AIM OF THE WORK

The study was designed to evaluate the alterations of serum levels of syndecan-1, lipids, interleukin-6 and C-reactive protein in type 2 diabetic patients and to assess the possible effect of statins on syndecan-1 level targeting the prevention of pathologic inflammatory events in these patients.

SUBJECTS AND METHODS

I. Subjects:

After the approval of the ethics committee of the Medical Research Institute. The present study was conducted on 50 subjects categorized as follows:

Group (I): Comprised 20 type 2 diabetic patients treated with conventional therapy for diabetes.

Group (II): Included 20 type 2 diabetic patients treated with conventional therapy for diabetes and received a daily dose of (40 mg/day) statin treatment (Simvastatin, CAS 79902-63-9) by oral administration for 10 weeks. [73]

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Control group: Ten healthy volunteers of comparable age and sex to the patients group were served as controls.

All patients were recruited from the internal medicine department at the Medical Research Institute, Alexandria University.

Subjects with any conditions other than diabetic complications that can affect serum levels of syndecan-1 and/or inflammatory markers were excluded such as tumors, collagenic disorders and hepatitis C.

Written consents were obtained from all participants, before entry in the study.

II. Methods:

The following were done to all the enrolled subjects:

A. Detailed history taking and full clinical examination with special stress on duration and treatment of diabetes, any complaints due to diabetic complications and determination of blood pressure.

B. Twelve leads standard electrocardiogram (ECG)

C. Blood sampling:

1. Fasting blood sample:

Five milliliters venous blood sample was taken from each subject after 6-8 hours fasting. Two milliliters of the sample were withdrawn on EDTA-disodium salt for determination of glycated hemoglobin (HbA1c). Another there milliliters venous blood sample was taken after 12-14 hours of fasting for determination of lipid profile. Serum was rapidly and carefully separated from the red blood cells by centrifugation at 3000 rpm for ten minutes. It was then divided as follows:

- An aliquot was immediately used for determination of some laboratory investigations such as: Fasting blood glucose concentration, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Creatine kinase (CK) activities, hs-CRP and lipid profile.
- Another aliquot stored at -20˚C, for serum syndecan-1, IL-6 and apo-E determination.

2. Post prandial blood sample:

Two milliliters venous blood sample was taken from all studied subjects exactly 2 hours after breakfast. Serum was separated and used for post prandial serum glucose estimation.

D. Urine sampling:

Second morning urine samples were collected from all participants for determination of albumin to creatinine ratio (ACR).

E. Laboratory investigations:

1. Determination of fasting and postprandial blood glucose levels: [74]

This was done by glucose oxidase method, where it was determined without deproteinization using an enzymatic reaction based on the following steps:

$$\text{Glucose} + H_2O \xrightarrow{\text{Glucose OxIdAse}} \text{Gluconic Acid} + O_2 + H_2O_2$$

$$H_2O_2 + \text{Reduced Chromagen} \xrightarrow{\text{Peroxidase}} \text{Oxidized Chromagen (Rose Color)} + H_2O$$

The rosy colored product which is proportional to the concentration of glucose in sample (T) was measured spectrophotometrically at 505 nm. The concentration of glucose solution was determined after comparison with a standard glucose solution (S) of known concentration (100 mg/dI) similarly treated.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1), Enzyme-Buffer	- Phosphate buffer - Glucose oxidase (GOD) - Peroxidase (POD) - 4-amino-antipyrene (PAP)	150 mmol/l ≤20,000 UI/l ≤1000 UI/l 0.8 mmol/l
Reagent 2 (R2), Chromogen	- Chloro-4-phenol	2 mmol/l
Reagent 3 (R3)	- Glucose standard	100 mg/dl

The working solution was prepared by transferring the vial content of R1 to the R2 vial.

Procedures:

1- One ml of working reagent and 10 µl of reagent blank, standard or sample were pippeted into a cuvette**.**

2- The cuvette then mixed well and the absorbance was recorded after 10 minutes at 505 nm.

Calculation:

$$\text{Glucose (mg /dl)} = \frac{\text{absorbance of T}}{\text{absorbance of S}} \text{ x concentration of S}$$

2. Determination of glycated hemoglobin (HbA1c) in blood: *(75)*

Principle:

A hemolyzed preparation of the whole blood is mixed continuously for 5 minutes with a weak binding cation-exchange resin. During this time, glycated hemoglobin (A1c) binds to the resin. After the mixing period, a filter is used to separate the supernatant containing the glycated hemoglobin from the resin. The percent glycated hemoglobin is determined by measuring the absorbance at 415 nm of the glycated hemoglobin fraction and the total hemoglobin fraction. The ratio of the two absorbances gives the percent glycated hemoglobin.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1)	- Potassium phtalate - sodium azide - pH 5	50 mmol/l 0.95 g/l
Reagent 2 (R2)	- Phosphate buffer - Sodium azide - Ph 6.5	30 mmol/l 0.95 g/l
Reagent 3 (R3)	- Phosphate buffer - Sodium azide - Ph 6.5	72 mmol/l 0.95 g/l
Microcolumns	- Pre-weighted amount of resin equilibrated with phosphate buffer	72 mmol/l

Procedures:

A-Hemolysate preparation and labile fraction elimination:

1- The column and reagents were brought to room temperature (21 – 26 °C).
2- 50 µl of blood were mixed with 200 µl of R1 within a test tube used as hemolysate.
3- The test tube was shaken thoroughly and let stand at room temperature for 10-15 minutes.
4- The upper cap of the column was removed and then snapped the tip off the button.
5- By using a flat end of a pipette, the upper disc was down to the resin surface and the column was left to drain waste completely.
6- 50 µl of hemolysate were added to the column and left to drain waste completely.
7- 200 µl of R2 were added in order to drain any sample residue left above the upper disc pipette.
8- 2 ml of R2 were added, and then were left to drain the waste.
9- The column then transferred into a test tube and received 4 ml of R3, then the HbA1c fraction elution was collected and the absorbance measured photometrically at 415 nm.

B- Measurement of total hemoglobin:

50 µl of hemolysate were mixed with 12 ml of R3 then the absorbance was measured photometrically at 415 nm.

Calculation:

$$\text{HbA1c (\%)} = \frac{\text{absorbance of A1c x volume of A1c}}{\text{absorbance of total Hb x volume of total Hb}} x100$$ where; the volume of HbA1c is 4 ml and the volume of total Hb is 12 ml.

3. Determination of total serum cholesterol: *(76)*

It was determined by enzymatic method according to the following reactions:

$$\text{Cholesterol ester} \xrightarrow{\text{Cholesterol esterase}} \text{Cholesterol + fatty acid}$$

$$\text{Cholesterol} + O_2 \xrightarrow{\text{Cholesterol oxidase}} \text{cholest-4-ene-3-one} + H_2O_2$$

$$2H_2O_2 + \text{phenol} + 4\ \text{aminoantipyrene} \xrightarrow{\text{Peroxidase}} \text{quinoneimine dye} + 4\ H_2O$$

The rosy colored quinoneimine chromogen in the sample (T) was measured spectrophtometrically at 505 nm and compared to the color of a similarly treated standard (S) of a known cholesterol concentration (200 mg/dl).

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1), Buffer	- Phosphate buffer - Chloro-4-phenol - Sodium cholate -Triton X 100	100 mmol/l 5 mmol/l 2.3 mmol/l 1.5 mmol/l
Reagent 2 (R2) ,Enzymes	- Cholesterol oxidase - Cholesterol esterase - Peroxidase - 4-amino-antipyrine - Polyethylene glycol 6000 (PEG)	≤ 100 IU/l ≤ 170 IU/l ≤ 1200 IU/l 0.25 mmol/l 167 µmol/l
Reagent 3 (R3)	- Cholesterol standard	200 mg/dl

The working solution was prepared by transferring the vial content of R1 to the R2 vial.

Procedures:

1- One ml of working reagent and 10 µl of reagent blank, standard or sample were pipetted into a cuvette.
2- The cuvette then mixed well and the absorbance was recorded after 5 minutes at 505 nm.

Calculation:

$$\text{Cholesterol (mg/dl)} = \frac{\text{absorbance of T}}{\text{absorbance of S}} \times \text{concentration of S}$$

4. Determination of serum high density lipoprotein cholesterol (HDL-C): [77]

It was determined enzymatically after precipitation of low density lipoproteins (LDL and VLDL) and chylomicrons by the addition of phosphotungstic acid (13.9 mmol/l) in the presence of magnesium chloride ions (570 mmol/l). The cholesterol concentration of HDL left in the supernatant after centrifugation was measured enzymatically and compared to the color of a standard of known cholesterol concentration by using total cholesterol reagent as described earlier.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1), Precipitant	- Phosphotungstic acid - Magnesium chloride ($MgCL_2$)	13.9 mmol/l 570 mmol/l
Reagent 2 (R2) ,Cholesterol standard	- Cholesterol standard	100 mg/dl

Procedures:

1- 250 µl of specimen and 500 µl of precipitating agent (R1) were pipetted into a centrifuge tube
2- The tube mixed vigorously and let stand for 10 minutes at room temperature, then centrifuged for 15 minutes at 3500-4000 rpm.
3- 25 µl of the collected supernatant was treated with 1 ml total cholesterol reagent and the same applied for reagent blank and standard.
4- The cuvette then mixed well and the absorbance was recorded after 5 minutes at 505nm.

Calculation:

Concentration of HDL-C was obtained according to the following equation:

$$\text{HDL-C (mg/dl)} = \frac{\text{absorbance of T}}{\text{absorbance of S}} \times \text{concentration of S} \times 3$$

where, (3) is a dilution factor.

5. Determination of serum low density lipoprotein cholesterol (LDL-C):[78]

It was determined by enzymatic method. After precipitation of LDL-cholesterol fraction by LDL precipitating mixture (polyvinyl Sulfate, Polyethylene glycol in appropriate pH 6.1 buffer). The harvested supernatant then treated enzymatically by means of coupled reaction forming quinoneimine rosy dye measure spectrophotometrically at 505 nm by using total serum cholesterol reagent kit as mentioned previously.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1), Precipitant	- Polyvinyl sulfate - Polyethylene glycol - pH	3 g/l 3 g/l 6.1
Reagent2 (R2), Cholesterol standard	- Cholesterol standard	200 mg/dl

Procedures:

1- 200 µl of the specimen and 200 µl of precipitating reagent (R1) were pipetted into a centrifuge tube.
2- The tube mixed thoroughly for one minute and let stand for 15 minutes at room temperature, then centrifuged for 15 minutes at 4000 rpm.
3- 20 µl of the collected supernatant was treated with 1 ml total cholesterol reagent, the same applied for reagent blank and standard.
4- The cuvette then mixed well and the absorbance was recorded after 5 minutes at 505nm.

Calculation:

The LDL-cholesterol in the supernatant was calculated as follow:

$$\text{LDL-C in supernatant (mg/dl)} = \frac{\text{absorbance of T}}{\text{absorbance of S}} \text{ x concentration of S x 2}$$

where; (2) is the sample dilution factor.

The LDL-C in the sample is calculated as follows:

LDL-C (mg/dl) = total cholesterol – cholesterol in supernatant.

6. Determination of serum Triglycerides (TG): *(79)*

It was determined by enzymatic hydrolysis with lipase enzyme according to the following reactions:

$$TG + H_2O \xrightarrow{\text{Lipase}} \text{Glycerol + Fatty Acids}$$

$$\text{Glycerol + ATP} \xrightarrow{\text{Glycerokinase}} \text{Glycerol 3 Phosphate + ADP}$$

$$\text{Glycerol 3 Phosphate} + O_2 \xrightarrow{\text{G 3 P Oxidase}} \text{Dihydroxyacetonephosphate}\textit{(DHAP)} + H_2O_2$$

$$2H_2O_2 + \text{4 -Aminoantipyrene + 4 -Chlorophenol} \xrightarrow{\text{Peroxidase}} \text{Quinoneimine Dye}\textit{ (Rose color)} + 4H_2O$$

The absorbance of rosy colored chromogen which is proportionate to TG concentration in the sample (T) was measured spectrophotometrically at 505 nm. The concentration of TG solution was determined after comparison with a standard TG solution (S) of known concentration (200 mg/dl) similarly treated.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1), Buffer	- PIPES (Piperazine-1,-Bis-(2-ethanesulfonic acid) buffer - Chloro-4-phenol - Magnesium chloride	100 mmol/l 9.8 mmol/l 3.5 mmol/l
Reagent 2 (R2) ,Enzymes	- Lipase - Peroxidase - Glycerol-3-phosphate oxidase - Glycerokinase - 4-amino-antipyrine - Adenosine triphosphate-Na (ATP)	≤ 1000 IU/l ≤ 1700 IU/l ≤ 3000 IU/l ≤ 660 IU/l 0.5 mmol/l 1.3 mmol/l
Reagent 3 (R3)	- Triglycerides standard	200 mg/dl

The working solution was prepared by transferring the vial content of R1 to the R2 vial.

Procedures:

1- One ml of working reagent and 10 µl of reagent blank, standard or sample were pipetted into a cuvette.
2- The cuvette then mixed well and the absorbance was recorded after 5 minutes at 37˚C at 505 nm.

Calculation:

$$\text{TG (mg/dl)} = \frac{\text{absorbance of T}}{\text{absorbance of S}} \times \text{concentration of S}$$

7. Determination of serum very low density lipoproteins (VLDL): [80]

Principle:

Very low density lipoproteins (VLDL) for all subjects under study were calculated mathematically according to the Friedwald's equation without the use of preparative ultracentrifugation.

Calculation:

$$\text{VLDL (mg/dl)} = \frac{\text{Triglycerides}}{5}$$

8. Determination of serum apolipoprotein-A1 (apo-A1): [81]

Principle:

Apo-A1 is measured by immunoturbidimetric method, through photometric measurement of the reaction between apo-A1 antigens of the specimen and specific antibody to human apo-A1. The turbidity induced is measured spectrophtometrically by end-point method at 600 nm.

Reagents:

Reagent	Component	Concentration
Reagent A	- Imidazole buffer - sodium azide - pH 7	50 mmol/l 0.95 g/l
Reagent B	- Suspension of latex particles coated with anti-human Apo-A1 antibodies, Sodium azide	0.95 g/l
Apo-A1 standard	- Human serum Apo-A1	200 mg/dl

All reagents were ready to use without mixing except standard solution which is reconstituted with 1 ml distilled water.

Construction of Calibration curve:

Serial dilutions of apo-A1 standard were prepared by using 9 g/l saline as a diluent, and then the concentration of apo-A1 standard was multiplied by the corresponding dilution factor indicated below to obtain Apo-A1 concentration of the dilutions.

Dilution	1	2	3	4	5
apo-A1 standard (µl)	30	60	120	180	240
Saline (µl)	210	180	120	60	---
Dilution factor	0.125	0.25	0.50	0.75	1.00

Procedures:

1- All reagents and instrument were brought to 37°C.
2- 1.2 ml reagent A and 10 µl distilled water (blank), standard or sample were pipetted into a cuvette
3- The cuvette then mixed well and inserted into spectrophotometer.
4- The absorbance (A1) was measured at 340 nm.
5- 300 µl reagent B was added to the cuvette.
6- The absorbance (A2) was recorded at 340 nm after exactly 5 minutes of addition of reagent B.

Calibration curve:

The absorbance difference values (A2 − A1) of each standard against its apo-A1 concentration was plotted automatically by the instrument, the blank is used as the standard of 0 concentration.

Apo-A1 concentration in the sample was calculated by interpolation of its absorbance difference (A2 − A1) on the calibration curve.

9. Determination of serum apolipoprotein-E (apo-E): *(82)*

Principle:

Serum levels of apo-E were assayed in all subjects by a quantitative sandwich enzyme-linked immunosorbent assay (ELISA) technique using a commercial kits provided by Assaypro, USA.

An anti-apo-E monoclonal coating antibody was adsorbed onto microwells. Apo-E present in the sample or a provided standard bound to immobilized antibodies adsorbed to microwells. After washing away any unbound substance, a secondary biotinylated apo-E polyclonal antibody was added and bound specifically to the captured apo-E and recognized by streptavidin-peroxidase conjugate. Following incubation, unbound enzyme conjugate anti-apo-E was removed during a wash step and substrate solution tetramethyl benzidine (TMB) reactive with streptavidin-peroxidase was added to the wells. A colored product was formed with variable intensities proportional to the original amount of apo-E present in the sample, the reaction was terminated by addition of acid and absorbance was measured at 450 nm. A standard curve was prepared from seven apo-E standard dilutions and unknown apo-E sample concentrations were determined.

Reagents and materials provided:

Reagents	Quantity
96-wells microtiter plates	2
Adhesive plate covers	4
Biotin –Conjugate anti-Apo-E polyclonal Antibody (50x)	1 vial (140 µl)
Apo-E standard : lyophilized	2 vials, 1.6 µg
Streptavidin-HRP conjugate (100x)	1 vial (80 µl)
Assay diluent (10x)	1 bottle (30 ml)
Washing buffer (20x)	2 bottles (30 ml)
Substrate solution (tetramethyl-benzidine, TMB)	1 vial (8ml)
Stop solution (0.5 N hydrochloric acid)	1 bottle (12 ml)

Preparation of Reagents:

1. All reagents were freshly diluted and brought to room temperature before use.
2. Assay diluent concentrate (10x) was diluted with distilled water (1: 10).
3. Standard: the standard was reconstituted with 0.8 ml of assay diluent. The concentration of the standard in the stock solution is 2 µg/ml. A series of standard were prepared containing 2, 1, 0.5, 0.25, 0.125, 0.063 and 0.031 µg/ml respectively. A tube containing assay diluent is considered as a blank (0 µg/ml).
4. Biotinlyated apo-E antibody (50x): the antibody was spin down and diluted the desired amount of the antibody 1:50 (V/V) with assay diluent.
5. Wash buffer concentrate (20x): the wash buffer was diluted 1:20 with distilled water.
6. Streptavidin-Peroxidase (100x): the SP was spin down and diluted the desired amount of the conjugate 1:100 with assay diluent.

Assay method:

1. Seven wells for standard and one well for blank were prepared. 50 µl each of dilutions of standard, blank and samples were added into the appropriate wells, covered with the plate sealer and incubated for 2 hours at 37ºC.
2. The microwell strips were washed twice with 300 µl wash buffer per well. After the last wash, wells were emptied and microwell strips were tapped on absorbent pad to remove excess wash buffer.
3. 50 µl of biotinylated apo-E antibody were added to each well and incubated for one hour.
4. At the end of incubation, the microwell strips were washed manually five times with 200 µl of wash buffer.
5. 50 µl of streptavidin-horseradish peroxidase conjugate were added to each well and incubated for 30 minutes.

6. The microtiter plate was washed after incubation.
7. 50 µl of chromagen substrate was added to each well and incubated for 12 minutes till the blue color developed.
8. The enzyme-substrate reaction was stopped by quickly pipetting 50 µl of 0.5 N hydrochloric acid into each well, including the blank wells to completely and uniformly inactivate the enzyme, results were read immediately after stopping the reaction.
9. Absorbance of each well was read at 450 nm.
10. A standard curve was constructed by plotting the absorbance values on the ordinate against the corresponding apo-E standard concentration on the abscissa.

Calculation:

The concentration of apo-E in each sample was determined by extrapolating optical density values to apo-E concentrations using the plotted standard curve **(Figure 8).**

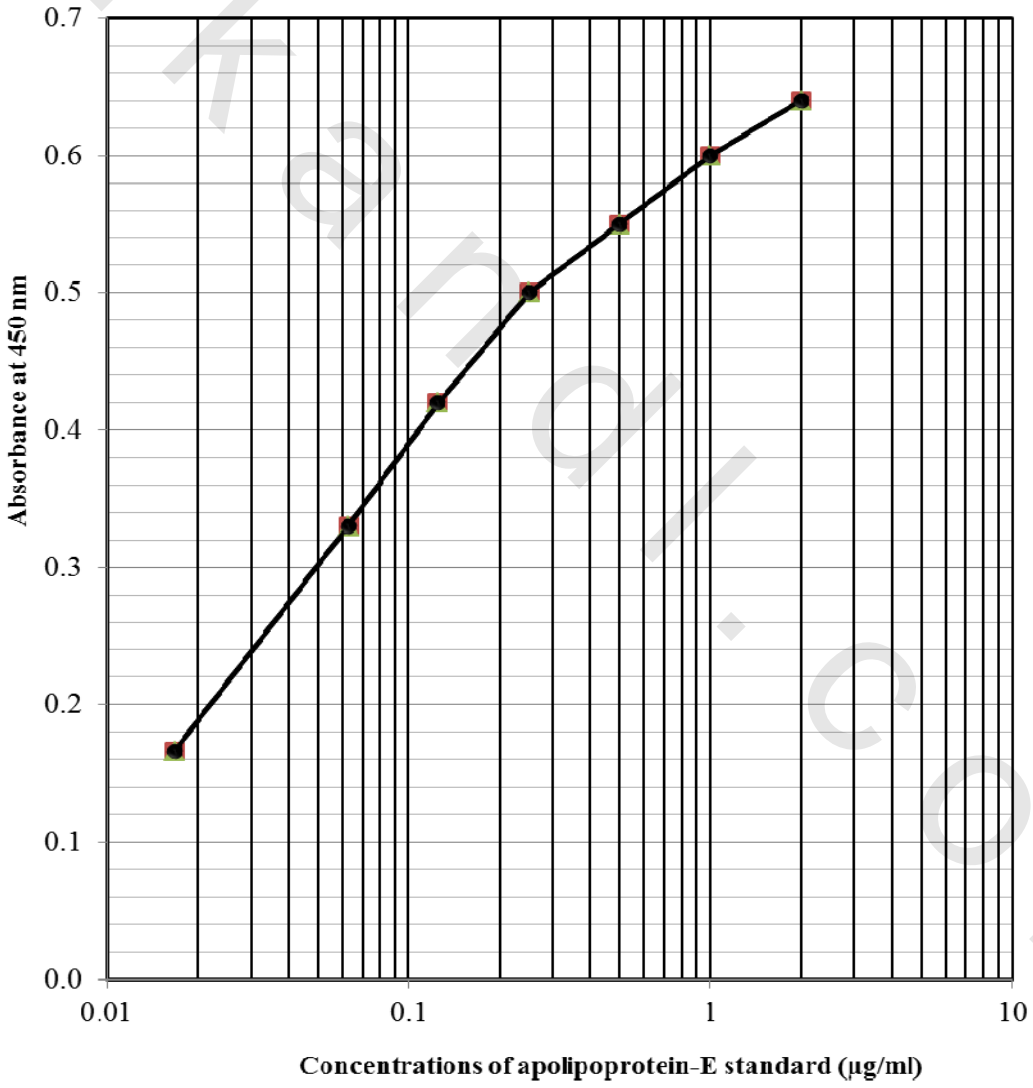


Figure (8): Apolipoprotein-E standard curve.

10. Determination of serum alanine aminotransferase (ALT) activity: [83]

It was done kinetically according to the following reactions:

$$\text{L.Alanine} + 2\text{-Oxoglutarate} \xrightleftharpoons{\text{ALT}} \text{L.Glutamate} + \text{Pyruvate}$$

$$\text{Pyruvate} + \text{NADH} + \text{H}^+ \xrightleftharpoons{\text{LDH}} \text{L.Lactate} + \text{NAD}^+$$

[LDH = lactate dehydrogenase]

The resulting decrease in absorbance of NADH at λ 340 nm was monitored kinetically for 3 minutes.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1), Working reagent	- EDTA	5 mmol/l
	- 2-oxoglutarate	15 mmol/l
	- L-Alanine	500 mmol/l
	- Lactate dehydrogenase (LDH)	≤ 1600 UI/l
	- NADH	≤ 0.18 UI/l
	- Tris buffer	100 mmol/l
	- pH at 30°C.	7.5 ±0.1

The working solution was prepared by dissolving the contents of R1 vial in 30 ml deionized water.

Procedures:

1- One ml working reagent and 100 µl sample were pipetted into a cuvette.
2- The cuvette then mixed well and the initial absorbance was recorded after 1 minute at 340 nm.
3- The absorbance was recorded again every minute during 3 minutes and the change in absorbance was calculated per minute (ΔAbs. /min)

Calculation:

The enzyme activity, expressed as units/l was calculated as follows:

ΔA/min × 1746 where; (1746) is a theoretical factor.

11. Determination of serum aspartate aminotransferase (AST) activity:[84]

AST activity was determined according to the following reactions:

$$\text{L.Aspartate} + \text{Alpha Ketoglutarate} \xrightleftharpoons{\text{AST}} \text{L.Glutamate} + \text{Oxaloacetate}$$

$$\text{Oxaloacetate} + \text{NADH}^{+} + \text{H}^{+} \xrightleftharpoons{\text{MDH}} \text{L.Malate} + \text{NAD}^{+}$$

[MDH = Malate dehydrogenase]

The resulting decrease in absorbance of NADH at λ 340 nm was monitored kinetically for 3 minutes.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1), Working reagent	- EDTA	5 mmol/l
	- 2-oxoglutarate	12 mmol/l
	- L-Aspartate	200 mmol/l
	- Malate dehydrogenase (MAD)	495 UI/l
	- NADH	≤ 0.18 UI/l
	- Tris buffer	80 mmol/l
	- pH at 30°C.	7.8 ±0.1

The working solution was prepared by dissolving the contents of R1 vial in 30 ml deionized water.

Procedures:

1- One ml working reagent and 100 µl sample were pipetted into a cuvette
2- The cuvette then mixed well and the initial absorbance was recorded after 1 minute at 340 nm.
3- The absorbance was recorded again every minute during 3 minutes and the change in absorbance was calculated per minute (ΔAbs. /min)

Calculation

The enzyme activity, expressed as units/l was calculated as follow:

ΔA/min × 1746 where; (1746) is a theoretical factor.

12. Determination of serum creatine kinase (CK): [85]

CK activity was determined as follows:

$$\text{Creatine Phosphate + ADP} \xrightarrow{\text{Creatine KINaSe}} \text{Creatine + ATP}$$

$$\text{Glucose + ATP} \xrightarrow{\text{Hexokinase}} \text{ADP + Glucose 6 Phosphate}$$

$$\text{Glucose 6 Phosphate + NADP}^{+} \xrightarrow{\text{G6PD}} \text{6 Phosphogluconate + NADPH + H}^{+}$$

The rate of NADPH formation is a measure of CK activity provided that the concentration of all other components in the 3 enzyme systems are present in excess, so the CK activity is the only limiting factor.

The resulting increase in absorbance of NADPH at 340 nm was monitored kinetically for 3 minutes.

Reagents:

Reagent	Component	Concentration
Reagent 1 (R1)	- AMP (Adenosine-5-monophosphate)	5 mmol/l
	- NADP (Nicotinamide adenine dinucleotide phosphate)	2 mmol/l
	- AP5A (Adenosine-5-pentaphosphate)	10 µmol/l
	- EDTA	2 mmol/I
	- Mg ions	10 mmol/l
	- ADP (Adenosine dinucleotide phosphate	2 mmol/l
Reagent 2 (R2)	- D-Glucose	200 mmol/l
	- N-Acetyl-Cysteine	20 mmol/l
	- Hekokinase (HK)	≤ 3000 IU/l
	-G6PD (Glucose-6-Phosphate Dehydrogenase)	≤ 2500 IU/l
	- Imidazole acetate	100 mmol/l
	- Creatine Phosphate	20 mmol/l
	- pH 6.7	

The working solution was prepared by transferring the vial content of R1 to the R2 vial.

Procedures:

1- One ml working reagent and 50 µl sample were pipetted into a cuvette.
2- The cuvette then mixed well and the initial absorbance was recorded after 1 minute at 340 nm.
3- The absorbance was recorded again every minute during 3 minutes and the change in absorbance was calculated per minute (ΔAbs./min)

Calculation:

The enzyme activity, expressed as units/l was calculated as follow:
ΔA/min × 3333 where; (3333) is a theoretical factor.

13- Determination of serum high sensitivity C-reactive protein (hs-CRP): [86]

Principle:

Hs-CRP levels in serum of all subjects were assayed by highly specific quantitative turbidimetric method. The latex particles coated with specific anti-human CRP are agglutinated when mixed with samples containing hs-CRP, the agglutination caused change in the absorbance dependent upon the CRP contents of the specimen, which in turn, measured photometrically at 540 nm.

Reagents:

Reagent	Component	Concentration
Reagent A	- Glycine buffer - sodium azide - pH 8.6	50 mmol/l 0.95 g/l
Reagent B	-Suspension of latex particles coated with anti-human CRP antibodies ,Sodium azide	0.95 g/l
Apo-A1 standard	- Human serum hs-CRP	12.4 mg/l

The working solution was prepared by mixing 4 ml of reagent A with 1 ml of reagent (B). Hs-CRP standard was reconstituted with 5 ml of distilled water.

Serial dilutions of hs-CRP standard were prepared by using 9 g/l saline as a diluent, and then the concentration of hs-CRP standard was multiplied by the corresponding dilution factor indicated below to obtain hs-CRP concentration of the dilutions.

Dilution	1	2	3	4	5
hs-CRP standard (µl)	30	60	120	180	240
Saline (µl)	210	180	120	60	---
Dilution factor	0.125	0.25	0.50	0.75	1.00

Procedures:

1- All reagents were brought to 37°C.
2- 1.5 ml of working reagent and 20 µL distilled water (blank), standard or sample were pipetted into a cuvette.
3- The cuvette then mixed well and the absorbance (A1) was measured at 540 nm after 10 seconds and after 5 minutes the absorbance of (A2) was recorded.

Construction of calibration curve:

The absorbance difference values (A2 − A1) of each standard against its hs-CRP concentration was plotted automatically by the instrument, the blank is used as the standard of 0 concentration.

Hs-CRP concentration in the sample was calculated by interpolation of its absorbance difference (A2 − A1) on the calibration curve.

14-Determination of serum Interleukin-6 (IL-6): [87]

Principle:

The IL-6 kit is a solid phase sandwich ELISA Purchased from Assaypro, USA. An anti- IL-6 monoclonal antibody has been pre-coated onto the microwells of the microtiter strips. Samples, standards of known IL-6 concentrations are pipetted into the microwells.

During incubation, IL-6 present in the sample or standard binds to antibodies adsorbed onto the microwells; a biotin conjugated polyclonal antibody specific to human IL-6 is added and binds to IL-6 captured by the receptors. Following incubation, unbound biotin conjugated IL-6 is removed by washing buffer. The enzyme streptavidin-horseradish peroxidase (HRP) is added, which binds to the biotin conjugated IL-6. After incubation unbound streptavidin-HRP is removed by washing buffer, and a substrate solution reactive with HRP is added to the wells to induce a colored reaction product, in which the intensity of the colored product is directly proportional to the concentration of IL-6 present in the samples. The reaction is terminated by adding 0.5 N HCL and absorbance is measured at 450 nm. A standard curve is prepared from seven IL-6 standard dilutions and IL-6 sample concentration is determined.

Reagents and materials provided:

Reagents	Quantity
96-wells microtiter plates	2
Adhesive plate covers	3
Biotin –Conjugate anti-IL-6 polyclonal Antibody (50x)	1 vial (140 µl)
IL-6 standard : lyophilized	1 vial, 2 µg
Streptavidin-HRP conjugate (100x)	1 vial (80 µl)
Assay diluent (10x)	1 bottle (30 ml)
Washing buffer (20x)	2 bottles (30 ml)
Substrate solution (tetramethyl-benzidine, TMB)	1 vial (8ml)
Stop solution (0.5 N hydrochloric acid)	1 vial (12 ml)

Reagent preparation:

1. All reagents were freshly diluted and brought to room temperature before use.
2. Assay diluent concentrate (10x) was diluted 1: 10 (V/V) with distilled water.
3. Standard curve: The 2 ng of IL-6 standard was reconstituted with 2 ml of assay diluent yielded a solution of 1 ng/ml. Serial dilutions of standard solution (1 ng/ml) was diluted 1:2 with assay diluent to produce 0.5, 0.25, 0.125, 0.063, 0.031, 0.016 and 0.008 ng/ml solutions. Assay diluent served as the zero standard (0 ng/ml).
4. Biotinlyated IL-6 antibody (50x): the antibody was spin down and diluted the desired amount of the antibody 1:50 (V/V) with assay diluent.
5. Wash buffer concentrate (20x): the wash buffer was diluted 1:20 (V/V) with distilled water.
6. Streptavidin-peroxidase (100x): the SP was spin down and diluted the desired amount of the conjugate 1:100 (V/V) with assay diluent.

Assay method:

1. All reagents, working standards and samples were brought to the room temperature.
2. The microwell strips were washed twice with 300 µl wash buffer per well. After the last wash, wells were emptied and microwell strips were tapped on absorbent pad to remove excess wash buffer.
3. 50 µl of assay diluent was added to standard wells B1, C1, D1, E1, F1, G1 and H1. Standard vial was then reconstituted with the appropriate volume as described in reagents preparation, 100 µl of standard (1ng/ml) was pipetted into well A1. 50 µl from A1 was transferred to well B1 with mixing contents of the well by repeated aspiration and ejection. This procedure was repeated from the well B1 to well C1 and from well C1 to D1 and so on, creating a row of IL-6 standard dilutions ranging from 0.5 to 0.008 ng/ml. 50 µl was discarded from the contents of the last microwell used G1 and the H1 well was served as the zero standard.
4. 50 µl of samples were added to sample wells.
5. The microtiter plate covered with sealing tape and incubated for two hours at room temperature on a microplate shaker.
6. At the end of incubation, the microwell strips were washed manually five times with 200 µl of wash buffer.
7. 50 µl of biotinylated IL-6 antibody were added to each well and incubated for two hours at room temperature.
8. The microwell strips were washed manually five times with 200 µl of wash buffer.
9. 50 µl of streptavidin-peroxidase conjugate were added to each well and incubated for 30 minutes.
10. The microtiter plate was washed after incubation.
11. 50 µl of TMB-substrate were added to each well and incubated for 12 minutes till the blue color developed.
12. The enzyme-substrate reaction was stopped by adding 50 µl of 0.5 N hydrochloric acid into each well, results were read immediately after stopping the reaction.
13. Absorbance of each well was read at 450 nm.
14. A standard curve was constructed by plotting the absorbance values on the ordinate against the corresponding IL-6 standard concentration on the abscissa **(figure 9)**.

Calculations:

The concentration of IL-6 in each sample was determined by extrapolating optical density (O.D) values to IL-6 concentrations using the plotted standard curve **(Figure 9).**

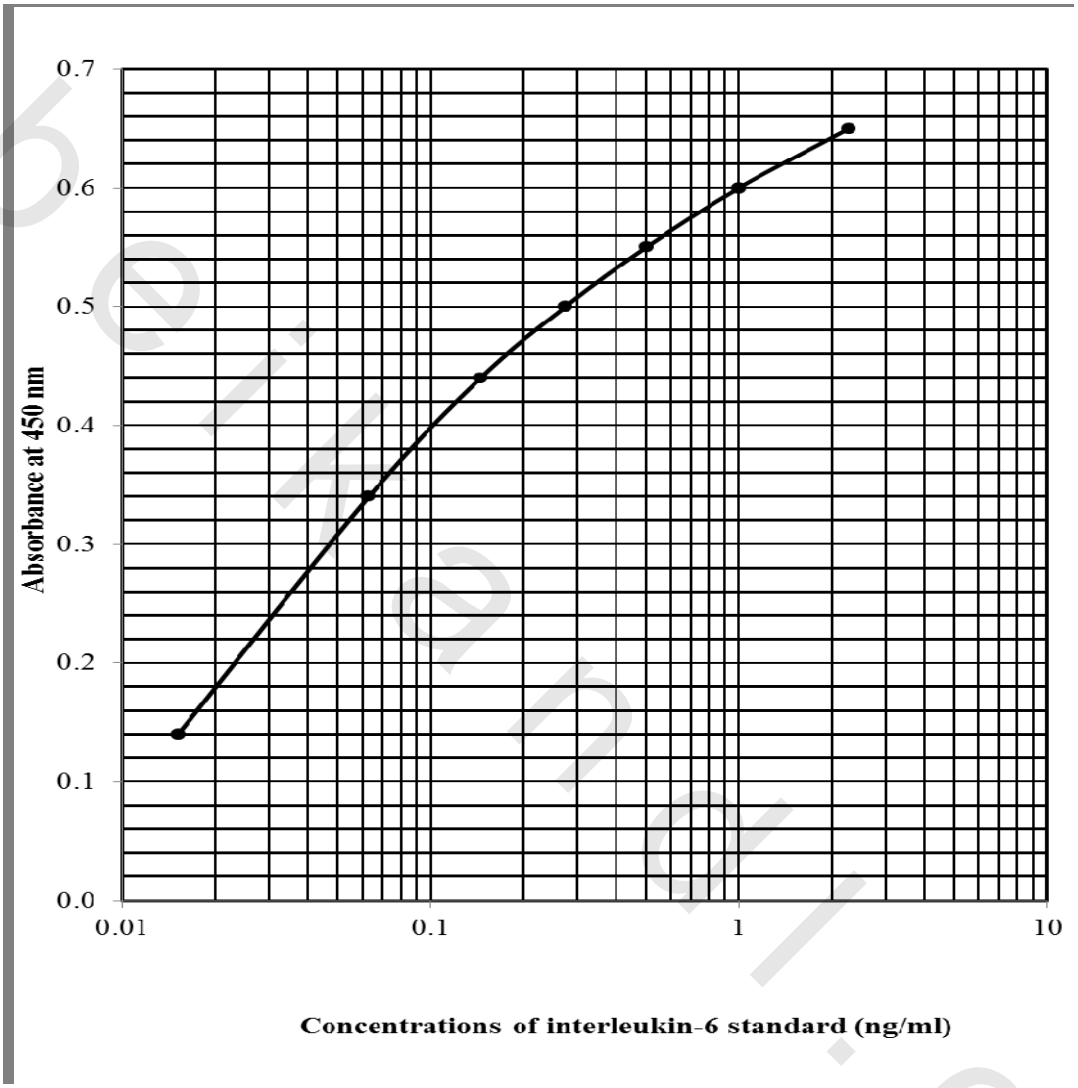


Figure (9): Interleukin-6 standard curve.

15. Determination of urinary microalbuminuria: [88]

***Urinary albumin determination:**

Urine microalbuminuria was determined by immunoturbidometry-Latex method using BioSystems kit, Spain.

Principle:

It was measured by using Immunoturbidimetric assay, in which, antigen-antibody reaction complex formed when albumin in urine samples specifically bind to anti-human albumin antigens yielding turbidity causing change in the absorbance that measured photometrically at 540 nm. The increased in turbidity is directly proportional to the amount of urinary albumin in the samples.

Reagents:

Reagent	Component	Concentration
Reagent 1, (R1)	- Borate buffer - sodium azide - pH	0.1 mol/l 0.95 g/l 10.0
Reagent 2, (R2)	-Suspension of latex particles coated with anti-human albumin antibodies Sodium azide	0.95 g/l
Albumin standard	- Human albumin	47 mg/l

The working solution was prepared by mixing 4 ml of R1 with 1 ml of R2. Albumin standard was reconstituted with 1ml of deionized water.

Procedure:

1. The working reagent was brought to37 ºC.
2. One ml working reagent and 7 µl standard or sample were pipetted into a cuvette.
3. The mixture was incubated for 10 seconds at 37ºC then absorbance (A1) was recorded at 540 nm.
4. After exactly further 120 seconds the absorbance (A2) was measured.

Calculation:

$\Delta A = (A2 - A1)$ sample or standard

$$\text{Albumin in urine (mg/l)} = \frac{\Delta \text{ absorbance of sample}}{\Delta \text{ absorbance of standard}} \times \text{concentration of standard}$$

***Urinary creatinine determination: [88]**

Principle:

It was determined kinetically without deproteinization using Jaffe' reaction. The complex formed by creatinine in the samples with picric acid in an alkaline medium (sodium hydroxide) was measured at an interval of one minute at 490 nm. A standard creatinine of known concentration (S) was similarly treated. The difference in optical density at 30 and 90 second (Δ) was used to determine the creatinine in the sample (T) and standard (S).

Reagents:

Reagent	Component	Concentration
Reagent 1, (R1)	Sodium hydroxide	0.4 mol/l
Reagent 2, (R2)	Picric acid	25 mmol/l
Reagent 3 (Standard)	Creatinine standard	2 mg/dl

The working solution was prepared by mixing 500 µl of R1 with 500 µl of R2.

Procedures:

1- The urine samples were diluted by using distilled water as following (10 µl urine: 490 µl dist. water), with a dilution factor equal 50.
2- One ml working reagent and 100 µl distilled water (blank), standard or sample were pipetted into a cuvette.
3- The absorbance (A1) was measured at 490 nm after 30 seconds and after 90 seconds the absorbance of (A2) was recorded.

Calculation:

The urinary creatinine in mg/dl is calculated according to the following general formula:

$\Delta A = (A2 - A1)$ sample or standard

Creatinine in urine (mg/dl) =

$$\frac{\Delta \text{absorbance of sample}}{\Delta \text{absorbance of standard}} \times \text{concentration of standard} \times 50$$

where; (50) is a dilution factor.

***Albumin/creatinine ratio (ACR)* [88]**

$$\text{ACR (mg/g)} = \frac{\text{Microalbumin in urine (mg/L)} \times 1000}{\text{creatinine in urine (mg/dl)} \times 10}$$

The urine creatinine value is multiplied by 10 to convert mg/dl to mg/l, and then divided the urine albumin value by the urine creatinine value to calculate the ratio, then multiplied by 1000 to express the value as (mg albumin/g creatinine).

16. Determination of serum syndecan-1 (SDC-1/CD138) levels:[89]

Principle:

Serum levels of syndecan-1 were assayed in all subjects by ELISA technique using commercial kits provided by Cell sciences, Inc.

An anti-syndecan-1 monoclonal coating antibody was adsorbed onto microwells. Syndecan-1 present in the sample or a provided standard bound to immobilized antibodies adsorbed to microwells. After washing away any unbound substance, a secondary biotinylated syndecan-1 polyclonal antibody was added and bound specifically to the captured syndecan-1 and recognized by streptavidin-horseradish peroxidase conjugate. Following incubation, unbound enzyme conjugate anti-syndecan-1 was removed during a wash step and substrate solution tetramethyl benzidine (TMB) reactive with streptavidin-HRP was added to the wells. A colored product was formed with variable intensities proportional to the original amount of syndecan-1 present in the sample, the reaction was terminated by addition of acid and absorbance was measured at 450 nm. A standard curve was prepared from seven syndecan-1 standard dilutions and unknown syndecan-1 sample concentrations were determined **(figure 10)**.

Reagents and materials provided:

Reagents	**Quantity**	**Reagents**	**Quantity**
Pre-coated, ready to use 96-well strip plate	2	Wash Buffer (200 concentrate)	1 bottle (10 ml)
Human syndecan-1 standard (256 ng/ml)	1 vial	Streptavidin-HRP conjugate	2 vial (5 µl)
Standard Diluent buffer (10 concentrate)	1 bottle (25ml)	HRP diluent	1 bottle (23 ml)
Biotinylated syndecan-1 antibody	2 vial (400 µl)	Chromogen substrate, TMB	1 bottle (11 ml)
Biotinylated anti-syndecan-1 diluent	1 bottle (7.5 ml)	Stop Solution, H_2SO_4	1bottle (11 ml)

Reagent preparation:

1. All kit components and samples were brought to room temperature before use.
2. Standard buffer diluent 10x concentrate was diluted 10 times with distilled water.
3. Standard: the standard was reconstituted with standard diluent to produce a stock solution with concentration 256 ng/ml. A series of standard were prepared containing 128, 64, 32, 16, 8 and 4 ng/ml solutions. A tube containing standard diluent is considered as a blank (0 ng/ml).

4. Dilution of biotinylated anti-syndecan-1: the antibody was spin down and diluted by addition of 240 µl biotinylated antibody to 6360 µl of biotinylated antibody diluent to designated 96 wells.
5. 10 mL of wash buffer concentrate (200x) was diluted 200 times with distilled water.
6. Dilution of streptavidin-HRP: 500 µl of HRP diluent were added to 5 µl vial of Streptavidin-HRP.

Assay procedure:

1. Seven wells for standards and one well for blank were prepared. 100 µl each of dilutions of standard, blank and samples were added into the appropriate wells, covered with the plate sealer and incubated for 2 hours at 37°C.
2. At the end of incubation, the microwell strips was washed manually five times with 200 µl of wash buffer.
3. 100 µl of biotinylated-syndecan-1 antibody was added to each well and incubated for one hour.
4. At the end of incubation, the microwell strips was washed manually five times with 200 µl of wash buffer.
5. 100 µl of streptavidin-HRP conjugate was added to each well and incubated for 30 minutes.
6. The microtiter plate was washed after incubation.
7. 100 µl of TMB-substrate was added to each well and incubated for 12 minutes till the blue color developed.
8. The enzyme-substrate reaction was stopped by adding 100 µl of H_2SO_4 into each well.
9. Absorbance of each well was read on spectrophotometer at 450 nm.
10. A linear standard curve was constructed by plotting the absorbance values on the ordinate against the corresponding syndecan-1 standard concentration on the abscissa.

Calculations:

The concentration of syndecan-1 in each sample was determined by extrapolating optical density values to syndecan-1 concentrations using the plotted standard curve **figure (10).**

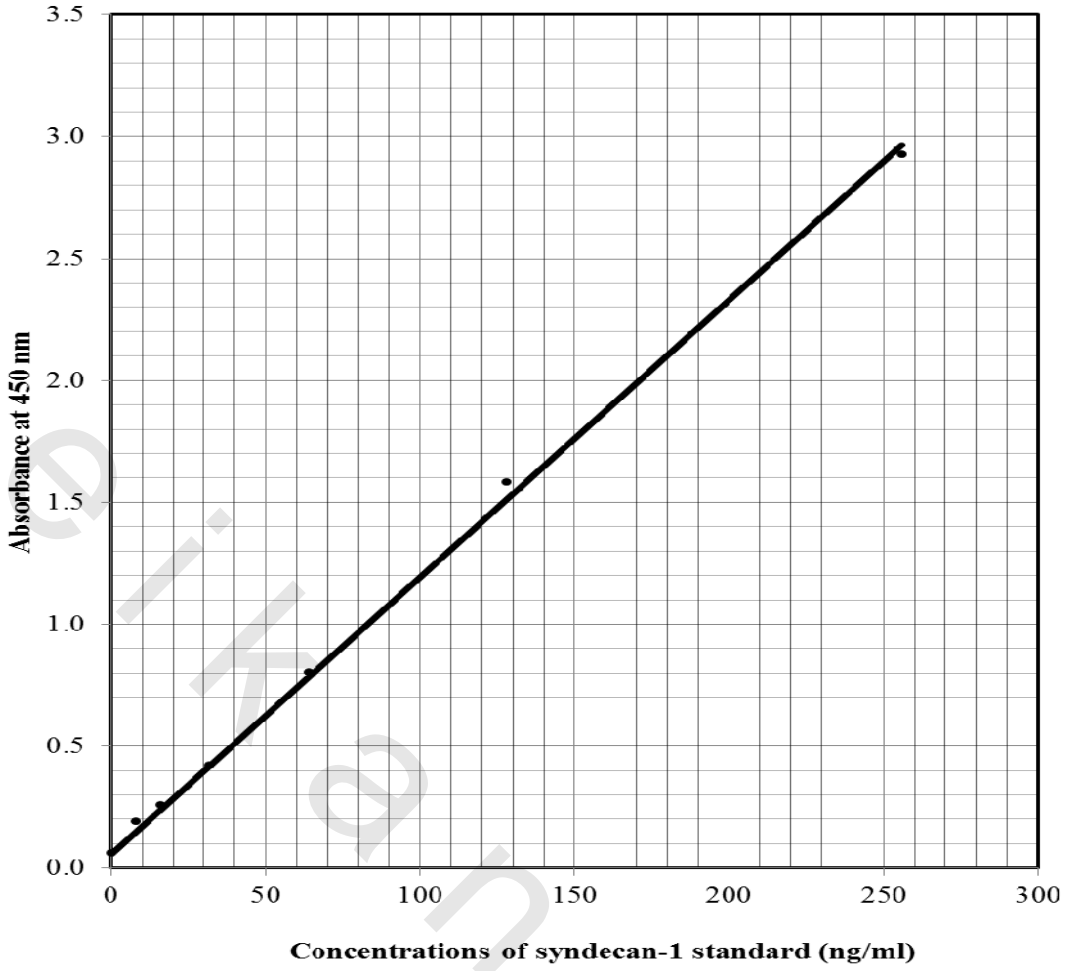


Figure (10): Syndecan-1 standard curve.

***All patients were informed about the main side effects of simvastatin and advised to:**

1. Avoid any drug that may increase the risk of statin-induced myopathy. These drugs include gemfibrozil, niacin, verapamil, diltiazem, amiodarone, cyclosporine, azoles and macrolides.

2. Report any muscle pain or weakness and to stop the medication immediately for severe muscle pain or brown urine (verified by 10 folds elevation in CPK after 4weeks of therapy).
   - ALT, AST and CPK assays were repeated after 4 weeks of treatment while all laboratory investigations were repeated for patients group after the 10 weeks of simvastatin therapy.
   - Any patient had 3 folds elevation in levels of ALT or AST, after 4 weeks of therapy, was also excluded from the study.

Statistical analysis of the data:

Data were analyzed using SPSS version 20.0 software. ***Student t-test*** and ***Mann-Whitney test*** of significance were utilized to compare measurements of different groups while ***Paired t-test*** of significance was utilized to compare the differences between values in the same group before and after treatment.

Person's correlations were adopted to calculate the correlation coefficient between each two parameters. P value <0.05 was considered statistically significant.

RESULTS

• Demographic Data:

The present study included 40 type 2 diabetic patients divided into two groups. **Group (I)**, included 20 type 2 diabetic patients treated with conventional treatment of diabetes and did not received simvastatin treatment, their age ranged between 38-58 years with a mean of 47.70 ± 4.52 years. This group included 7 (35%) males and 13 (65%) females. **Group (II),** included 20 type 2 diabetic patients treated with conventional treatment of diabetes and received 40 mg daily simvastatin dose therapy for 10 weeks, their age ranged between 36-52 years with a mean of 45.15 ± 4.63 years. This group included 7 (35%) males and 13 (65%) females. Ten healthy subjects are included as controls, their age ranged between 36-50 years with a mean of 42.40 ± 4.67 years. This group included 4 (40%) males and 6 (60%) females as shown in **table (2)**.

Table (2): Age and sex of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI) (n=20)		**Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII) (n=20)**		**Controls (n = 10)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Sex						
Male	7	35.0	7	35.0	4	40.0
Female	13	65.0	13	65.0	6	60.0
Age (Years)						
Min. – Max.	38.00 – 58.00		36.00 – 52.00		36.00 – 50.00	
Mean ± SD	47.70 ± 4.52		45.15 ± 4.63		42.40 ± 4.67	

- **Blood pressure:**

Individual data and mean values ± SD of systolic and diastolic blood pressures (BP) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects are shown in **tables (3, 4)** respectively. The statistical analysis of the data is shown in **table (5)**.

a) Systolic blood pressure:

Table (3) showed levels of systolic blood pressure of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of systolic BP in diabetic patients treated with conventional therapy alone (gpI, base line value) was 121.25 ± 6.04 mmHg and 120.00 ± 6.28 mmHg after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment in combination with conventional therapy (gpII) the mean value was 122.50 ± 5.96 mmHg before starting simvastatin treatment and 118.50 ± 5.40 mmHg after therapy. The mean value of systolic blood pressure in control subjects was 116.50 ± 6.69 mmHg.

The base line mean values for systolic blood pressure in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P=0.006) and (P=0.019) respectively as shown in **table (5)**.

No significant difference in systolic blood pressure level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.514) as shown in **table (5)**.

Systolic blood pressure showed insignificant change in both groups of diabetic patients after 10 weeks of starting study compared to the corresponding mean value of control group; (P=0.170) and (P=0.385) respectively as shown in **table (5)**.

Systolic blood pressure showed insignificant change in diabetic patients on conventional therapy after 10 weeks of follow up compared to the corresponding mean base line value; (P=0.525) as shown in **table (5)**, while, it showed significant reduction in diabetic patients with simvastatin therapy compared to the corresponding mean value before starting simvastatin treatment; (P=0.032) as shown in **table (5)**.

Table (3): Systolic blood pressure levels (mmHg) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1.	125	120	120	120	120
2.	120	120	125	120	110
3.	130	125	120	120	100
4.	115	110	120	120	120
5.	110	110	115	120	115
6.	125	125	130	125	120
7.	120	120	125	125	120
8.	120	120	120	115	120
9.	135	125	130	120	120
10.	120	130	135	120	120
11.	125	120	110	120	
12.	120	120	120	110	
13.	125	130	120	100	
14.	120	115	125	120	
15.	120	120	130	120	
16.	115	110	125	120	
17.	110	110	120	115	
18.	125	125	125	120	
19.	120	125	115	120	
20.	125	120	120	120	
Mean	**121.25**	**120.00**	**122.50**	**118.50**	**116.50**
± SD	**6.04**	**6.28**	**5.96**	**5.40**	**6.69**

b) Diastolic blood pressure:

Table (4) showed levels of diastolic blood pressure of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of diastolic blood pressure in diabetic patients treated with conventional therapy alone (gpI, base line value) was 81.25 ± 5.59 mmHg and 80.75 ± 5.20 mmHg after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment in combination with conventional therapy (gpII) the mean value was 81.75 ± 5.45 mmHg before starting simvastatin treatment and 78.75 ± 4.25 mmHg after simvastatin treatment. The mean value of diastolic blood pressure in control subjects was 78.00 ± 3.50 mmHg.

The base line mean values for diastolic blood pressure in both groups (gpI and gpII) of diabetic patients showed insignificant difference when compared to the corresponding mean value of control group; (P=0.105) and (P=0.058) respectively as shown in **table (5)**.

No significant difference in diastolic blood pressure level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.776) as shown in **table (5)**.

Diastolic blood pressure showed insignificant change in both groups of diabetic patients after 10 weeks of starting study compared to the corresponding mean value of control group; (P=0.159) and (P=0.634) respectively as shown in **table (5)**.

Diastolic blood pressure showed insignificant change in diabetic patients on conventional therapy after 10 weeks of follow up compared to the corresponding mean base line value; (P=0.771) as shown in **table (5)**, while, it showed significant reduction in diabetic patients with simvastatin treatment compared to the corresponding mean value before starting simvastatin treatment; (P=0.030) as shown in **table (5)**.

Table (4): Diastolic blood pressure levels (mmHg) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1.	85	80	80	80	80
2.	80	80	85	80	75
3.	80	75	80	80	80
4.	80	85	85	80	80
5.	75	75	90	80	70
6.	90	85	80	80	80
7.	80	85	80	75	75
8.	85	80	75	80	80
9.	80	80	85	80	80
10.	80	80	90	90	80
11.	90	95	80	75	
12.	95	90	90	80	
13.	80	80	75	70	
14.	70	75	70	80	
15.	75	75	80	80	
16.	80	80	80	80	
17.	80	80	90	80	
18.	80	75	80	75	
19.	80	80	80	70	
20.	80	80	80	80	
Mean	**81.25**	**80.75**	**81.75**	**78.75**	**78.00**
± SD	**5.59**	**5.20**	**5.45**	**4.25**	**3.50**

Table (5): Statistical analysis of systolic and diastolic blood pressures (mmHg) levels of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
Systolic BP (mmHg)					
Min. - Max.	110.0 - 135.0	110.0 - 130.0	110.0 - 135.0	100.0 - 125.0	100.0 - 120.0
Mean ± SD	121.25 ± 6.04	120.0 ± 6.28	122.50 ± 5.96	118.50 ± 5.40	116.50 ± 6.69
Median	120.00	120.00	120.00	120.00	120.00
P	0.525		0.032*		
p_1	0.006*	0.170	0.019*	0.385	
p_2			0.514	0.423	
Diastolic BP (mmHg)					
Min. - Max.	70.0 – 95.0	75.0 – 95.0	70.0 – 90.0	70.0 – 90.0	70.0 – 80.0
Mean ± SD	81.25 ± 5.59	80.75 ± 5.20	81.75 ± 5.45	78.75 ± 4.25	78.00 ± 3.50
Median	80.00	80.00	80.00	80.00	80.00
P	0.771		0.030*		
p_1	0.105	0.159	0.058	0.634	
p_2			0.776	0.191	

P: vs.values before treatment within the same group (paired t-test).
p_1:vs.control (student t-test).
p_2: vs.corresponding values of the other patient's group (student t-test).
*: $p \leq 0.05$ considered statistically significant

• Laboratory Investigations:

1. Parameters of glycemic control:

Individual data and mean values ± SD of fasting blood glucose (FBG), two hours post prandial blood glucose (PPG) and glycated hemoglobin (HbA1c) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects are shown in **tables (6,7 and 8)** respectively. The statistical analysis is shown in **table (9)**.

a) Fasting blood glucose (FBG):

Table (6) showed levels of fasting blood glucose of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of FBG in diabetic patients treated with conventional therapy alone (gpI, base line value) was 188.65 ± 49.81 mg/dl and 186.70 ± 57.27 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 190.50 ± 43.65 mg/dl before starting simvastatin treatment and 130.25 ± 35.56 mg/dl after simvastatin treatment. The mean value of fasting blood glucose in control subjects was 80.60 ± 6.67 mg/dl.

The base line mean values of fasting blood glucose in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; ($P<0.001$) as shown in **table (9)**.

No significant difference in FBG level was observed on comparing the base line mean values of the two studied groups of diabetic patients; ($P=0.901$) as shown in **table (9)**.

Fasting blood glucose level showed significant elevation in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; ($P<0.001$) as shown in **table (9)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; ($P<0.001$) as shown in **table (9)**.

Fasting blood glucose level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean base line value; ($P=0.909$) as shown in **table (9)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; ($P<0.001$) as shown in **table (9)**.

Table (6): Serum levels of fasting blood glucose (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1.	140	138	232	192	88
2.	192	196	230	194	84
3.	148	158	109	89	82
4.	108	112	194	117	90
5.	200	192	117	122	72
6.	118	116	114	102	82
7.	214	210	240	112	86
8.	196	190	231	128	76
9.	168	164	168	98	74
10.	269	245	240	112	72
11.	290	280	210	198	
12.	241	310	223	142	
13.	211	212	205	92	
14.	210	114	175	122	
15.	174	207	210	192	
16.	196	192	212	142	
17.	240	260	122	105	
18.	124	114	210	126	
19.	136	132	190	112	
20.	198	192	178	108	
Mean	**188.65**	**186.70**	**190.50**	**130.25**	**80.60**
± SD	**49.81**	**57.27**	**43.65**	**35.56**	**6.67**

b) Post prandial blood glucose (PPG):

Table (7) showed levels of two hours post prandial blood glucose of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of PPG in diabetic patients treated with conventional therapy alone (gpI, base line value) was 312.50 ± 88.96 mg/dl and 311.15 ± 82.06 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 313.80 ± 64.36 mg/dl before starting simvastatin treatment and 227.00 ± 53.81 mg/dl after simvastatin treatment. The mean value of post prandial blood glucose in control subjects was 112.40 ± 10.78 mg/dl.

The base line mean values of post prandial blood glucose in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (9)**.

No significant difference in PPG level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.958) as shown in **table (9)**.

Post prandial blood glucose level showed significant elevation in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (9)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (9)**.

Post prandial blood glucose level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.960) as shown in **table (9)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (9)**.

Table (7): Serum levels of two hours post prandial blood glucose (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	219	217	380	320	124
2	346	342	400	340	112
3	230	282	289	182	114
4	186	188	316	282	126
5	310	312	156	184	94
6	332	338	210	185	126
7	328	325	314	214	104
8	402	400	280	210	102
9	320	329	210	185	108
10	360	368	398	210	114
11	528	510	318	226	
12	294	290	310	211	
13	346	330	310	122	
14	460	428	368	290	
15	189	198	342	289	
16	310	318	367	260	
17	380	360	285	214	
18	234	238	348	225	
19	236	212	368	189	
20	240	238	307	202	
Mean	**312.50**	**311.15**	**313.80**	**227.00**	**112.40**
± SD	**88.96**	**82.06**	**64.36**	**53.81**	**10.78**

c) Glycated hemoglobin (HbA1c):

Table (8) showed levels of glycated hemoglobin of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of HbA1c in diabetic patients treated with conventional therapy alone (gpI, base line value) was 10.26 ± 1.28 % and 10.07 ± 1.18 % after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 10.51 ± 1.50 % before starting simvastatin treatment and 7.60 ± 1.18 % after simvastatin treatment. The mean value of glycated hemoglobin in control subjects was 4.85 ± 0.46 %.

The base line mean values of glycated hemoglobin in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (9)**.

No significant difference in HbA1c level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.582) as shown in **table (9)**.

Glycated hemoglobin level showed significant elevation in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (9)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (9)**.

glycated hemoglobin level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.620) as shown in **table (9)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (9)**.

Table (8): Blood levels of glycated hemoglobin (%) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	10.4	10.2	10.2	7.1	4.9
2	9.1	9.2	10.5	7.4	5.2
3	9.3	8.7	8.7	7.2	5.6
4	8.4	8.4	7.9	5.4	5.1
5	11.1	10.9	10.8	6.3	4.8
6	11.4	11.8	9.1	6.2	3.9
7	11.3	11.4	9.2	7.4	4.6
8	11.2	10.9	12.2	9.1	4.5
9	10.4	10.6	9.1	6.8	5.1
10	11.2	10.2	12.4	8.1	4.8
11	11.6	11.4	9.1	6.2	
12	9.4	9.3	10.2	8.8	
13	10.6	10.8	11.4	7.6	
14	12.6	10.9	9.3	6.9	
15	9.5	9.4	13.1	8.6	
16	11.4	11.2	12.6	9.1	
17	9.3	9.2	10.2	7.4	
18	10.8	10.6	12.4	10	
19	8.3	8.6	11.5	8.7	
20	7.9	7.6	10.2	7.6	
Mean	**10.26**	**10.07**	**10.51**	**7.60**	**4.85**
± SD	**1.28**	**1.18**	**1.50**	**1.18**	**0.46**

Table (9): Statistical analysis of fasting blood glucose (mg/dl), two hours post prandial blood glucose (mg/dl) and blood glycated hemoglobin (%) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Control (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
FBS (mg/dl)					
Min. - Max.	108.0 – 290.0	112.0 – 310.0	109.0 – 240.0	89.0 – 198.0	72.0 – 90.0
Mean ± SD	188.65 ± 49.81	186.70 ± 57.27	190.50 ± 43.65	130.25 ± 35.56	80.60 ± 6.67
Median	196.00	192.00	207.50	119.50	82.00
P	0.909		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.901	0.001*	
PPG (mg/dl)					
Min. - Max.	186.0 – 528.0	188.0 – 510.0	156.0 – 400.0	122.0 – 340.0	94.0 – 125.0
Mean ± SD	312.50 ± 88.96	311.15 ± 82.06	313.80 ± 64.36	227.00 ± 53.81	112.40 ± 10.78
Median	315.00	321.50	315.00	212.50	113.00
P	0.960		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.958	<0.001*	
HbA1c (%)					
Min. - Max.	7.90 – 12.60	7.60 – 11.80	7.90 – 13.10	5.40 – 10.0	3.90 – 5.60
Mean ± SD	10.26 ± 1.28	10.07 ± 1.18	10.51 ± 1.50	7.60 ± 1.18	4.85 ± 0.46
Median	10.50	10.40	10.20	7.40	4.85
P	0.620		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.582	<0.001*	

P: vs.values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs.corresponding values of the other patient's group (Mann Whitney test).
*: $p \leq 0.05$ considered statistically significant

2-Lipid profile:

Individual data and mean values ± SD of total serum cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein (VLDL), triglycerides (TG), apolipoprotein-A1 (apo-A1) and apolipoprotein-E (apo-E) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects are shown in **tables (10,11,12,13,14,15 and 16)** respectively. The statistical analysis is shown in **table (17, 18)**.

a) Total serum cholesterol (TC):

Table (10) showed levels of total serum cholesterol of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of TC in diabetic patients treated with conventional therapy alone (gpI, base line value) was 249.95 ± 26.63 mg/dl and 247.70 ± 25.92 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 255.35 ± 35.85 mg/dl before starting simvastatin treatment and 121.30 ± 16.56 mg/dl after simvastatin treatment. The mean value of total serum cholesterol in control subjects was 113.80 ± 9.35 mg/dl.

The base line mean values of total serum cholesterol in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; ($P<0.001$) as shown in **table (17)**.

No significant difference in TC level was observed on comparing the base line mean values of the two studied groups of diabetic patients; ($P=0.592$) as shown in **table (17)**.

Total serum cholesterol level showed significant elevation with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; ($P<0.001$) as shown in **table (17)**, while, it showed significant reduction with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; ($P<0.001$) as shown in **table (17)**.

Total serum cholesterol level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; ($P=0.788$) as shown in **table (17)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; ($P<0.001$) as shown in **table (17)**.

Table (10): Serum levels of total cholesterol (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	250	250	265	108	112
2	270	272	260	98	116
3	284	280	240	152	122
4	256	250	210	122	114
5	250	280	260	124	98
6	238	240	246	126	102
7	182	192	212	107	112
8	280	275	280	125	124
9	285	280	238	104	128
10	248	242	240	116	110
11	250	248	214	102	
12	246	240	286	146	
13	250	255	226	124	
14	186	189	280	122	
15	263	260	260	142	
16	261	242	302	140	
17	262	260	294	122	
18	260	245	263	106	
19	246	240	339	142	
20	232	214	192	98	
Mean	**249.95**	**247.70**	**255.35**	**121.30**	**113.80**
± SD	**26.63**	**25.92**	**35.85**	**16.56**	**9.35**

b) Serum high density lipoprotein cholesterol (HDL-C):

Table (11) showed levels of high density lipoprotein cholesterol of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of HDL-C in diabetic patients treated with conventional therapy alone (gpI, base line value) was 32.36 ± 6.86 mg/dl and 32.32 ± 5.78 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 31.41 ± 7.03 mg/dl before starting simvastatin treatment and 43.53 ± 5.62 mg/dl after simvastatin treatment. The mean value of HDL-C in control subjects was 72.45 ± 9.44 mg/dl.

The base line mean values of high density lipoprotein cholesterol in both groups (gpI and gpII) of diabetic patients showed significant reductions when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (17)**.

No significant difference in HDL-C level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.666) as shown in **table (17)**.

HDL-C level showed significant reduction with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (17)**, while, it showed significant elevation with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (17)**.

high density lipoprotein cholesterol level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.982) as shown in **table (17)**, while, it showed significant elevation in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (17)**.

Table (11): Serum levels of high density lipoprotein cholesterol (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	30.6	31.1	25.4	40.2	60.4
2	28.3	26.8	29.8	41.1	77.2
3	37.6	35.8	29.3	40.7	69.8
4	42.2	42.4	32.4	45.1	65.9
5	30.8	30.2	43.2	54.6	68.9
6	24.6	28.1	39.1	50.2	79.4
7	29.2	27.8	39.8	50.4	82.4
8	31.8	32.1	29.4	46.1	58.2
9	40.7	41	32.6	38.9	87.1
10	40.6	40.6	29.8	42.1	75.2
11	32.6	33	36.8	44.2	
12	29.2	29.8	23.6	38.1	
13	23.3	22.2	34.8	46.7	
14	20.9	24.6	26.6	38.9	
15	25.8	28.1	39.2	49.1	
16	35.6	36.1	25.1	39.8	
17	29.8	30.2	22.4	34.7	
18	32.6	32.4	26.4	42.4	
19	32.6	31.8	19.2	35.2	
20	48.4	42.2	43.2	52.1	
Mean	**32.36**	**32.32**	**31.41**	**43.53**	**72.45**
± SD	**6.86**	**5.78**	**7.03**	**5.62**	**9.44**

c) Serum low density lipoprotein cholesterol (LDL-C):

Table (12) showed levels of low density lipoprotein cholesterol of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of LDL-C in diabetic patients treated with conventional therapy alone (gpI, base line value) was 181.20 ± 10.02 mg/dl and 179.35 ± 10.10 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 186.95 ± 41.97 mg/dl before starting simvastatin treatment and 69.43 ± 11.91 mg/dl after simvastatin treatment. The mean value of LDL-C in control subjects was 61.99 ± 9.16 mg/dl.

The base line mean values of low density lipoprotein cholesterol in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (17)**.

No significant difference in LDL-C level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.555) as shown in **table (17)**.

LDL-C level showed significant elevation with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (17)**, while, it showed significant reduction with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (17)**.

Low density lipoprotein cholesterol level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.564) as shown in **table (17)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (17)**.

Table (12): Serum levels of low density lipoprotein cholesterol (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	192	190	198	74.2	68.2
2	182	180	184	84.6	63.6
3	194	188	194	62.2	74.4
4	169	170	147	73.4	54.6
5	178	176	187	68.2	57.2
6	190	189	124	53.1	48.4
7	178	172	162	56.2	66.2
8	195	190	205	62.3	74.4
9	178	170	140	72.6	50.8
10	198	194	199	89.2	62.1
11	176	178	168	58.1	
12	162	160	234	76.2	
13	167	158	124	66.2	
14	182	186	218	74.7	
15	190	184	197	75.4	
16	178	186	247	75.2	
17	189	185	228	82.4	
18	172	174	185	57.5	
19	173	172	274	83.6	
20	181	185	124	43.2	
Mean	**181.20**	**179.35**	**186.95**	**69.43**	**61.99**
± SD	**10.02**	**10.10**	**41.97**	**11.91**	**9.16**

d) Serum very low density lipoprotein (VLDL):

Table (13) showed levels of very low density lipoprotein of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of VLDL in diabetic patients treated with conventional therapy alone (gpI, base line value) was 41.41 ± 8.10 mg/dl and 40.56 ± 7.96 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 41.30 ± 6.75 mg/dl before starting simvastatin treatment and 27.14 ± 5.43 mg/dl after simvastatin treatment. The mean value of VLDL in control subjects was 17.70 ± 2.91 mg/dl.

The base line mean values of very low density lipoprotein in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (17)**.

No significant difference in VLDL level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.963) as shown in **table (17)**.

VLDL level showed significant elevation with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (17)**, while, it showed significant reduction with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (17)**.

Very low density lipoprotein level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.740) as shown in **table (17)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (17)**.

Table (13): Serum levels of very low density lipoprotein (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	42	41.6	42	27.6	14.2
2	52.6	51.6	36.8	26.4	20.2
3	34.8	34	39.6	28	22.8
4	39.6	38.4	38.6	24	18.2
5	42	42.4	37.6	26	18.5
6	42.8	41.6	37.2	24.8	17.5
7	34.8	35.2	42	22.8	14.2
8	43.2	42	57.8	36.8	19.1
9	26	26.4	36	24.4	18.6
10	56.4	56	42	34.8	13.7
11	42	39.6	36.4	24.2	
12	38.4	38	35.6	27.2	
13	52	42	56.4	35.2	
14	26.8	27.2	34	21.6	
15	44.8	42	42	22.4	
16	35.6	34	34.4	20.4	
17	46	48	43.2	33.6	
18	39.6	38	50.8	25.6	
19	36	36.8	45.2	37	
20	52.8	56.4	38.4	20	
Mean	**41.41**	**40.56**	**41.30**	**27.14**	**17.70**
± SD	**8.10**	**7.96**	**6.75**	**5.43**	**2.91**

e) Serum triglycerides (TG):

Table (14) showed levels of triglycerides of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of TG in diabetic patients treated with conventional therapy alone (gpI, base line value) was 207.05 ± 40.51 mg/dl and 201.30 ± 37.15 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 206.35 ± 33.83 mg/dl before starting simvastatin treatment and 131.85 ± 21.28 mg/dl after simvastatin treatment. The mean value of TG in control subjects was 86.70 ± 14.67 mg/dl.

The base line mean values of triglycerides in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (18)**.

No significant difference in TG level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.953) as shown in **table (18)**.

TG level showed significant elevation with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (18)**, while, it showed significant reduction with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (18)**.

Triglycerides level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.643) as shown in **table (18)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (18)**.

Table (14): Serum levels of triglycerides (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	210	208	210	138	72
2	263	258	184	132	102
3	174	170	198	140	110
4	198	192	190	120	94
5	210	212	188	130	82
6	214	208	186	124	87
7	174	176	210	114	72
8	216	210	289	162	96
9	130	132	180	122	89
10	282	280	210	152	63
11	210	198	182	121	
12	192	190	178	136	
13	260	210	282	176	
14	134	136	170	108	
15	224	210	210	112	
16	178	170	172	102	
17	230	240	216	158	
18	198	190	254	128	
19	180	184	226	162	
20	264	252	192	100	
Mean	**207.05**	**201.30**	**206.35**	**131.85**	**86.70**
± SD	**40.51**	**37.15**	**33.83**	**21.28**	**14.67**

f) Serum apolipoprotein-A1 (apo-A1):

Table (15) showed levels of apolipoprotein-A1 of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of apo-A1 in diabetic patients treated with conventional therapy alone (gpI, base line value) was 99.06 ± 17.30 mg/dl and 99.37 ± 17.14 mg/dl after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 99.31 ± 16.12 mg/dl before starting simvastatin treatment and 162.80 ± 22.01 mg/dl after simvastatin treatment. The mean value of apo-A1 in control subjects was 186.92 ± 18.21 mg/dl.

The base line mean values of apolipoprotein-A1 in both groups (gpI and gpII) of diabetic patients showed significant reductions when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (18)**.

No significant difference in apo-A1 level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.963) as shown in **table (18)**.

Apo-A1 level showed significant reduction with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (18)**, while, it showed significant elevation with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (18)**.

Apolipoprotein-A1 level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.955) as shown in **table (18)**, while, it showed significant elevation in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (18)**.

Table (15): Serum levels of apolipoprotein-A1 (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	98.2	96.4	84.2	129.8	158.2
2	110.4	110	104.1	176.7	201.3
3	114.2	112	89.2	145.8	162.6
4	112.6	114	102.4	156.6	168.4
5	98.2	96.8	119.7	169.2	210.4
6	90.1	98.1	115.4	155.4	184.4
7	86.2	85	122.2	194.2	204.2
8	114.8	113	93.6	178.6	189.1
9	126.2	124	116.6	185.8	198.2
10	118	120	92.4	148.6	192.4
11	92.4	90.2	118.5	180.2	
12	72.8	78	98.2	140.6	
13	68.8	66.4	99.6	185.7	
14	62.6	61.8	83.9	136.3	
15	95.4	94.7	97.4	188.8	
16	104.6	110	72.2	165.7	
17	87.7	89	78.5	134.6	
18	102.2	104	95.8	152.6	
19	110.4	108	76.6	134.5	
20	115.4	116	125.6	196.4	
Mean	**99.06**	**99.37**	**99.31**	**162.80**	**186.92**
± SD	**17.30**	**17.14**	**16.12**	**22.01**	**18.21**

g) Serum apolipoprotein-E (apo-E):

Table (16) showed levels of apolipoprotein-E of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of apo-E in diabetic patients treated with conventional therapy alone (gpI, base line value) was 4.58 ± 0.59 µg/ml and 4.41 ± 0.61 µg/ml after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 4.76 ± 0.85 µg/ml before starting simvastatin treatment and 2.22 ± 0.51 µg/ml after simvastatin treatment. The mean value of apo-E in control subjects was 1.76 ± 0.37 µg/ml.

The base line mean values of apolipoprotein-E in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (18)**.

No significant difference in apo-E level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.429) as shown in **table (18)**.

Apo-E level showed significant elevation with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (18)**, while, it showed significant reuction with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (18)**.

Apolipoprotein-E level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.375) as shown in **table (18)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (18)**.

Table (16): Serum levels of apolipoprotein-E (µg/ml) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	5.3	5.1	5.6	2.3	1.6
2	4.5	4.2	5.2	2.6	2.1
3	4.4	4.1	4.4	2.2	2.2
4	5.2	5.3	2.4	2.4	1.8
5	3.3	3.6	4.6	3.3	1.6
6	4.85	5	4.1	1.1	1.4
7	3.4	3.1	5.1	2.2	1.4
8	4.2	4	4.8	2.7	1.2
9	4.38	4.2	4.5	1.7	2.1
10	5.3	5.2	4.7	2.4	2.2
11	4.2	4.1	4.6	2.1	
12	4.1	4.1	5.3	2.1	
13	4.7	4.2	6.2	1.9	
14	4.8	4.6	4.4	2.6	
15	5.2	5.1	5.8	2.2	
16	5.3	5.4	3.4	2.8	
17	4.8	4.5	4.3	1.4	
18	4.3	4.1	5.2	1.6	
19	4.4	4.2	5.2	2.4	
20	4.3	4	5.4	2.3	
Mean	**4.58**	**4.41**	**4.76**	**2.22**	**1.76**
± SD	**0.59**	**0.61**	**0.85**	**0.51**	**0.37**

Table (17): Statistical analysis of total serum cholesterol (mg/dl), high density lipoprotein cholesterol (mg/dl), low density lipoprotein cholesterol (mg/dl) and very low density lipoprotein (mg/dl) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Control (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
Cholesterol (mg/dl)					
Min. - Max.	182.0 – 285.0	189.0 – 280.0	192.0 – 339.0	98.0 – 152.0	98.0 – 128.0
Mean ± SD	249.95 ± 26.63	247.70 ± 25.92	255.35 ± 35.85	121.30 ± 16.56	113.80 ± 9.35
Median	250.00	249.00	260.00	122.00	113.00
p	0.788		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	0.196	
p_2			0.592	<0.001*	
HDL (mg/dl)					
Min. - Max.	20.90 – 48.40	22.20 – 42.40	19.20 – 43.20	34.70 – 54.60	58.20 – 87.10
Mean ± SD	32.36 ± 6.86	32.32 ± 5.78	31.41 ± 7.03	43.53 ± 5.62	72.45 ± 9.44
Median	31.30	31.45	29.80	42.25	72.50
p	0.982		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.666	<0.001*	
LDL (mg/dl)					
Min. - Max.	162.0 – 198.0	158.0 – 194.0	124.0 – 274.0	43.20 – 89.20	48.40 – 74.40
Mean ± SD	181.20 ± 10.02	179.35 ± 10.10	186.95 ± 41.97	69.43 ± 11.91	61.99 ± 9.16
Median	179.50	182.00	190.50	73.00	62.85
p	0.564		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	0.095	
p_2			0.555	<0.001*	
VLDL (mg/dl)					
Min. - Max.	26.0 – 56.40	26.40 – 56.40	34.0 – 57.80	20.0 – 37.0	13.70 – 22.80
Mean ± SD	41.41 ± 8.10	40.56 ± 7.96	41.30 ± 6.75	27.14 ± 5.43	17.70 ± 2.91
Median	42.00	40.60	39.10	25.80	18.35
p	0.740		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.963	<0.001*	

P: vs. Values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs. Corresponding values of the other patient's group (Mann Whitney test)
*: $p \leq 0.05$ considered statistically significant

Table (18): Statistical analysis of serum triglycerides (mg/dl), apolipoprotein-A1 (mg/dl) and apolipoprotein-E (µg/ml) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Control (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
TG (mg/dl)					
Min. - Max.	130.0 – 282.0	132.0 – 280.0	170.0 – 289.0	100.0 - 176.0	63.0 – 110.0
Mean ± SD	207.05 ± 40.51	201.30 ± 37.15	206.35 ± 33.83	131.85 ± 21.28	86.70 ± 14.67
Median	210.00	203.00	195.00	129.00	88.00
p	0.643		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.953	<0.001*	
apo-A1 (mg/dl)					
Min. - Max.	62.60 – 126.20	61.80 – 124.0	72.20 – 125.60	129.80 – 196.40	158.20 – 210.40
Mean ± SD	99.06 ± 17.30	99.37 ± 17.14	99.31 ± 16.12	162.80 ± 22.01	186.92 ± 18.21
Median	100.20	101.05	97.80	161.15	190.75
p	0.955		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	0.006*	
P_2			0.963	<0.001*	
apo-E (µg/ml)					
Min. - Max.	3.30 – 5.30	3.10 – 5.40	2.40 – 6.20	1.10 – 3.30	1.20 – 2.20
Mean ± SD	4.58 ± 0.59	4.41 ± 0.61	4.76 ± 0.85	2.22 ± 0.51	1.76 ± 0.37
Median	4.55	4.20	4.75	2.25	1.70
P	0.375		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	0.017*	
p_2			0.429	<0.001*	

P: vs. Values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs. Corresponding values of the other patient's group (Mann Whitney test).
*: $p \leq 0.05$ considered statistically significant

3. Liver function tests:

Individual data and mean values ± SD of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects are shown in **tables (19, 20)** respectively. The statistical analysis is shown in **table (21)**.

a) Serum alanine aminotransferase (ALT):

Table (19) showed levels of alanine aminotransferase of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of ALT in diabetic patients treated with conventional therapy alone (gpI, base line value) was 20.80 ± 6.64 u/l and after 4 and 10 weeks of follow up the mean values were 22.65 ± 10.33 u/l and 23.35 ± 12.46 u/l respectively. While, in diabetic patients receiving simvastatin treatment (gpII), the mean value was 20.40 ± 5.35 u/l before starting simvastatin treatment and 23.70 ± 3.69 u/l and 28.65 ± 4.21 u/l after 4 and 10 weeks of simvastatin treatment respectively. The mean value of ALT in control subjects was 15.90 ± 3.81 u/l.

The base line mean values for serum ALT levels in both groups (gpI and II) of diabetic patients showed significant elevations *(values still within normal range)* when compared to the corresponding mean value of control group; (P=0.040) and (P=0.025) respectively as shown in **table (21).**

No significant difference in serum ALT level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.835) as shown in **table (21).**

Serum ALT levels showed insignificant change in diabetic patients on conventional therapy alone (gpI) after 4 and 10 weeks of follow up compared to the corresponding mean base line value; (P=0.505) and (P=0.424) respectively, while, it showed significant elevation *(values still within normal range)* in diabetic patients after 4 and 10 weeks of simvastatin treatment compared to the corresponding mean value before starting simvastatin treatment; (P=0.029) and (P<0.001) respectively as shown in **table (21)**.

Table (19): Serum levels of alanine aminotransferase (u/l) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)			Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)			Controls (n=10)
	Base line value (n=20)	After 4 weeks (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 4 weeks of statin (n=20)	After 10 weeks of statin (n=20)	
1.	21	15	25	22	28	34	12
2.	14	16	18	25	24	28	10
3.	16	22	19	15	20	24	16
4.	12	10	11	20	22	26	18
5.	29	19	50	17	20	26	15
6.	18	18	25	12	17	23	20
7.	25	16	11	8	16	22	21
8.	14	43	18	24	25	28	12
9.	32	33	22	20	24	27	20
10.	26	24	17	22	24	30	15
11.	12	8	10	16	20	28	
12.	19	33	16	24	28	32	
13.	17	20	22	14	26	31	
14.	15	9	15	18	24	29	
15.	17	14	10	22	28	38	
16.	17	20	25	26	30	36	
17.	29	40	37	26	24	32	
18.	30	35	44	24	26	26	
19.	23	25	22	28	25	28	
20.	30	33	50	25	23	25	
Mean	**20.80**	**22.65**	**23.35**	**20.40**	**23.70**	**28.65**	**15.90**
± SD	**6.64**	**10.33**	**12.46**	**5.35**	**3.69**	**4.21**	**3.81**

b) Serum aspartate aminotransferase (AST):

Table (20) showed levels of aspartate aminotransferase of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of AST in diabetic patients treated with conventional therapy alone (gpI, base line value) was 17.00 ± 3.39 u/l and after 4 and 10 weeks of follow up the mean values were 17.35 ± 5.57 u/l and 18.75 ± 6.77 u/l respectively. While, in diabetic patients receiving simvastatin treatment (gpII), the mean value was 17.55 ± 2.42 u/l before starting simvastatin treatment and 23.35 ± 3.51 u/l and 29.85 ± 3.82 u/l after 4 and 10 weeks of simvastatin treatment respectively. The mean value of AST in control subjects was 17.10 ± 3.54 u/l.

The base line mean values for serum AST levels in both groups (gpI and II) of diabetic patients showed insignificant difference when compared to the corresponding mean value of control group; (P=0.941) and (P=0.684) respectively as shown in **table (21).**

No significant difference in serum AST level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.612) as shown in **table (21).**

Serum AST levels showed insignificant change in diabetic patients on conventional therapy alone after 4 and 10 weeks of follow up compared to the corresponding mean base line value; (P=0.812) and (P=0.308) respectively, while, it showed significant elevations *(values still within normal range)* in diabetic patients with simvastatin treatment after 4 and 10 weeks of starting simvastatin treatment when compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (21)**.

Table (20): Serum levels of aspartate aminotransferase (u/l) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)			Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)			Controls (n=10)
	Base line value (n=20)	After 4 weeks (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 4 weeks of statin (n=20)	After 10 weeks of statin (n=20)	
1.	22	13	23	16	20	28	16
2.	18	20	16	14	18	26	12
3.	13	16	13	19	28	34	21
4.	16	11	19	20	24	30	18
5.	20	12	30	16	22	28	12
6.	12	11	15	18	26	35	18
7.	23	19	11	17	21	28	14
8.	13	24	14	20	24	28	18
9.	18	14	15	17	23	29	22
10.	16	14	21	14	19	25	20
11.	13	12	12	14	20	27	
12.	16	21	10	18	25	30	
13.	11	19	22	16	20	24	
14.	18	10	14	16	18	27	
15.	16	13	11	18	25	33	
16.	20	22	30	20	24	28	
17.	19	31	31	22	28	35	
18.	20	22	25	22	30	37	
19.	16	21	18	16	27	29	
20.	20	22	25	18	25	36	
Mean	**17.00**	**17.35**	**18.75**	**17.55**	**23.35**	**29.85**	**17.10**
± SD	**3.39**	**5.57**	**6.77**	**2.42**	**3.51**	**3.82**	**3.54**

Table (21): Statistical analysis of serum alanine aminotransferase (u/l), aspartate aminotransferase (u/l) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)			Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)			Controls (n=10)
	Base line value (n=20)	After 4 weeks (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 4 weeks of statin (n=20)	After 10 weeks of statin (n=20)	
ALT (u/l)							
Min. - Max.	12.0 – 32.0	8.0 – 43.0	10.0 – 50.0	8.0 – 28.0	16.0 – 30.0	22.0 – 38.0	10.0 – 21.0
Mean ± SD	20.80 ± 6.64	22.65 ± 10.33	23.35 ± 12.46	20.40 ± 5.35	23.70 ± 3.69	28.65 ± 4.21	15.90 ± 3.81
Median	18.50	20.00	20.50	22.00	24.00	28.00	15.50
P		0.505	0.424		0.029*	<0.001*	
P_1	0.040*	0.057	0.077	0.025*	<0.001*	<0.001*	
P_2				0.835	0.671	0.079	
AST (u/l)							
Min. – Max.	11.0 – 23.0	10.0 – 31.0	10.0 – 31.0	14.0 – 22.0	18.0 – 30.0	24.0 – 370	12.0 – 22.0
Mean ± SD	17.00 ± 3.39	17.35 ± 5.57	18.75 ± 6.77	17.55 ± 2.42	23.35 ± 3.51	29.85 ± 3.82	17.10 ± 3.54
Median	17.00	17.50	17.00	17.50	24.00	28.50	18.00
P		0.812	0.308		<0.001*	<0.001*	
P_1	0.941	0.898	0.478	0.684	<0.001*	<0.001*	
P_2				0.612	<0.001*	<0.001*	

p: vs.values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs.corresponding values of the other patient's group (Mann Whitney test).
*: $p \leq 0.05$ considered statistically significant.

4. Serum creatine kinase (CK):

Individual data and mean values ± SD of serum creatine kinase (CK) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects are shown in **table (22)** respectively. The statistical analysis is shown in **table (23)**.

Table (22) showed levels of serum creatine kinase of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of CK in diabetic patients treated with conventional therapy alone (gpI, base line value) was 76.50 ± 45.65 u/l and after 4 and 10 weeks of follow up the mean values were 78.30 ± 45.89 u/l and 77.40 ± 45.43 u/l respectively. While, in diabetic patients receiving simvastatin treatment (gpII), the mean value was 78.90 ± 17.54 u/l before starting simvastatin treatment and 90.55 ± 19.95 u/l and 114.65 ± 22.48 u/l after 4 and 10 weeks of simvastatin treatment respectively. The mean value of CK in control subjects was 44.40 ± 7.92 u/l.

The base line mean values for serum CK levels in both groups (gpI and II) of diabetic patients showed significant elevations *(values still within normal range)* when compared to the corresponding mean value of control group; (P=0.037) and (P<0.001) respectively as shown in **table (23).**

No significant difference in serum CK level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.827) as shown in **table (23).**

Serum CK levels showed insignificant change in diabetic patients on conventional therapy alone (gpI) after 4 and 10 weeks of follow up compared to the corresponding mean base line value; (P=0.902) and (P=0.950) respectively. In addition, serum CK level in diabetic patients with simvastatin treatment (gpII) showed insignificant elevation after 4 weeks of simvastatin treatment compared to the corresponding mean value before starting simvastatin treatment; (P=0.057) as shown in **table (23)**, while, it showed significant elevation *(values still within normal range)* in diabetic patients with simvastatin treatment after 10 weeks of starting simvastatin treatment compared to the corresponding mean value before starting simvastatin therapy; (P<0.001) as shown in **table (23)**.

Table (22): Serum levels of creatine kinase (u/l) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)			Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)			Controls (n=10)
	Base line value (n=20)	After 4 weeks (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 4 weeks of statin (n=20)	After 10 weeks of statin (n=20)	
1.	61	60	62	102	122	148	52
2.	102	98	100	84	90	102	58
3.	78	76	74	112	128	138	42
4.	47	48	52	95	104	114	48
5.	100	102	98	74	82	92	48
6.	130	135	130	68	78	89	42
7.	42	42	40	83	90	102	29
8.	53	55	57	84	100	126	42
9.	153	160	165	100	118	142	38
10.	81	88	90	92	110	162	45
11.	46	42	40	75	62	118	
12.	44	40	40	65	85	105	
13.	61	63	60	52	60	86	
14.	30	38	32	56	78	98	
15.	53	55	50	96	104	124	
16.	30	34	36	87	80	117	
17.	170	172	168	65	92	138	
18.	168	167	162	48	55	82	
19.	41	44	48	72	84	116	
20.	40	47	44	68	89	94	
Mean	**76.50**	**78.30**	**77.40**	**78.90**	**90.55**	**114.65**	**44.40**
± SD	**45.65**	**45.89**	**45.34**	**17.54**	**19.95**	**22.48**	**7.92**

Table (23): Statistical analysis of serum creatine kinase (u/l) levels of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)			Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)			Controls (n=10)
	Base line value (n=20)	After 4 weeks (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 4 weeks of statin (n=20)	After 10 weeks of statin (n=20)	
CK (u/l)							
Min. - Max.	30.0 – 170.0	34.00 – 172.0	32.0 – 168.0	48.0 – 112.0	55.0 – 128.0	82.0 – 162.0	29.0 – 58.0
Mean ± SD	76.50 ± 45.65	78.30 ± 45.89	77.40 ± 45.43	78.90 ± 17.54	90.55 ± 19.95	114.65 ± 22.48	44.40 ± 7.92
Median	57.00	57.50	58.50	79.00	89.50	115.00	43.50
P		0.902	0.950		0.057	<0.001*	
P_1	0.037*	0.029*	0.032*	<0.001*	<0.001*	<0.001*	
P_2				0.827	0.280	0.002*	

P: vs.values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs.corresponding values of the other patient's group (Mann Whitney test).
*: $p \leq 0.05$ considered statistically significant

5. Inflammatory markers:

Individual data and mean values ± SD of serum high sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects are shown in **tables (24, 25)** respectively. The statistical analysis is shown in **table (26)**.

a) High-sensitivity C-reactive protein (hs-CRP):

Table (24) showed levels of high sensitivity C-reactive protein of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of hs-CRP in diabetic patients treated with conventional therapy alone (gpI, base line value) was 7.64 ± 1.16 mg/l and 7.38 ± 1.27 mg/l after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 7.68 ± 1.63 mg/l before starting simvastatin treatment and 3.67 ± 1.09 mg/l after simvastatin treatment. The mean value of hs-CRP in control subjects was 0.70 ± 0.30 mg/l.

The base line mean values of high sensitivity C-reactive protein in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (26)**.

No significant difference in hs-CRP level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.929) as shown in **table (26)**.

Hs-CRP level showed significant elevation with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (26)**, while, it showed significant reduction with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (26)**.

high sensitivity C-reactive protein level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.503) as shown in **table (26)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (26)**.

Table (24): Serum levels of high-sensitivity C-reactive protein (mg/l) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	7.2	7	8.2	1.7	0.68
2	9.4	9.2	3.5	1.9	0.85
3	7.4	7.2	9.5	3.1	0.54
4	5.8	5.4	9.2	3.2	0.22
5	8.7	8.4	9.4	3.3	0.79
6	5.7	5.2	7.2	3.3	0.62
7	7.2	7.1	5.8	1.2	1.1
8	7.2	7.4	10.4	5.2	0.45
9	7.4	7.1	5.7	5.2	0.56
10	8.2	8.1	8.2	3.6	1.2
11	6.8	6.2	6.7	3.7	
12	9.1	9.2	6.4	3.7	
13	9.4	8.7	8.5	3.8	
14	8.2	8.1	7.4	3.9	
15	8.1	7.8	8.4	4.2	
16	7.6	7.8	7.1	4.2	
17	6.9	6.2	6.6	4.2	
18	5.9	5.2	9.2	4.4	
19	9.4	9.2	7.6	4.8	
20	7.2	7	8.6	4.8	
Mean	**7.64**	**7.38**	**7.68**	**3.67**	**0.70**
± SD	**1.16**	**1.27**	**1.63**	**1.09**	**0.30**

b) Serum interleukin-6 (IL-6):

Table (25) showed levels of interleukin-6 of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of IL-6 in diabetic patients treated with conventional therapy alone (gpI, base line value) was 0.28 ± 0.16 ng/ml and 0.27 ± 0.14 ng/ml after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 0.31 ± 0.24 ng/ml before starting simvastatin treatment and 0.06 ± 0.01 ng/ml after simvastatin treatment. The mean value of IL-6 in control subjects was 0.04 ± 0.02 ng/ml.

The base line mean values of interleukin-6 in both groups (gpI and gpII) of diabetic patients showed significant elevations when compared to the corresponding mean value of control group; (P<0.001) as shown in **table (26)**.

No significant difference in IL-6 level was observed on comparing the base line mean values of the two studied groups of diabetic patients; (P=0.722) as shown in **table (26)**.

IL-6 level showed significant elevation with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; (P<0.001) as shown in **table (26)**, while, it showed significant reduction with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; (P<0.001) as shown in **table (26)**.

Interleukin-6 level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; (P=0.835) as shown in **table (26)**, while, it showed significant reduction in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; (P<0.001) as shown in **table (26)**.

Table (25): Serum levels of interleukin-6 (ng/ml) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	0.162	0.16	0.324	0.05	0.021
2	0.377	0.298	0.125	0.051	0.051
3	0.202	0.2	0.163	0.051	0.031
4	0.101	0.29	0.124	0.052	0.028
5	0.098	0.088	0.842	0.052	0.023
6	0.124	0.126	0.166	0.053	0.051
7	0.125	0.122	0.182	0.049	0.042
8	0.191	0.174	0.191	0.076	0.056
9	0.428	0.398	0.128	0.082	0.061
10	0.532	0.498	0.123	0.053	0.022
11	0.421	0.48	0.526	0.054	
12	0.5	0.482	0.1	0.054	
13	0.512	0.318	0.142	0.056	
14	0.542	0.396	0.612	0.059	
15	0.128	0.126	0.128	0.059	
16	0.168	0.172	0.152	0.059	
17	0.158	0.156	0.812	0.06	
18	0.198	0.192	0.388	0.06	
19	0.395	0.382	0.554	0.072	
20	0.282	0.384	0.324	0.074	
Mean	**0.28**	**0.27**	**0.31**	**0.06**	**0.04**
± SD	**0.16**	**0.14**	**0.24**	**0.01**	**0.02**

Table (26): Statistical analysis of serum high-sensitivity C-reactive protein (mg/l) and interleukin-6 (ng/ml) levels of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Control (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
hs-CRP (mg/l)					
Min. - Max.	5.70 – 9.40	5.20 – 9.20	3.50 – 10.40	1.20 – 5.20	0.22 – 1.20
Mean ± SD	7.64 ± 1.16	7.38 ± 1.27	7.68 ± 1.63	3.67 ± 1.09	0.70 ± 0.30
Median	7.40	7.30	7.90	3.75	0.65
p	0.503		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.929	<0.001*	
IL-6 (ng/ml)					
Min. - Max.	0.10 – 0.54	0.09 – 0.50	0.10 – 0.84	0.05 – 0.08	0.02 – 0.06
Mean ± SD	0.28 ± 0.16	0.27 ± 0.14	0.31 ± 0.24	0.06 ± 0.01	0.04 ± 0.02
Median	0.20	0.25	0.17	0.06	0.04
p	0.835		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	0.001*	
p_2			0.722	<0.001*	

P: vs.values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs.corresponding values of the other patient's group (Mann Whitney test).
*: $p \leq 0.05$ considered statistically significant

6. Urinary albumin to creatinine ratio (ACR):

Individual data and mean values ± SD of urinary albumin to creatinine ratio of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects are shown in **table (27)**. The statistical analysis is shown in **table (28)**.

Table (27) showed levels of urinary albumin to creatinine ratio of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of ACR in diabetic patients treated with conventional therapy alone (gpI, base line value) was 18.24 ± 4.40 mg/g and 17.96 ± 4.12 mg/g after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 19.58 ± 4.73 mg/g before starting simvastatin treatment and 15.11 ± 2.96 mg/g after simvastatin treatment. The mean value of ACR in control subjects was 11.76 ± 1.33 mg/g.

The base line mean values of urinary albumin to creatinine ratio in both groups (gpI and gpII) of diabetic patients showed significant elevations *(values still within normal range)* when compared to the corresponding mean value of control group; ($P<0.001$) as shown in **table (28)**.

No significant difference in ACR level was observed on comparing the base line mean values of the two studied groups of diabetic patients; ($P=0.359$) as shown in **table (28)**.

Urinary albumin to creatinine ratio level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; ($P=0.837$) as shown in **table (28)**, while, it showed significant reduction *(values still within normal range)* in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; ($P<0.001$) as shown in **table (28)**.

Table (27): Urinary albumin to creatinine ratio levels (mg/g) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1.	23.8	17	26.4	15.4	12.2
2.	17.6	14.8	26.4	17.5	11.4
3.	15.6	12.1	17.4	14.8	11.3
4.	22.2	15.2	11.2	17.4	10.8
5.	12.4	19.2	19.3	21.4	9.8
6.	20.6	19	16.8	10.2	11.1
7.	9.4	25	20.5	14.2	10.8
8.	15.2	17.1	18.4	18.2	12.6
9.	17.8	20.2	16.5	12.3	13.4
10.	26.4	17.4	19.2	16.7	14.2
11.	15.1	22.2	16	12.9	
12.	13.3	9.8	25.2	13.5	
13.	20	15	28.2	12.8	
14.	19.7	24.8	15.2	17.6	
15.	22.4	18.1	19.8	13.6	
16.	25.7	23.2	11.2	19.2	
17.	19.2	22.1	17.1	10.4	
18.	15.8	13	23.1	12.1	
19.	16.7	17.1	22.4	16.1	
20.	17.2	16.8	21.2	15.8	
Mean	**18.24**	**17.96**	**19.58**	**15.11**	**11.76**
± SD	**4.40**	**4.12**	**4.73**	**2.96**	**1.33**

Table (28): Statistical analysis of urinary albumin to creatinine ratio (mg/g) levels of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		**Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)**		**Controls (n=10)**
	Base line value (n=20)	**After 10 weeks (n=20)**	**Before statin treatment (n=20)**	**After 10 weeks of statin treatment (n=20)**	
ACR (mg/g)					
Min. – Max.	9.40 – 26.40	9.80 – 25.0	11.20 – 28.20	10.20 – 21.40	9.80 – 14.20
Mean ± SD	18.24 ± 4.40	17.96 ± 4.12	19.58 ± 4.73	15.11 ± 2.96	11.76 ± 1.33
Median	17.70	17.25	19.25	15.10	11.35
P	0.837		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	0.002*	
p_2			0.359	0.016*	

P: vs.values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs.corresponding values of the other patient's group (Mann Whitney test).
*: $p \leq 0.05$ considered statistically significant.

7. Serum Syndecan-1 (SDC-1/CD138):

Individual data and mean values ± SD of serum syndecan-1 of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects are shown in **table (29)**. The statistical analysis is shown in **table (30)**.

Table (29) showed levels of serum syndecan-1 of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of healthy control subjects. The mean value of syndecan-1 in diabetic patients treated with conventional therapy alone (gpI, base line value) was 88.21 ± 6.48 ng/ml and 85.84 ± 8.15 ng/ml after 10 weeks of follow up, while, in diabetic patients receiving simvastatin treatment (gpII) the mean value was 88.59 ± 9.69 ng/ml before starting simvastatin treatment and 366.47 ± 119.06 ng/ml after simvastatin treatment. The mean value of syndecan-1 in control subjects was 118.6 ± 9.52 ng/ml.

The base line mean values of syndecan-1 in both groups (gpI and gpII) of diabetic patients showed significant reductions when compared to the corresponding mean value of control group; ($P<0.001$) as shown in **table (30)**.

No significant difference in syndecan-1 level was observed on comparing the base line mean values of the two studied groups of diabetic patients; ($P=0.885$) as shown in **table (30)**.

Syndecan-1 level showed significant reduction with no improvement in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to corresponding mean value of control group; ($P<0.001$) as shown in **table (30)**, while, it showed significant elevation with improvement in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value of control group; ($P<0.001$) as shown in **table (30)**.

Syndecan-1 level showed insignificant change in diabetic patients on conventional treatment solely after 10 weeks of follow up (gpI) compared to the corresponding mean base line value; ($P=0.315$) as shown in **table (30)**, while, it showed significant elevation in diabetic patients with simvastatin treatment (gpII) compared to the corresponding mean value before starting simvastatin treatment; ($P<0.001$) as shown in **table (30)**.

Table (29): Serum levels of syndecan-1 (ng/ml) of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

No.	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Controls (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
1	82.8	88	92	624.2	102
2	92.6	98	84	528.5	114
3	97.2	95.1	92.1	519.2	112
4	99.2	98.2	102	376.5	122
5	85.4	88.2	81	342.2	126
6	88.6	102	88.1	333.6	132
7	88.2	78.2	114	675.4	118
8	85.2	88	86	285.6	124
9	78.7	78	74	282.4	108
10	98.4	89	92	330.6	128
11	77.4	90	88.1	319.8	
12	88.6	87	78	311.6	
13	95.6	77	102	310.2	
14	82.9	76	82	308.2	
15	92.1	82	92	307.7	
16	78.2	87	87.4	307.1	
17	88.3	78.2	80	298.4	
18	87.2	85	93.6	292.3	
19	85.4	78	75.2	288.4	
20	92.1	74	88.2	287.4	
Mean	**88.21**	**85.84**	**88.59**	**366.47**	**118.60**
± SD	**6.48**	**8.15**	**9.69**	**119.06**	**9.52**

Table (30): Statistical analysis of serum syndecan-1 (ng/ml) levels of diabetic patients either receiving conventional treatment of diabetes solely or in combination with statin and of control subjects.

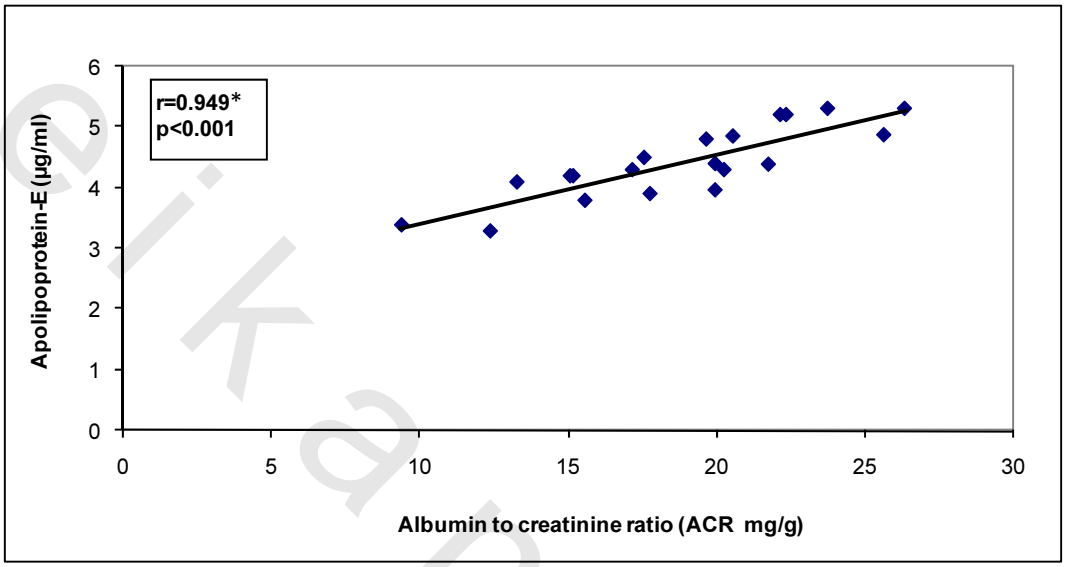
	Diabetic patients receiving conventional treatment of diabetes without statin treatment (gpI)		Diabetic patients receiving conventional treatment of diabetes and statin treatment (gpII)		Control (n=10)
	Base line value (n=20)	After 10 weeks (n=20)	Before statin treatment (n=20)	After 10 weeks of statin treatment (n=20)	
Syndecan-1 (ng/ml)					
Min. – Max.	77.4 – 99.2	74.0 – 102	74.0 – 114	282.40 – 675.40	102 – 132
Mean ± SD	88.21 ± 6.48	85.84 ± 8.15	88.59 ± 9.69	366.47 ± 119.06	118.6 ± 9.52
Median	88.25	87.00	88.10	310.90	120
P	0.315		<0.001*		
p_1	<0.001*	<0.001*	<0.001*	<0.001*	
p_2			0.885	<0.001*	

P: vs.values before treatment within the same group (Paired t-test).
p_1:vs.control (Mann Whitney test).
p_2: vs.corresponding values of the other patient's group (Mann Whitney test).
*: $p \leq 0.05$ considered statistically significant

Correlation study:

Figure (11) shows the statistical correlation between apolipoprotein-E (apo-E) and urinary albumin to creatinine ratio (ACR) levels in diabetic patients receiving conventional treatment of diabetes (gpI) at the beginning of the study.

A significant positive correlation has been found between the levels of apo-E and ACR in diabetic patients receiving conventional treatment of diabetes at the beginning of the study. (r= 0.949*, P<0.001).

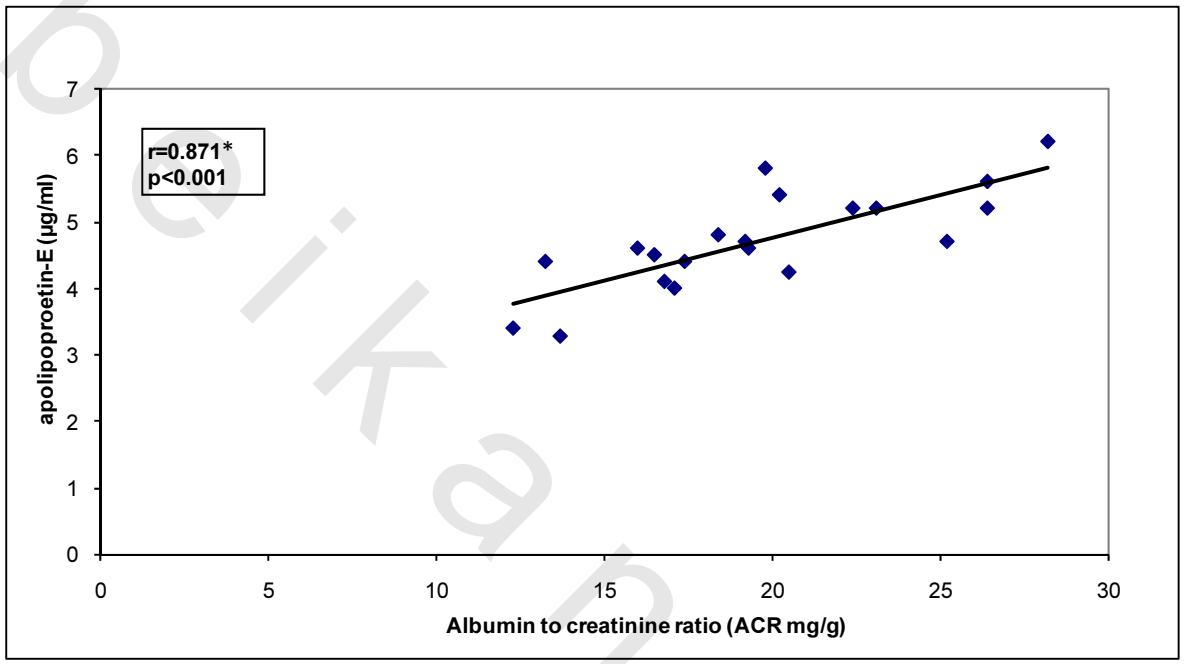


r: Pearson coefficient, *: Statistically significant at p ≤0.05.

Figure (11): The statistical correlation between apolipoprotein-E and urinary albumin to creatinine ratio (ACR) in diabetic patients receiving conventional treatment of diabetes (gpI) at the beginning of the study.

Figure (12) shows the statistical correlation between apolipoprotein-E and urinary albumin to creatinine ratio levels in diabetic patients receiving conventional treatment of diabetes before statin treatment (gpII).

A significant positive correlation has been found between the levels of apolipoprotein-E and urinary albumin to creatinine ratio levels in simvastatin-treated diabetic patients (gpII) before starting statin treatment. (r=0.871, P<0.001).

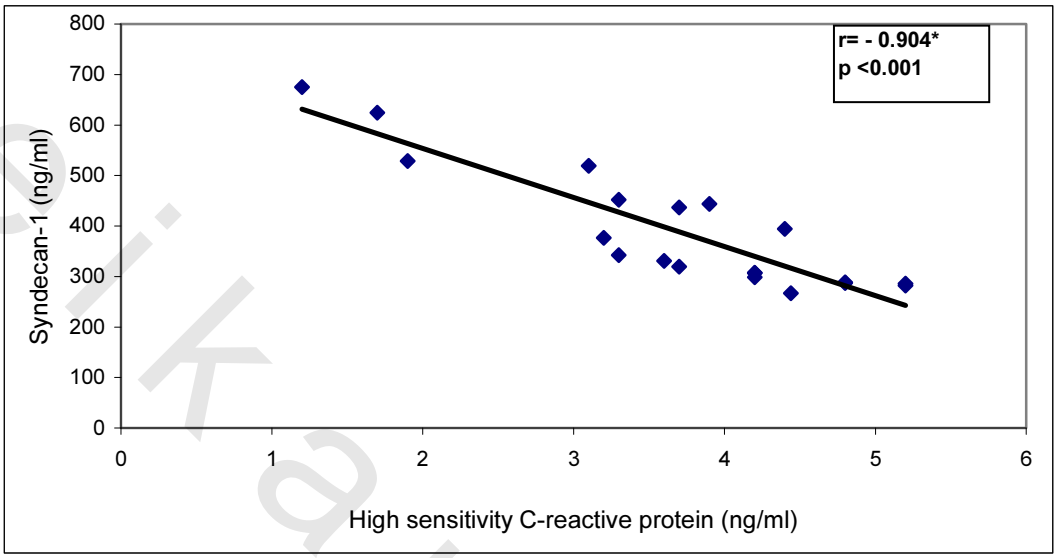


r: Pearson coefficient, *: Statistically significant at p ≤0.05.

Figure (12): The statistical correlation between apolipoprotein-E and urinary albumin to creatinine ratio (ACR) in diabetic patients receiving conventional treatment of diabetes (gpII) before starting statin treatment.

Figure (13) shows the statistical correlation between syndecan-1 and high sensitivity C-reactive protein (hs-CRP) levels in simvastatin-treated diabetic patients after 10 weeks of statin treatment.

A significant negative correlation has been found between the levels of syndecan-1 and hs-CRP in simvastatin-treated diabetic patients after 10 weeks of statin treatment. (r= -0.904, P<0.001).

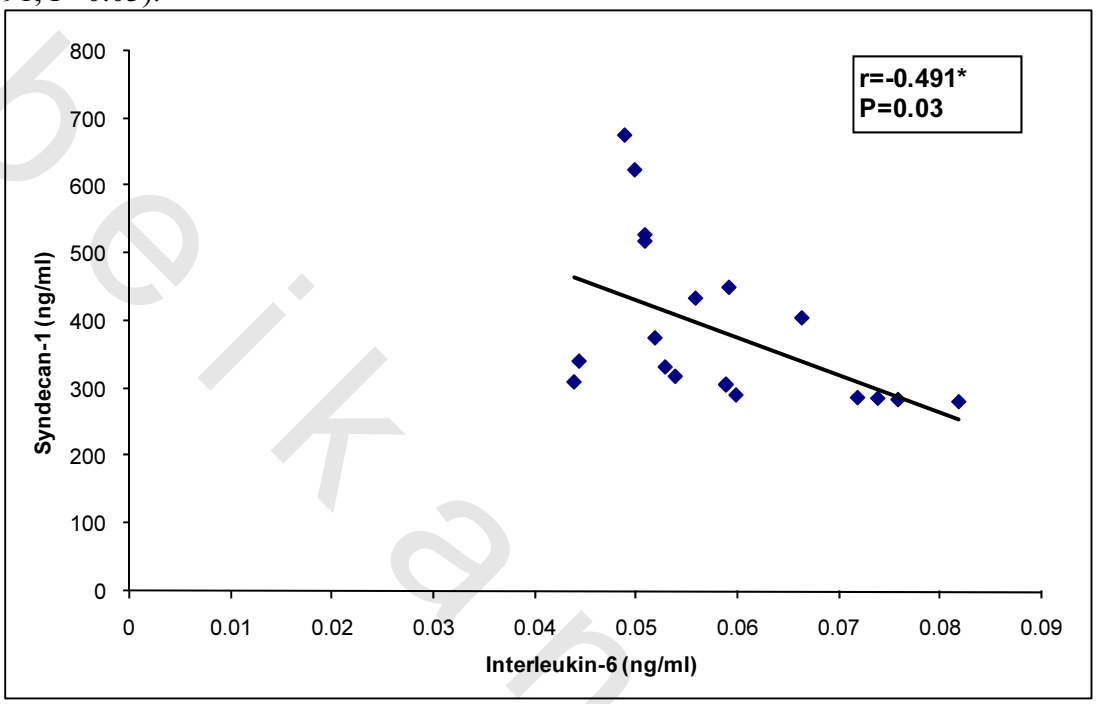


r: Pearson coefficient, *: Statistically significant at p ≤0.05.

Figure (13): The statistical correlation between syndecan-1 and high sensitivity C-reactive protein in simvastatin-treated diabetic patients after 10 weeks of statin treatment.

Figure (14) shows the statistical correlation between syndecan-1 and interleukin-6 (IL-6) levels in simvastatin-treated diabetic patients after 10 weeks of statin treatment.

A significant negative correlation has been found between the levels of syndecan-1 and IL-6 in simvastatin-treated diabetic patients after 10 weeks of statin treatment. (r=-0.491, P=0.03).



r: Pearson coefficient, *: Statistically significant at p ≤0.05.

Figure (14): The statistical correlation between syndecan-1 and interleukin-6 in simvastatin-treated diabetic patients after 10 weeks of statin treatment.