

# High Sensitive C – Reactive Protein Level as a Risk Factor for Cardiovascular Diseases in Sudanese with Type 2 Diabetes Mellitus and Obese individuals

Razaz Adil Hassan<sup>1</sup>, Sara Osman Yousif Hamid<sup>2</sup>, Altaf Suleman Mosad Taaha<sup>2</sup>, and Mariam Abbas Ibrahim Abdelghafour<sup>2\*</sup>

<sup>1</sup>Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, Al- Neelain University, Khartoum, Sudan

<sup>2</sup>Clinical Chemistry Department, College of Medical Laboratory Science, Sudan University of Science and Technology, Khartoum, Sudan

\*Corresponding author: Mariam A. I. Abdelghafour

| Received: 06.04.2019 | Accepted: 14.04.2019 | Published: 30.04.2019

DOI: [10.21276/sijb.2019.2.4.1](https://doi.org/10.21276/sijb.2019.2.4.1)

## Abstract

**Background:** There is evidence that support the use of high sensitive C-reactive protein (hs-CRP) to monitor cardiovascular risk in diabetic and non diabetic individuals. This study aims to assess hs-CRP level in Sudanese with type 2 diabetes mellitus (D.M) and obese individuals; as a risk factor for cardiovascular diseases. **Materials and methods:** This cross-sectional study was conducted in Khartoum-Sudan from April to December 2018, 50 diagnosed Sudanese patients with diabetes mellitus attending Alarbaeen hospital in Khartoum state and 50 obese Sudanese individuals were enrolled in this study. Blood samples were analyzed for cholesterol and hs-CRP levels using Mindray BS-200 automated analyzer. **Results:** There were no significant differences in hs-CRP and total cholesterol levels in type 2 D.M when compared with obese. Both diabetic patients and obese had high levels of hs-CRP and total cholesterol. hs-CRP and total cholesterol levels revealed no significant difference when male compared with female in type 2 D.M as well as in obese. The majority of the study participants were found to have hs-CRP level more than 3 mg/L, which indicate a high risk to have cardiovascular diseases according to American Heart Association. There was no correlation between hs-CRP levels and total cholesterol levels in the study subjects. Age showed inverse significant correlation with hs-CRP levels in type 2 D.M and no correlation among obese. **In conclusion:** The higher levels of hs-CRP with higher levels of total cholesterol may be a predictive factor for developing of CVD in Sudanese with type 2 D.M as well as in obese.

**Keywords:** CVD, Type 2 DM, Obesity, hs-CRP, Sudanese.

**Copyright © 2019:** This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

## INTRODUCTION

Obesity, type 2 diabetes mellitus (T2DM), and atherosclerosis are closely linked and may be determinants of an increased acute-phase response [1]. Long term levels of C-reactive protein (CRP), as measured by high-sensitivity assays (hs-CRP), can predict future risk of cardiovascular disease (CVD) in both men and women [2, 3]. Elevated levels of C-reactive protein (CRP) have been associated with increased risk of cardiovascular disease (CVD) among the general population [4]. People with diabetes, hypertension and obesity have CRP levels that are higher than those in people without these conditions in the general population. Type 2 diabetes mellitus (T2DM) accounts for approximately 90% of the diabetes cases worldwide [5] and is linked mainly to excess body weight and physical inactivity. The glucotoxicity and lipotoxicity that occur in diabetic patients could be reversed early by good management,

which may assist in preventing or delaying the long-term complications of T2DM, particularly vascular complications [6].

It is recognized that the risk of cardiovascular events is amplified in patients with T2DM, and dyslipidemia is a contributing factor [7]. Weight gain and obesity are key factors in increasing the prevalence of both cardiovascular disease (CVD) and T2DM [8]. Data on mortality in diabetic patients showed that 52% of people with T2DM died of CVD, primarily heart disease and stroke [8], however the aim of this study was to associate between hs-CRP and cholesterol levels among diabetic patients and obese as risk factors for cardiovascular diseases.

## MATERIALS AND METHODS

**Study design:** This is a cross-sectional study.

### Study Area and Period

The study was conducted in Alarbaeen hospital and Afra gym center, Khartoum state, Sudan. The study was carried out from April to December 2018.

### Study Population

Fifty Sudanese Patients with type 2 diabetes mellitus and 50 obese individuals were enrolled in this study.

### Inclusion Criteria

Sudanese patients who were diagnosed with Type 2 diabetes mellitus and obese individuals who were selected according to their body mass index (BMI) more than 30 kg/m<sup>2</sup> (according to WHO definition for obesity) were enrolled in this study.

### Exclusion Criteria

Diabetic patients and obese with recent or ongoing infection or fever, chronic inflammatory disorder (rheumatoid arthritis, systemic lupus Erythematosus, etc.), hypertension, cardiovascular diseases, liver diseases, renal diseases were excluded from the study.

### Ethical Consideration

The study was approved by scientific committee of Medical Laboratory Science, Clinical Chemistry Department –Alneelain University, then an informed consent was obtained from all participants.

### Data Collection and Anthropometric Measurements

Clinical data was collected by questionnaire. The body mass index (BMI) was calculated as weight (kg) divided by the square of height (in meters).

### Sampling

After consent a sample of venous blood (5 mL) was collected in plain container to obtain serum after centrifugation and was refrigerated until used.

### Biochemical Measurements

The laboratory measurements of high sensitivity C-reactive protein (hs-CRP) and total cholesterol levels were carried out using Mindray BS-200 automated analyzer.

### Quality Control

Pathological and normal control sera were measured, to assure the accuracy and precision of results.

### Statistical Analysis

The Data was analyzed using SPSS version 21. Values were expressed as percentage and Mean  $\pm$  SD. Independent T-test and one-way Anova analysis were used for comparison between groups. Pearson's correlation test was done to determine the association between study variables. P-value  $\leq$  0.05 were considered to be statistically significant.

## RESULTS

A total of 100 subjects were enrolled in this study, 50 were diagnosed with type 2 DM and 50 were obese with mean age  $44 \pm 10.6$  years and  $48 \pm 9.8$  years old respectively. The means of hs-CRP and total cholesterol levels did not show significant differences in patients with type 2 DM compared with the obese ( $p = 0.30$ ,  $p = 0.06$ ) respectively (Table-1). hs-CRP and total cholesterol levels revealed no significant differences in male when compared with female in type 2 D.M as well as in obese subjects (Table-2). hs-CRP levels of type 2 D.M and obese were divided into four groups shown in table-3. The majority of the study subjects were found to have hs-CRP level more than 3 mg/L, which indicate a high risk to have cardiovascular diseases according to American Heart Association(AHA). Correlation of hs-CRP levels with age and total cholesterol levels were presented in table 4. There was no correlation between hs-CRP levels and total cholesterol levels in the study subjects. Age showed inverse significant correlation with hs-CRP levels in type 2 D.M ( $r = -0.358$ ,  $p = 0.01$ ) and negative correlation but not significant among obese subjects.

**Table-1: Comparison of the means  $\pm$  SD of age, hs-CRP and total cholesterol levels in type 2 D.M and obese individuals**

Variables	Type 2 D.M n=50	Obese n= 50	P-value
Age (years)	$44 \pm 10.6$	$48 \pm 9.8$	0.053
hs-CRP (mg/L)	$10.5 \pm 4.8$	$11.4 \pm 4.5$	0.30
Total cholesterol (mg/dL)	$237 \pm 40$	$212 \pm 45$	0.06

**Table-2: Comparison of the means  $\pm$  SD of hs-CRP and total cholesterol levels in type 2 D.M and obese individuals in reference to gender**

Variables	Type 2 D.M			Obese		
	Male n= 22	Female n= 28	P-value	Male n= 22	Female n= 28	P-value
hs-CRP (mg/L)	12.2 $\pm$ 4.4	10.8 $\pm$ 4.6	0.28	10.5 $\pm$ 5.4	10.5 $\pm$ 4.4	0.98
Total cholesterol (mg/dL)	211 $\pm$ 50	213 $\pm$ 42	0.86	234 $\pm$ 41	238 $\pm$ 41	0.70

**Table-3: Categorization of hs-CRP level in type 2 D.M and obese individuals as risk factor for CVD**

	hs-CRP level (mg/L)				P-value
	<7	7-11	12-14	>14	
	N (%)	N (%)	N (%)	N (%)	
Type 2 D.M n= 50	12 (24)	11 (22)	15 (30)	12 (24)	0.000
Obese n= 50	17(34)	11 (22)	10 (20)	12 (24)	0.000

**Table-4: Correlation of hs-CRP levels with age and total cholesterol levels**

hs-CRP (mg/L)	Type 2 D.M n=50		Obese n=50	
	Age (years)	T. cholesterol (mg/dL)	Age (years)	T. cholesterol (mg/dL)
	r = - 0.358 P = 0.01	r = 0.092 P = 0.525	r = - 0.190 P = 0.187	r = 0.087 P = 0.548

## DISCUSSION

This study has shown that there were no differences in hs-CRP and total cholesterol levels between type 2 diabetic patients and obese. Both study group had high levels of hs-CRP and total cholesterol. The majority of diabetic patients and obese were found to have levels of hs-CRP more than 3 mg/L, which indicate high risk to have CVDs according to AHA categorization, <1, 1 to 3, and more than 3 mg/L (low, average, and high-risk) respectively. The mean of total cholesterol levels was more than 200 mg/dL in diabetic patients as well as in obese. These findings comes in line with Abdelmarouf H *et al.*, study in type 2 diabetic patients that reported, 70% of diabetic patients had high levels of hs-CRP range (2.45-10 mg/L). Also was reported an association between higher levels of hs-CRP and obesity [9]. Two studies showed increase significant differences of hs-CRP levels in type 2 diabetic patients when compared with non diabetics [10, 11]. Furthermore Angelo C *et al.*, study demonstrated that diabetics found to have more than five times higher CRP than non diabetics. Diabetics found to be at high risk to have CVD than non diabetics and CRP may be a potential predictor of CVD, especially in obese diabetics [11]. A case-control study done among Sudanese overweight and obese adults showed that, positive significant correlation between

hs-CRP level and body mass index. In addition, a relation between obesity and risk of developing CVDs was found [12].

It has been reported that, high levels of CRP in diabetes and obesity may be due to increase in adipose tissue mass that enhances cytokines production (e.g tumor necrosis factor- $\alpha$  and interleukins) by adipocytes, which stimulate synthesis of CRP [11].

In this study there were no differences in hs-CRP and total cholesterol levels in both study groups regarding gender. Conversely, two studies noted that, the hs-CRP mean of females was significantly higher than males [12, 13].

Our study showed a positive correlation but not significant between levels of hs-CRP and total cholesterol in diabetic patients and obese. This finding match a study results done in Sudanese with type 2 Type 2 diabetes mellitus that documented a non significant correlation between hs-CRP levels and total cholesterol [11]. In contrast other study reported that, higher levels of hs-CRP were positively (significant) correlated with total cholesterol levels [13].

In the present study there was a significant inverse correlation of hs-CRP levels with age in

diabetic patients. Also an inverse correlation but not significant between hs-CRP levels and age in obese were found. This finding was counteracted by Abdelmarouf H *et al.*, report, that subjects with the highest age were have high levels of hs-CRP [9].

It is reported by some studies; that hs-CRP seems to be a significant predictor of diabetes risk even if BMI, family history of DM and other factors were adjusted [14, 15]. Furthermore, in patients with diabetes a high CRP levels may be associated with a two fold increase in CV mortality after adjusting for age, sex and glucose tolerance tests [16, 17]. As indicated by AHA CRP is an independent indicator of cardiovascular risk, estimation of CRP levels is recommended by AHA in patients who on the basis of multiple risk factor scoring with cholesterol levels, weight, level of exercise, smoking history and presence of diabetes and hypertension. An elevated CRP levels in these patients can indicate the degree of risk which may give knowledge to doctor and patient [12].

## CONCLUSION

This study found that, the majority of type 2 diabetics and obese subjects were found to have high risk of developing CVDs according AHA categorization for hs-CRP levels. Also the both subjects were with high levels of total cholesterol which is one of the risk factors.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

## REFERENCES

- Lyon, C. J., Law, R. E., & Hsueh, W. A. (2003). Minireview: adiposity, inflammation, and atherogenesis. *Endocrinology*, 144(6), 2195-2200.
- Ridker, P. M., Hennekens, C. H., Buring, J. E., & Rifai, N. (2000). C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *New England Journal of Medicine*, 342(12), 836-843.
- Koenig, W., Khuseyinova, N., Baumert, J., Thorand, B., Loewel, H., Chambless, L., ... & Herder, C. (2006). Increased concentrations of C-reactive protein and IL-6 but not IL-18 are independently associated with incident coronary events in middle-aged men and women: results from the MONICA/KORA Augsburg case-cohort study, 1984-2002. *Arteriosclerosis, thrombosis, and vascular biology*, 26(12), 2745-2751.
- Pai, J. K., Pischon, T., Ma, J., Manson, J. E., Hankinson, S. E., Joshipura, K., ... & Rimm, E. B. (2004). Inflammatory markers and the risk of coronary heart disease in men and women. *New England Journal of Medicine*, 351(25), 2599-2610.
- Stolar, M. (2010). Glycemic control and complications in type 2 diabetes mellitus. *The American journal of medicine*, 123(3), S3-S11.
- Brunzell, J. D., Davidson, M., Furberg, C. D., Goldberg, R. B., Howard, B. V., Stein, J. H., & Witztum, J. L. (2008). Lipoprotein management in patients with cardiometabolic risk: consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes care*, 31(4), 811-822.
- Bays, H. E., Chapman, R. H., Grandy, S., & SHIELD Investigators' Group. (2007). The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: comparison of data from two national surveys. *International journal of clinical practice*, 61(5), 737-747.
- Kvan, E., Pettersen, K. I., Sandvik, L., Reikvam, A., & INPHARM Study Investigators. (2007). High mortality in diabetic patients with acute myocardial infarction: cardiovascular comorbidities contribute most to the high risk. *International journal of cardiology*, 121(2), 184-188.
- Mohieldein, A. H., Hasan, M., & El-Habiby, M. I. (2017). High Sensitivity C-Reactive Protein as Atherogenic Marker Among Type 2 Diabetes. *European Scientific Journal*, 13(33): 1857-7881.
- Mahajan, A., Tabassum, R., Chavali, S., Dwivedi, O. P., Bharadwaj, M., Tandon, N., & Bharadwaj, D. (2009). High-sensitivity C-reactive protein levels and type 2 diabetes in urban North Indians. *The Journal of Clinical Endocrinology & Metabolism*, 94(6), 2123-2127.
- Dongway, A. C., Faggad, A. S., Zaki, H. Y., & Abdalla, B. E. (2015). C-reactive protein is associated with low-density lipoprotein cholesterol and obesity in type 2 diabetic Sudanese. *Diabetes, metabolic syndrome and obesity: targets and therapy*, 8, 427-435.
- Gamil, S. S., Adam, M. E., & Bakheit, K. H. (2014). Plasma levels of C-reactive protein a cardiovascular risk factor indicator in Sudanese overweight and obese adults. *Journal of Endocrinology, Diabetes & Obesity*, 3(1), 1063.
- Abha, G., Dilip, K., Satyam, R., & Arvind, K. (2015). To study the association of high sensitivity C-reactive protein with newly diagnosed DM type 2. *Journal Indian Academy of Clinical Medicine*, 16(1): 12-15.
- Pradhan, A. D., Manson, J. E., Rifai, N., Buring, J. E., & Ridker, P. M. (2001). C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *Jama*, 286(3), 327-334.

15. Flores-Alfaro, E., Parra-Rojas, I., Salgado-Bernabé, A. B., Chávez-Maldonado, J. P., & Salazar-Martinez, E. (2008). Cardiovascular risk evaluated by C-reactive protein levels in diabetic and obese Mexican subjects. *Circulation Journal*, 72(7), 1170-1174.
16. Jager, A., van Hinsbergh, V. W., Kostense, P. J., Emeis, J. J., Yudkin, J. S., Nijpels, G., ... & Stehouwer, C. D. (1999). von Willebrand factor, C-reactive protein, and 5-year mortality in diabetic and nondiabetic subjects: the Hoorn Study. *Arteriosclerosis, thrombosis, and vascular biology*, 19(12), 3071-3078.
17. Pfützner, A., & Forst, T. (2006). High-sensitivity C-reactive protein as cardiovascular risk marker in patients with diabetes mellitus. *Diabetes technology & therapeutics*, 8(1), 28-36.