Sudan Journal of Medical Sciences
Volume 14, Issue no. 3, DOI 10.18502/sjms.v14i3.5213
Production and Hosting by Knowledge E

Research Article

High Sensitive C Reactive Protein As Predictor Marker for Cardiovascular Diseases in Sudanese Type 2 Diabetic Patients

Hala Abdalazeem Aljack

Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Omdurman Islamic University, Khartoum-Sudan

Abstract

Background: type 2 diabetes mellitus is frequently associated with inflammatory condition that lead to chronic complications. hs-CRP level had been reported as markers of cardiovascular diseases (CVDs) complications. Therefore, the aim of this study was to assess hs-CRP level in type 2 DM patients and their relation to diabetes cardiovascular complications.

Materials and methods: In case control study (205) diagnosed type 2 DM patients and (100) controls were included. Serum high Sensitive C Reactive Protein (hs-CRP), Triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL-C) and low density lipoprotein (LDL-C) were measured.

Results: Type 2 DM patients had increased level of hs-CRP and decreased HDL-C level *p*-value (0.020 and 0.000) respectively. Females had increased serum hs-CRP, TC, HDL-C and LDL-C *p*-value (0.005, 0.000, 0.000 and 0.000) respectively. Moreover, patients received statin drugs showed decreases in hs-CRP, TC and LDL-C *p*-value (0.030, 0.000 and 0.000) respectively. BMI correlate positively with TG (r: 0.37, *P*-value 0.017) and hs-CRP (r: 0.56, *P*-value 0.000), while it correlated negatively with HDL-C (r: -0.36, *P*-value 0.029).

Conclusion: The data suggested that, hs-CRP is useful diagnostic and predictor marker for CVDs in obese type 2 DM patients.

Keywords: High sensitive C reactive protein, cardiovascular diseases, type 2 DM, obesity, Sudan.

Corresponding Author:
Hala Abdalazeem Aljack;
email:
hala.abdalazeem@yahoo.com

Received 21 February 2019
Accepted 12 May 2019
Published 30 September 2019

Production and Hosting by Knowledge E

Editor-in-Chief:
Prof. Mohammad A. M. Ibnouf

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder, characterized by hyperglycemic condition due to defect in secretion of insulin by β cells of pancreas or defect in insulin action [1-3]. Recently, DM become most common chronic disorder (4) with increasing prevalence worldwide (5). It was estimated that, 425 million people had DM in 2017, and the number is expected to rise to 629 million by 2045 [6]. In Sudan, the prevalence of DM is rising from 9.3% in 2010 to 10.6 % in four states in 2013 [7].

Type 2 diabetes mellitus is a complex condition, result from resistance of insulin action combine with impaired pancreatic function [8]. If left uncontrolled, Type 2 DM can cause chronic microvascular and macrovascular complications [9]. Some previous studies confirmed that, Type 2 DM gradually causes chronic low grade of inflammation which plays vital role in the progression of diabetic complications [10].

Type 2 DM patients are at a high risk to develop CVDs and the risk increased when patients suffer from nephropathy [11]. The CVDs are observed to increase in type 2 DM with elevated inflammatory markers [12]. The inflammatory marker hs-CRP is pentameric protein synthesize by hepatic cells under control of cytokines [11]. It has been identified as a strong predictor marker for CVDs [13-15]. Previous studies documented that, diabetic patients undergo high serum hs-CRP level [16], that lead to activation of inflammatory pathways and progression of CVD [17, 18]. Accordingly this study was conducted to evaluate the hypothesis that, hs-CRP is associated with CVDs in type 2 DM patients.

2. Materials and Methods

In case control study we examined n205 type 2 DM patients, (94 males and 111 females), age ranged (from 39 to 75) years old. n100 sex and age match health apparently subjects were recruited as control. DM patients with inflammatory, liver and/or renal diseases were excluded. Written inform consents were obtained from each participations. This study was approved by local committee of Al-Neelain University, Sudan.

2.1. Measurement of BMI

Body mass index (BMI) was calculated using (weight kg/hight m^2) formula.

2.2. Measurement of hs-CRP

Serum levels of hs-CRP in patients were measured using the Particle enhanced immuno-turbidimetric assay method Cobas C-311®. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies, and then the precipitate was determined turbidimmetrically.

2.3. Measurement of lipid profile

Serum TG, TG and HDL-cholesterol were estimated by Cobas C-311® automated chemistry analyzer (Roche diagnostics, Germany).

2.4. TG measurement

Using the principle enzymatic colorimetric method which based on complete hydrolysis of triglycerides by lipoprotein lipase to glycerol, followed by oxidation and peroxidation process to form a red dyestuff. The color intensity of the red dyestuff formed is directly proportional to the triglyceride concentration and can be measured photometrically.

2.5. TC measurement

Estimation of total cholesterol based on serial enzymatic reactions lead to formation of red quinone-imine dye which can be measured photometrically. The color intensity of the dye formed is directly proportional to the cholesterol concentration.

2.6. HDL-C measurement

In the presence of magnesium ions, dextran sulfate selectively forms water-soluble complexes with LDL, VLDL and chylomicrons. The cholesterol concentration of HDL-cholesterol is determined enzymatically after formation of a purple-blue dye. The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.

2.7. LDL-C measurement

Levels of LDL-C were calculated using Friedwald equation as fallow:

$$LDL - C = TC - \left(HDL - C + \frac{TG}{5} \right)$$

3. Statistical Analysis

All statistical analyses was performed using the SPSS software (Statistical Package for the Social Sciences) (version 21.0; SPSS Inc.). Descriptive statistic (frequency and percentage) were obtained. Independent *t*-test was employed to compare mean between

groups. Pearson's correlation was used to correlate between study parameters and variables. Quantitative variables were demonstrated as mean ± SD, significant differences were considered as *P*-value ≤ 0.05.

4. Results

The study comprised of 205 Type 2 diabetic patients, Demographic and general characteristics of patients group are shown in (table 1).

The mean level of hs-CRP was significantly increased in case group (4.83 ± 0.42) compared with control group (3.48 ± 0.38) with (*p*-value 0.020), while there was significant decrease in HDL-C in case (39.4 ± 8.88) compared with control (45.2 ± 12.4) with (*p*-value 0.000). In addition, the mean levels of TG, TC and LDL-C showed insignificant differences when compared case group with control group (Table 2).

The results of the study showed the mean level of hs-CRP was significantly higher in female (5.91 ± 2.61) compared with male (3.54 ± 2.55) with (*p*-value 0.005). furthermore, The lipid profile results showed significant increase in TC, HDL-C and LDL-C mean levels in female when compared with male (*p*-value 0.000) and insignificant difference in mean level of TG (table 3).

Patients group who take cholesterol lowering agent (statin) had significantly lower levels of hs-CRP, TC and LDL-C as compared with untreated Patients (*p*-value 0.030, 0.000 and 0.000) respectively, while other parameter showed insignificant differences between two groups (table 4).

In correlation analysis, hs-CRP and TG levels correlate positively with BMI (*p*-value 0.000 and 0.017) respectively while HDL-C inversely related with BMI (r: 0.37 *p*-value 0.029) as in (table 5) (Figure 1).

Table 1: General characteristics of type 2 diabetic patients.

Characteristic	Frequency (percentage %)
Gender	Male: 94 (46%) Female: 111 (54%)
Age (years)	< 55 years: 96 (47%) > 55 years: 109 (53%)
BMI	Normal weight: 47 (23%) Overweight: 94 (46%) Obese: 64 (31%)
Diabetic control	Controlled: 64 (31.2%) Uncontrolled: 141 (68.8%)
Education status	Low: 36 (18%) Moderate: 132 (65%) High: 35 (17%)
Life style	Low: 69 (35.0%) Moderate: 113 (57.4%0) Good: 15 (7.6%)
Physical exercise	Yes: 93 (47.9%) No: 101 (52.1%)
Family history of DM	First degree: 108 (36.5%) Second degree: 137 (46.3%) No: 51 (17.2%)
Family history of CVD	Yes: 26 (14.1%) No: 159 (85.9%)
Cholesterol lowering agent	Yes: 84 (47.2%) No: 94 (52.8%)

Table 2: Study parameters in case and control groups.

Parameter	Case (Mean±SD)	Control (Mean ± SD)	P-value
hs-CRP (mg/l)	4.83 ± 0.42	3.48 ± 0.38	0.020
TG (mg/dl)	117 ± 48.3	114 ± 60.4	0.620
T.Cholestrol (mg/dl)	171 ± 33.7	163 ± 42.2	0.055
HDL-Cholestrol (mg/dl)	39.4 ± 8.88	45.2 ± 12.4	0.000
LDL-Cholestrol (mg/dl)	101 ± 35.8	103 ± 31.1	0.647

The results expressed as (Mean ± SD) and *P* value less than 0.05 was statistically considered significant

Table 3: Biochemical parameters according to gender.

Parameters	Male (Mean±SD)	Female (Mean±SD)	P-value
hs-CRP (mg/l)	3.54 ± 2.55	5.91 ± 2.61	0.005
TG (mg/dl)	119 ± 60.2	121 ± 62.7	0.794
T.Cholestrol (mg/dl)	150 ± 39.1	171 ± 40.1	0.000
HDL-Cholestrol (mg/dl)	37.1 ± 7.51	41.4 ± 9.49	0.000
LDL-Cholestrol (mg/dl)	91.3 ± 34.5	109 ± 35.0	0.000

The results expressed as (Mean ± SD) and *P*-value less than 0.05 was statistically considered significant.

Table 4: Study parameters in patient group classified according to intake of cholesterol lowering agent.

Parameters	Patients who were taken cholestrol lowering agent (Mean ± SD)	Patients who were not taken cholestrol lowering agent (Mean ± SD)	P-value
hs-CRP (mg/l)	3.52 ± 3.23	4.98 ± 5.43	0.030
TG (mg/dl)	121 ± 69.1	125 ± 58.8	0.706
T.Cholestrol (mg/dl)	146 ± 38.2	176 ± 40.7	0.000
HDL-Cholestrol (mg/dl)	38.8 ± 8.71	39.0 ± 8.35	0.847
LDL-Cholestrol (mg/dl)	85.8 ± 32.1	114 ± 33.9	0.000

The results expressed as (Mean ± SD) and *P*-value less than 0.05 was statistically considered significant.

Table 5: Correlation of biochemical parameters with study variables.

Correlation	R	P-value
hs-CRP with BMI	**0.56****	**0.000**
hs-CRP with age	-0.12	0.094
hs-CRP with duration	-0.01	0.942
TG with BMI	**0.37***	**0.017**
TG with age	0.02	0.800
TG with duration	0.07	0.355
T.Cholestrol with BMI	0.07	0.332
T.Cholestrol with age	-0.08	0.250
T.Cholestrol with duration	0.50	0.484
HDL-C with BMI	**-0.36***	**0.029**
HDL-C with age	-0.03	0.725
HDL-C with duration	0.05	0.505
LDL-C with BMI	0.06	0.428
LDL-C with age	-0.11	0.110
LDL-C with duration	0.04	0.599

(R): Pearson correlation test, (____): negative correlation, *P*-value less than 0.05 was statistically considered significant.

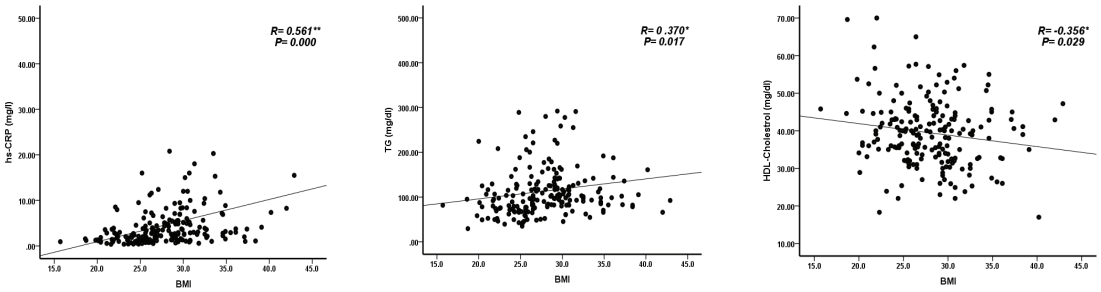

Figure 1: Dot blots regression of hs-CRP with BMI, TG with BMI and HDL-C with BMI. R= Pearson correlation test. (____): negative correlation *P*-value less than 0.05 were statistically considered significant.

5. Discussion

In this study we found that, type 2 DM was common in female than male. The predominance of females with diabetes is attributed to the hormonal effects, higher ability of the body to store iron and physical inactivity indeed most of them were housewives [19]. In our study the majority of patients are elderly and overweight. Thus postulated combination of genetic predisposition, environmental, nutritional factors, obesity, physical inactivity, stress, and aging [20], might be involved in Sudanese type2 DM. Moreover, characteristic data revealed significant higher of uncontrolled DM patients and lower socioeconomic status. Previous study associated between low educational level correlate with DM, and socioeconomic status inversely associated with DM prevalence [21].

Serum hs-CRP level was significantly higher in type 2 DM patients versus controls. Our results was in agreement with others that, pro-inflammatory cytokine hs-CRP was significantly higher in type 2 diabetic patients [22, 23]. Recently, the inflammatory pathway play critical role in type 2 pathogenesis, development and progression of the diabetes complications [11]. On the other hand, accordance to previous reports [24, 25], we found that, women had higher hs-CRP levels than with men. This sex difference is incompletely understood, many studies speculated that, adiposity and hormone replacement therapy or that looked only at postmenopausal women still found higher levels of CRP in women [25].

In addition, the results of lipid profile showed insignificant difference in TG, TC and LDL-C levels in patient and control groups. Previous study reported that, the mean TG, TC and LDL-C concentrations were insignificantly differ in type 2 DM and control subject

[26]. HDL-C level is significantly lower in type 2 DM patients as in line with previous study noted that, type 2 patients had lower level of HDL-C compared with control participants. In lipids metabolism in DM patients have reported that, decreasing in HDL-C may be due to a reduction in lipoprotein lipase (LPL) activity, which would impair the maturation of HDL particles. In type 2 DM, particularly in poor glycemic control patients who are relatively insulin deficient, LPL activity is decreased [27]. Furthermore female type 2 DM patients had higher levels of TC, HDL-C and LDL-C than diabetic male which is in line with previous studies [28], which attributed to the effect of sex hormones and distribution of body fat leading to these differences [28].

Moreover patients received Statin treatment revealed lower levels of hs-CRP, TC and LDL-C. Previous evidence indicating that, treatment with atorvastatin lead to reduce LDL-C and hs-CRP levels in patients with type 2 DM [29].

Likewise to previous reports stated that, hs-CRP level is correlate positively with BMI [30]. In addition, the correlation between serum TG and BMI observed the highest triglyceride levels in overweight and obese patients [31] while HDL-C was negatively correlate with BMI [32], our study showed BMI correlate positively with TG and hs-CRP, while it correlated negatively with HDL-C.

6. Conclusion

The study concluded that, hs-CRP had significantly higher in type 2 DM patients. BMI positively associated with hs-CRP and TG while negatively correlate with HDL-C. Therefore, hs-CRP is useful diagnostic predictor marker for CVD in type 2 DM patients. Therefore, periodic monitoring should recommended especially for overweight and obese type 2 DM patients.

Acknowledgment

The authors gratefully acknowledge Dr. Nazik Mahmoud (Specialist of Diabetes and Endocrinology) at diabetic center of Military hospital for her valuable assistance in this study.

Conflict of Interest

All authors have declared that no conflict of interest exists.

References

[1] Khodaeian M, Enayati S, Tabatabaei-Malazy O, Amoli MM. Association between genetic variants and diabetes mellitus in Iranian populations: a systematic review of observational studies. Journal of diabetes research. 2015;2015:21.

[2] Liu J, Li J, Li W-J, Wang C-M. The role of uncoupling proteins in diabetes mellitus. Journal of diabetes research. 2013;2013:7.

[3] Ozougwu J, Obimba K, Belonwu C, Unakalamba C. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. Journal of Physiology and Pathophysiology. 2013;4(4):46-57.

[4] Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010;87:4-14.

[5] Noor S, Bushara S, Sulaiman A, Elmadhoun W, Ahmed M. Undiagnosed diabetes mellitus in rural communities in Sudan: prevalence and risk factors/Diabete non diagnostique dans les communautes rurales du Soudan: prevalence et facteurs de risque. Eastern Mediterranean Health Journal. 2015;21(3):164-70.

[6] Aynalem SB, Zeleke AJ. Prevalence of Diabetes Mellitus and Its Risk Factors among Individuals Aged 15 Years and Above in Mizan-Aman Town, Southwest Ethiopia, 2016: A Cross Sectional Study. International journal of endocrinology. 2018;2018:1-7.

[7] Balla SA, Ahmed HA, Awadelkareem MA. Prevalence of diabetes, knowledge, and attitude of rural, population towards diabetes and hypoglycaemic event, Sudan 2013. Am J Health Res. 2014;2(6):356-60.

[8] Baranwal JK, Maskey R, Majhi S, Lamsal M, Baral N. Association between level of HbA1c and lipid profile in T2DM patients attending diabetic OPD at BPKIHS. Health Renaissance. 2017;13(3):16-23.

[9] Moreira TS, Hamadeh MJ. The role of vitamin D deficiency in the pathogenesis of type 2 diabetes mellitus. e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism. 2010;5(4):e155-e65.

[10] Likitesh A, Prabhakar K, Reddy Prasad K. Estimation of high sensitivity c-reactive protein levels as a early marker of diabetic nephropathy. european journal of pharmaceutical and medical research.4(4):315-8.

[11] Khan MI, Usman K, Ashfaq F, Himanshu D, Ali W, Idris M. Association of Hs-CRP and HbA1C with Microalbuminuria in Type-2 Diabetic patients in North India. Biomedical Research. 2012;23(3):380-4.

[12] Patil A, Ganu J. High sensitive C-reactive protein and microalbumin in type 2 diabetes mellitus. Asian Pac J Health Sci. 2014;1(4):319-21.

[13] Sindhu S, Singh HK, Salman MT, Fatima J, Verma VK. Effects of atorvastatin and rosuvastatin on high-sensitivity C-reactive protein and lipid profile in obese type 2 diabetes mellitus patients. Journal of pharmacology & pharmacotherapeutics. 2011;2(4):261-65.

[14] Ding D, Wang M, Su D, Hong C, Li X, Yang Y, et al. Body mass index, high-sensitivity C-reactive protein and mortality in Chinese with coronary artery disease. PloS one. 2015;10(8):e0135713.

[15] Clearfield MB. C-reactive protein: a new risk assessment tool for cardiovascular disease. Journal-american osteopathic association. 2005;105(9):409-16.

[16] Hayashino Y, Mashitani T, Tsujii S, Ishii H. Serum high-sensitivity C-reactive protein levels are associated with high risk of development, not progression, of diabetic nephropathy among Japanese type 2 diabetic patients: a prospective cohort study (Diabetes Distress and Care Registry at Tenri [DDCRT7]). Diabetes Care. 2014;37(11):2947-52.

[17] Bashir S, Shabbir I, Aasim M. Role of C-reactive protein as a marker for microalbuminuria in type 2 diabetics. Journal of Ayub Medical College Abbottabad. 2014;26(1):32-4.

[18] Mojahedi MJ, Bonakdaran S, Hami M, Sheikhian MR, Shakeri MT, Aiatollahi H. Elevated serum C-reactive protein level and microalbuminuria in patients with type 2 diabetes mellitus. Iran J Kidney Dis. 2009;3(1):12-6. 27.

[19] Ozder A. Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study. Lipids in health and disease. 2014;13(1):183.

[20] Kohei K. Pathophysiology of type 2 diabetes and its treatment policy. JMAJ. 2010;53(1):41-6.

[21] Rahmanian K, Shojaei M, Jahromi AS. Relation of type 2 diabetes mellitus with gender, education, and marital status in an Iranian urban population. Reports of biochemistry & molecular biology. 2013;1(2):64-8.

[22] Momin AA, Naik PS, Bhoite GM. Albumin/Creatinine Ratio, As Predictor of Microalbuminuria, a Risk Factor For Nephropathy In Type 2 Diabetes Mellitus Patients. International Journal of Health Sciences and Research (IJHSR). 2012;1(2):36-40.

[23] Valiollah S, Mojtaba E, Vahid I, Ali SM, editors. Association of C Reactive Protein with Insulin Resistance in Type 2 Diabetic. Proceedings of International Conference on Bioscience, Biochemistry and Bioinformatics (ICBBB 2011); 2011.

[24] Mahajan A, Tabassum R, Chavali S, Dwivedi OP, Bharadwaj M, Tandon N, et al. High-sensitivity C-reactive protein levels and type 2 diabetes in urban North Indians. The Journal of Clinical Endocrinology & Metabolism. 2009;94(6):2123-7.

[25] Qasim AN, Budharaju V, Mehta NN, St Clair C, Farouk S, Braunstein S, et al. Gender differences in the association of C–reactive protein with coronary artery calcium in Type–2 diabetes. Clinical endocrinology. 2011;74(1):44-50.

[26] Gordon L, Ragoobirsingh D, St Errol Y, Choo-Kang E, McGrowder D, Martorell E. Lipid profile of type 2 diabetic and hypertensive patients in the Jamaican population. Journal of laboratory physicians. 2010;2(1):25-30.

[27] Cui R, Qi Z, Zhou L, Li Z, Li Q, Zhang J. Evaluation of serum lipid profile, body mass index, and waistline in Chinese patients with type 2 diabetes mellitus. Clinical interventions in aging. 2016;11:445-52.

[28] Zeqollari A, Spahiu K, Vyshka G, Çakërri L. Lipid Profile in Diabetes Mellitus Type 2 Patients in Albania and The Corellation with BMI, Hypertension, and Hepatosteatosis. Journal family medicin community health. 2014;1(4):1018.

[29] Son JW, Kim DJ, Lee CB, Oh S, Song KH, Jung CH, et al. Effects of patient–tailored atorvastatin therapy on ameliorating the levels of atherogenic lipids and inflammation beyond lowering low–density lipoprotein cholesterol in patients with type 2 diabetes. Journal of diabetes investigation. 2013;4(5):466-74.

[30] Amanullah S, Jarari A, Govindan M. Association of hs-CRP with diabetic and non-diabetic individuals. Jordan journal of biological sciences. 2010;3(1):7-12.

[31] Omotoye FE, Fadupin GT. Effect of Body Mass Index on Lipid Profile of Type 2 Diabetic Patients at an Urban Tertiary Hospital in Nigeria. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2016;15(9):65-70.

[32] Elfaki EM, Raheem EMA, Ahmed SE. Evaluation of Lipid Metabolism among Sudanese Patients with Type 2 Diabetes Mellitus. International Journal of Pure and Applied Sciences and Technology. 2014;23(1):28-33.