The Effect of Age and Gender on Fetuin-A and Some Biochemical parameters in Blood Sera of Iraqi patients with T2DM: A comparative study

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Received 21, July, 2014
Accepted 18, February, 2015

Abstract:

The serum protein test includes measurement of the level of total protein(albumin, globulin). Fetuin-A is a blood protein made in liver. It can inhibit insulin receptor, enhance insulin sensitivity and make the individuals more likely to develop type 2 diabetes, then disorder in lipid profile (Total cholesterol(TC), low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c), Triglyceride(TG) and very low density lipoprotein cholesterol (VLDL-c) .

To evaluate Fetuin-A, total protein, albumin, globulin, HbAlc and lipid profile in 200 adult and elderly Iraqi patients with type 2 Diabetes Mellitus were taken and compare them with 200 subjects as a healthy control. The laboratory analysis(for patients and control) were performed to determine these parameters .The results show that FBG. HbA1c, Lipid profile for (patients and control) (except HDL-c) were increase with age with a significant difference ($p<0.01$) between patients and control in each age and with no significant difference ($p>0.05$) between male and female. Serum total protein, globulin, Fetuin-A, increase with age while albumin decrease with age(in patients and control).

Key words: Fetuin-A, HbA1c, Lipid profile, Protein, Albumin, Globulin.

Introduction:

Type 2 diabetes is a defect metabolically characterized by an insulin resistance that has become a new global response to the epidemic [1]. Insulin cannot convert the glucose to any nutrients after a meal in the liver but can stop the burning of fat stores, this gives the diabetic person a double whammy fatty acids accumulate from food and liver consequently more fat is deposited in tissues [2,3]. Glycosylated hemoglobin (HbA1c) comes from the combination between glucose and hemoglobin, so it is used primarily to monitor the long term control of diabetes mellitus. The level of HbA1c is increased in the red blood cells of persons with poorly controlled diabetes mellitus, since the glucose stay attached to hemoglobin for the life of red blood cell about three months, the level of HbA1c reflects the average blood glucose concentration over the past 120 days [4]. The proteins from fat tissue called (adipocytokines) regulate the metabolism of blood glucose and may ultimately prove to be a target for new diabetes therapies. Fetuins are blood proteins which are made in hepatocytes and secreted in to the serum. They belongs to a group of binding proteins mediating the transport and availability of a wide variety of cargo substances in the blood stream [3]. Fetuin- A (Alpha 2 – Hermans albumin is mainly synthesized in the liver, it helps in keeping the blood from leaking out of blood vessels Sehmid Glucoprotein) (AHsG) is a circulating glycoprotein

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and a member of systatin protease that can inhibit insulin receptor outophos-phorylation and subsequent downstream signaling in vitro[2,4]. Fetuin- A is more abundant in fetus blood than adults hence the name "Fetuin "from Latin word fetus. The measurement of serum total protein means (albumin plus globulin), albumin also helps to carry some medicines and other substances through the blood and is important for tissue growth and healing. Globulin is made up of different proteins called Alpha, Beta and Gamma types. Some globulins are made by the liver, while others are made by immune system. Certain globulin bind with hemoglobin other globulins transport metals such as iron in the blood and help fight infections [5,6].

Aim of the study

The aim of the current study is to evaluate of Fetuin-A, total protein, albumin , globulin, HbAlc and lipid profile in adult and elderly Iraqi patients with type 2 Diabetes Mellitus and compare the results with a healthy control subjects (both groups are on same age ,sex and number.)

Materials and Methods:

The present study comprised of (200) patients with type 2 Diabetes Mellitus (100 male, 100 female) and (200 subjects healthy control (100 male, 100 female) they were attending the specialized center for endocrinology and diabetes in Baghdad from (May 2011-May 2014). Patients and control grouped in to 4 groups depending on their age .First group (40-50 years), second (51-60years) third (61-70 years) and fourth group age (more than70 years)(each age group 25 subjects). Venous blood samples were aspirated after an over night fast and examined for plasma lipid profile and glucose by enzymatic colorimetric methods. Serum Fetuin – A was determined by using ELISA system (Elisa kit Bosterbio-USA) ,and biuret method was used to determine total protein , albumin and globulin while immune method was used to determine HbA1c. Descriptive analysis was used to show the mean and standard deviation of variables .The significance of difference between mean values was estimated by Student T-Test. The probability, $P<0.01$ highly significant $P< 0.05$ = significant, $p> 0.05$ = no significant. Correlation analysis was used to test the linear relationship between parameters.

ANOVA test was used to show the differences between variables of differentiated groups.

Results and Discussion:

As shown in table (1) there was a highly significant difference ($P<0.01$) in mean values of all factors between the patients and control group(except ,Age, total protein ,albumin, and globulin which there values in patients more than control but with no significant difference $P>0.05$).

Total protein may be elevated due to dehydration (loss of water from the body because of diabetic) and this causes decrease in albumin concentration and globulin increase in kidney dysfunction which always happened with diabetes this result was in agreement with other studies [7,8,9,10].

Not:

***= no significant difference between this value and the value before it p>0.05**

****= significant difference between this value and the value before it p<0.05**

*****= Highly significant difference between this value and the value before it p<0.01**

Table (1) : The mean± SD of F.B.G,HbA1c, TC , LDL-c , HDL-c , TG , VLDL-c ,Total protein, Albumin, Globulin and Fetuin – A in sera of patients(with type 2 diabetes) and control groups.

Biochemical Parameters	Control group No.(200)	Patients group No.(200)	P value
Age range (year)	55.4±4	*55.7±4.3	>0.05
F.B.G mg/dl	90±3.7	***345.32±7	<0.01
HbA1c %	5.38±0.01	***13.135±0.7	<0.01
TC. mg/dl	146.587.±4	***302.375±5	<0.01
LDL-c mg/dl	86.675±3	***237±5	<0.01
HDL-c mg/dl	37.641±2.8	***48.2±2.04	<0.01
TG mg/dl	94.237±2.8	***213.925±3	<0.01
VLDL-c mg/dl	18.8±1.1	***42.78±1.2	<0.01
TP mg/dl	727.8±0.4	*827.48±0.3	>0.05
Alb. mg/dl	414±1.4	*425.3±1.3	>0.05
Glub. mg/dl	313.8±1.2	*349.5±1.1	>0.05
Fetuin – A mg/dl	82.1±0.02	***127±0.16	<0.01

* p>0.05 no.sig. ** p<0.05 sig. ***P<0.01Hs

The results in Table (2) show that the values of all factors of all ages in(male patients) were increase with age with a highly significant difference P<0.01 (except HDL-c and Alb, were decreased with no significant difference P>0.05), total protein, globulin and VLDL-c increased with age with no-significant difference (p>0.05) between them, and , also the value of Fetuin-A between the two age groups (40-50) and (50-60) increase with no significant difference P>0.05. These results in agreement with other studies [11,12] which found that serum Fetuin-A levels elevated in subjects newly diagnosed type 2 diabetes with impaired glucose tolerance and it increased with age , while there was a significant difference between the older age and other ages this was in agreement with (Joachim H. Ix, et al,) [13], who found that higher Fetuin-A is associated with incident diabetes in older persons (aged ≥75years).

Study for Joachim H Ix. etal [14] , concluded that serum Fetuin-A is a novel risk factor for incident diabetes that is independent of markers of insulin resistance commonly available in clinical practice, and may be partially mediated through visceral adiposity.

HbA1c increase with age because Glycolated hemoglobin is a monitor for having diabetes [15, 16] due to the long duration of sickness, diet, poorly or lack of physical exercise, may be obesity because always weight increase with age, poorly controlled diabetes, all these factors lead marked to increase in proportion of glucose and impede the patients response to treatment [16].

The upper results for male in (Tables 2 and 3) indicated that there were highly significant differences p<0.01 in values of all factors between control and patients ,but as in table (3), the results show that there was no significant difference p>0.05 between the value of any factors, except, the value of Fetuin- A for the older age as compared with other ages was highly significant difference p<0.01, while for the age 61-70 and other ages ,the result was significant p<0.05.

Table (2) The mean± SD of F.B.G, HbA1c, TC, LDL-c, HDL-c, TG , VLDL-c, Total protein, Albumin, Globulin and Fetuin – A in male patients .

Age years Biochemical parameters	40-50	51-60	61-70	71- up	P value
F.B.G mg/dl	291.8± 8	***331.6± 7	***362.4± 6	***400.8±5	P<0.01
HbA1c %	11.4±0.04	***12.6±0.02	***13.9±0.09	***14.9±0.08	P<0.01
TC. mg/dl	286±2	***300±2	***321±2	***332.5±2	P<0.01
LDL-c mg/dl	206.3±2	***220.3±2	***236.9±2	***246.4±2	P<0.01
HDL-c mg/dl	40.5±1	*40.3±1	*38.9±1	*37.5±2	p>0.05
TG mg/dl	195.4±1	***215±2	***225±2	***242±2	P<0.01
VLDL-c mg/dl	39.8±1.3	*43±1	*45±1	*48.4±1	P>0.05
TP mg/dl	732.2±0.5	*775±0.17	*788.5±0.3	*823.4±0.2	p>0.05
Alb. mg/dl	447.5±0.4	*433.6±0.22	*412.1±0.35	*364.5±0.1	p>0.05
Glub. mg/dl	284.7±0.14	331.4±0.133	376.4±0.15	*498.9±0.1	p>0.05
Fetuin – A mg/dl	74.6±0.2	*75.1±0.01	**105±0.01	***252±0.01	P<0.01

*p>0.05 no sig. ** p<0.05 sig. ***p<0.01 Hs

Table (3) The mean± SD of F.B.G, HbA1c, TC , LDL-c, HDL-c ,TG , VLDL-c ,Total protein, Albumin, Globulin and Fetuin – A in male control .

Age years Biochemical Parameters	40-50	51-60	61-70	71- up	P value
F.B.G mg/dl	86.6±3.8	*90.6±3.7	*93.44±3.6	*95.2±3.6	p>0.5
HbA1c %	5.3±0.01	*5.35±0.01	*5.51±0.01	*5.7±0.01	p>0.05
TC. mg/dl	150.2±1	*156.5±1	*158.3±1.1	*160.7±1	p>0.05
LDL-C mg/dl	84.1±1	*92.4±1.1	*95.46±1	*97.4±4.3	p>0.05
HDL-C mg/dl	49.1±3	*47.3±2	*45.9±2.1	*45.7±2.1	p>0.05
TG mg/dl	83.4±4	*84±3	*84.7±3	*88.3±2	p>0.05
VLDL-C mg/dl	16.6±1.3	*16.8±1	*16.94±2	*17.6±1.3	p>0.05
TP mg/dl	722±0.5	*729.0±0.3	*729.5±0.3	*753±0.2	p>0.05
Alb.mg/dl	421±0.4	*417.5±0.22	*415±0.35	*410±0.1	p>0.05
Glub.mg/dl	301±0.14	*311.5±0.133	*314.5±0.15	*343±0.2	p>0.05
Fetuin – A mg/dl	51±0.02	*52±0.01	**86±0.010	***152±0.01	P

The same pattern was seen for female tables (4,5). Fetuin –A has been demonstrated to bind the insulin receptor (tyrosine kinase) in muscle and fat leading to insulin resistance in these tissues and promotes insulin resistance in muscles and fat [3,17,18] then increase with increasing F.B.G.

In table (5) there were no significant difference between the values of fetuin –A at all ages but at age (71 up)years there was a highly significant difference between it and other ages and for the age (61-70) years their was a significant difference between its value and other ages .This may occurred in liver dysfunction , congestive heart failure , high blood pressure in elderly patients .

There was no significant difference between male and female P>0.05 for all factors between (patients, patients) ,(control, control).

Table (4) The mean± SD of F.B.G,HbA1c, TC , LDL-c , HDL-c ,TG , VLDL-c, Total protein, Albumin, Globulin and Fetuin – A in female patients

Age years Biochemical parameters	40-50	51-60	61-70	71- up	P value
F.B.G mg/dl	285.32±7	***330.42±8	***360±6	***400.8±5	P<0.01
HbA1c %	11.1±0.07	***12.4±0.08	***13.81±0.9	***14.89±0.1	P<0.01
TC mg/dl	285.1±1	***298±1	***319±2	***33072	P<0.01
LDL-c mg/d l	206.1±1	***219.7±2	***226.3±1	***245.1±2	P<0.01
HDL-c mg/dl	40.5±1	*40.3±1	*38.9±1	*37.5±2	p>0.05
TG mg/dl	192.5±4	***202±3	***219±3	***237.5±2	P<0.01
VLDL-c mg/dl	38.5±1	*40.4±1.4	*43.8±1.3	*47.4±1.4	p>0.05
TP mg/dl	726.4±o.14	*765.4±0.14	*776.1±0.21	*811.8±0.13	p>0.05
Alb. mg/dl	4.362±0.2	*423.1±.18	*418.1±0.13	*343.1±0.16	p>0.05
Glub. mg/dl	2.902±0.13	*342.3±o.12	*358.0±0.11	*467.7±0.12	p>0.05
Fetuin – A mg/dl	0.739±0.2	*0.749±0.07	***1.03±0.3	***2.49±0.07	P

Table (5) The mean± SD of F.B.G, HbA1c, TC , LDL-c, HDL-c ,TG , VLDL-c ,Total protein, Albumin, Globulin and Fetuin – A in female control.

Age years Biochemical parameters	40-50	51-60	61-70	71- up	P value
F.B.G mg/dl	85.3±3.8	*89.2±3.5	*92.4±3.1	*94.8±3	p>0.05
HbA1c %	5.2±0.01	*5.25±0.02	*5.3±0.02	*5.43±0.02	p>0.05
TC mg/dl	143.3±6.1	*144.4±6.1	*146±5.5	*147.1±5.2	p>0.05
LDL-c mg/dl	84.6±2	*84.9±1.8	*85.9±1.5	*86.2±1.3	p>0.05
HDL-c mg/dl	50.13±2	*48.5±1.8	*47.8±1.6	*46.7±1.3	p>o.o5
TG mg/dl	82.6±2	*82.9±1.9	*83.3±1.7	*84.6±1.6	p>0.05
VLDL-c mg/dl	16.52±2	*16.58±3.3	*16.66±3.1	*16.92±3.1	p>0.05
TP mg/dl	712±4	*714.5±3.8	*719.9±4.2	*743±3.1	p>0.05
Alb. mg/dl	420.1±2	*415.2±1.8	*413.0±1.6	*411.6±1.4	p>0.05
Glub. mg/dl	291.9±2.1	*304.5±2	*306±1.8	*332.4±1.5	p>0.05
Fetuin-A mg/dl	0.5±0.01	*0.52±0.01	**0.83±0.02	***1.31±0.03	P

These results were disagreement with the results obtained by Gunduz FO,et al,who found that serum Fetuin-A levels were significantly lower in patients with T2DM than controls, correlations between, Fetuin-A and HbA1c levels were not observed [19]. Also Aiyun Song,et al reported that there was a non significant association between elevated serum Fetuin-A concentrations and impaired glucose regulation (all p≥0.12)[20].

In conclusion serum Fetuin-A is a novel risk factor for incident diabetes and insulin resistance i.e., patients with type 2DM had increased their Fetuin-A especially with age(71-up)years

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تاثير العمر والجنس على مستوى البروتين الكبدي الجنيني – A وبعض المؤشرات البيوكيميائيه في مصول المرضى العراقيين المصابين بداء السكري من النمط الثاني .:دراسة مقارنه

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الخلاصة:

يتضمن اختبار البروتين الكلي قياس مستوى(الألبومين ، الكلوبيولين) .الفتيون –A هو بروتين ينتج بالكبد ويطرح الى مجرى الدم ويستطيع تثبيط عمل مستلمات الأنسولين ويزيد من تحسس الأنسولين ويجعل الشخص البالغ اكثر قابليه على الاصابه بداء السكري من النمط الثاني ،اضطراب بالدهون (الكولسترول الكلي ،البروتين ألدهني عالي الكثافة ،البروتين ألدهني واطئ الكثافة ،الدهون الثلاثية ،البروتين ألدهني واطئ الكثافة جدا) .

و لتقدير كمية، البروتين الكبدي الجنيني- A والبروتين الكلي ،الألبومين ، الكلوبيولين ،الدهون والهيمكلوبين السكري (التراكمي)تم اخذ 200 شخص بالغ ،من الكبار في السن مصابين بداء السكري من النمط الثاني (100 نساء، 100 رجال) ومقارنه النتائج بـ 200 شخص (100 نساء ،100 رجل)أصحاء كمجموعه مقارنه. تم اجراء التحاليل ألمختبريه (للمرضى والأصحاء) لتقدير هذه المؤشرات.

أظهرت النتائج ان نسبه الكلوكوز عند الصيام ،الهيمكلوبين السكري (تراكمي) والدهون كلها عدا (الدهون البروتينيه عاليه الكثافة)تزداد بتقدم العمر بوجود فرق معنوي عالي ($P<0.01$) بين المرضى والأصحاء ولا يوجد فرق معنوي ($P>0.05$)بين الرجال والنساء .

كما لوحظ ان البروتين الكلي والكلوبيولين والبروتين الجنيني يزداد بتقدم العمر والألبومين يقل بتقدم العمر (عند المرضى والأصحاء) .