasm . Between controls with T2DM patients, there wasa highly significant increase in TC, TG, LDL, and VLDL cholesterol, but a substantial decrease in HDL cholesterol. According to a study (13), RBP4 expression and blood cholesterol (TC) levels are connected. adipocyte hypertrophy, adipose tissue inflammation, and endocrine dysfunction may be caused by an excess of adipocyte cholesterol that is produced as a result of hypercholesterolemia, which interferes with adipocyte differentiation and maturation. The fundamental process may be that hypercholesterolemia leads to adipocyte cholesterol excess since adipose inflammatory can also promote get free of pro-inflammatory molecules (such TNF-α and IL-1). Furthermore, the collection of pro- inflammatory substances impede set free of RBP4 from adipocytes into the bloodstream (14). Wessel et al. (2019) discovered a strong positive association between RBP-4 levels and high very low-density lipoproteins (VLDL) compared to tiny low-density lipoproteins (LDL), while finding a strong negative correlation between RBP-4 and HDL-C. RBP4 shows a significant positive link with blood triglyceride (TG) levels in people withtype 2 diabetes. The identical connection between TG and HDL was discovered in RBP4 single nucleotides polymorphism (15). All of these findings point to RBP4's potential involvement in the pathophysiological development of atherosclerosis by changing plasma lipoprotein giving out associated with atherosclerosis (16).

In contrast to certain publications (17, 18), but in line with other studies (19, 20), plasma RBP4 levels were not raised in T2DM participants in our investigation. Furthermore, we failed to find a significant association between the two and HOMA-IR-based insulin resistance. However, due to its link to triglycerides, we did discover

ISSN: 2583-4053
Volume-2 Issue-5 || October 2023 || PP. 210-214
https://doi.org/10.55544/jrasb.2.5.31

that RBP4 was higher in people who were classified as having T2DM. In contrast, Ingelsson et al. also noted RBP4 elevations in T2DM and showed that the presence of more T2DM components was associated with incrementally higher RBP4levels. It should be noted that although retinol levels were elevated in the T2DM-diagnosed participants as well, there was no correlation between any of the specific T2DM components, and there were no anomalies in the RBP4/retinol ratio.As was expected, there was a strong association between retinol and RBP4 that appeared to be linear across the whole range of RBP4 values measured. When considered as a whole, the data are consistent with the hypothesis that the major abnormality in TEDM is not retinol but rather increased levels of circulating RBP4(21). Results indicate that dyslipidemia, obesity, and vascular dysfunction are closely related to RBP4. RBP4 similarly originates solely from hepatocytes, although RBP4 released by the liver has no negative effects on glucose homeostasis. Additionally, RBP4 has demonstrated promise in the diagnosis and treatment of cardiovascular illness, including the ability to foretell the prevalence of hypertensive, coronary heart disease in the widespread populations, evaluating the prediction of individuals with heart failure and coronary artery disease, among other conditions. Future cardiovascular disease biomarkers are anticipated to include RBP4. (22). RBP-4 may be the characteristic cytokines of IR and the acuteness of CVD in people with Type 2 diabetic patient because both diseases share the same theorized mechanisms that produce endothelial dysfunction and, consequently, inflammation (23,24,25). Conclusion: Elevation of retinol in diabetic patients is considered a risk indicator for them with the early onset of cardiovascular disease, and this is a result of the continuous increase in the concentrations of sugar levels in the blood,and thus a defect in the metabolism of fats occurs, which leads to its rise,and this isan indicator of the entry of a diabetic patient with one of the complications, which is heart disease.

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ISSN: 2583-4053

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