



# **A Study of Carotid Doppler and Highly Specific C Reactive Protein in Type II Diabetes Mellitus and Its Correlation with Macrovascular Complications**

**Vijayashree S. Gokhale <sup>a#</sup>, Rupesh S. Parati <sup>a\*o</sup>, Ponvijaya Yadav <sup>aω</sup>  
and Keyuri Mehta <sup>aω</sup>**

<sup>a</sup> Department of Medicine, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, India.

## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

## **Article Information**

DOI: 10.9734/JPRI/2021/v33i60B34850

## **Open Peer Review History:**

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/81352>

**Original Research Article**

**Received 20 October 2021**  
**Accepted 22 December 2021**  
**Published 25 December 2021**

## **ABSTRACT**

**Background:** Diabetes has a multitude of macrovascular complications, one of them being Carotid artery Atherosclerosis leading to stenosis and predisposing patient to Stroke. A hypothesis put forward is the presence of low-grade inflammation in Diabetic patients, which may enhance atherosclerosis. A study was planned to assess Carotid artery stenosis and HsCRP levels in Diabetic patients, so as to identify at risk group and take measures to prevent complications such as stroke and ischemic heart disease.

**Aim:** To study the patients by clinical parameters, ultrasound carotid doppler study, and estimation of HsCRP with patients of type II DM.

**Study Design:** Cross sectional observational study.

**Place and Duration of Study:** Study was conducted at Department of General Medicine, Dr D Y Patil Medical College, Pune from July 2019 – September 2021.

**Methodology:** The study included 50 subjects with type 2 DM (as per inclusion and exclusion criterion). All participants were explained the nature of the study and after informed consent all subjects were clinically examined and were subjected to carotid artery doppler and HsCRP levels.

<sup>#</sup>Professor & Head of Unit;

<sup>o</sup>Resident

<sup>\*</sup>Corresponding author: E-mail: [rupeshparati@gmail.com](mailto:rupeshparati@gmail.com);

**Results:** In our study 16% had carotid stenosis of <50% while 8% had >50%. However, 42% had increased intima-media thickness. On the other hand, 52% subjects had raised HsCRP levels.

**Conclusion:** In our study, Carotid Stenosis and impending stenosis was seen in significant number of Diabetic patients of more than 5 years duration, who also had higher HsCRP levels.

*Keywords: Diabetes; carotid artery stenosis; carotid artery doppler; HsCRP (Highly specific C reactive protein).*

## 1. INTRODUCTION

Diabetes is a conglomerate of disorder with hyperglycemia being the distinguishing trait. Contemporary medical science uses a vast array of primary lifestyle and pharmaceutical interventions with an objective intended at preventing and controlling hyperglycemia [1]. The paramount focus is to ensure the adequate delivery of glucose to the tissue, and addressing the insulin resistance simultaneously [1,2]. Treatment of diabetes aims at decreasing the likelihood that the tissues of the body are harmed by hyperglycemia. Chronic hyperglycemia being an important escalating factor for macro-microvascular complication and ongoing inflammatory process, requires adequate to strict glycemic control [3]. The preponderance of protecting the body from hyperglycemia cannot be overstated; there are both direct and the indirect effects of chronic hyperglycemia on vascular anatomy and physiology and act as the major pedigree of morbidity and mortality in both type I and type II diabetes. The substantial inimical effects of hyperglycemia are divided into macrovascular complications viz; coronary artery disease, peripheral vascular disease, and cerebrovascular disease and microvascular complications like diabetic triopathy (nephropathy, retinopathy, neuropathy) [4,5,6]. As the incidence and prevalence of diabetes is on increasing trend in India and rest of the world, the early diagnosis, prevention and lifestyle modification will alter the progression of the disease and delay the development of vascular complication which in turn may prevent the major life threatening complication likely to arise in future [6,7]. The present study is an example of evidence-based medicine in which we subject a study participant to a non-invasive technique of assessing carotid atherosclerosis or stenosis by Doppler ultra sound along with assessment of HsCRP, an inflammatory marker which has generated considerable interest as a marker of atherosclerosis and in the prediction of clinical Coronary-Cerebral vascular events, especially in resource limited country like India [7,8].

## 2. MATERIALS AND METHODS

50 patients enrolled for study were explained the procedure and the purpose of the study and the informed consent were taken from the patients. Required physical examination and necessary investigations were done. Carotid Doppler was done in patient with type II DM. The examinations at baseline were performed on an Acuson 128 XP10 with a 7.5-MHz linear array probe (Acuson, Malvern, PA). The degree of carotid artery narrowing was obtained according to 6 categories, corresponding to NASCET (North American Symptomatic Carotid Endarterectomy Trial) angiographic graduation.

Serum HsCRP level were assessed using a modification of Behring Latex Enhanced CRPSA on the Behring Nephelometer analyser system with a 2% inter assay coefficient of variation.

### 2.1 Inclusion Criteria

1. Patient with history of Type 2 DM.

### 2.2 Exclusion Criteria

1. Patient with previous history of neck surgery or an invasive intervention of carotid artery.
2. Patient with history of any autoimmune or inflammatory disorder.

### 2.3 Data Analysis

Data collected using preformed data collection form and case record form. Data entry was done in Microsoft Excel and analyzed using SPSS (Statistical Package for Social Sciences) Software version 20. Student t test (Two tailed) was applied to find the significance of mean pattern of parameters in relation to macrovascular complication; Pearson correlation co-efficient was applied to find correlation between HsCRP and CIMT with  $p < 0.05$  as statistically significant value at 95% Confidence interval.

### 3. RESULTS AND DISCUSSION

In the present study, elderly age group with female preponderance was observed. Tables 1 and 2 show the distribution of study cases according to age and gender respectively.

**Table 1. Age distribution of study subjects**

Age Group	Frequency	Percent
41-50yrs	11	22.0
51-60yrs	13	26.0
61-70yrs	18	36.0
>70yrs	8	16.0
<b>Total</b>	<b>50</b>	<b>100.0</b>

**Table 2. Gender distribution of study subjects**

Gender	Frequency	Percent
Female	16	32.0
Male	34	68.0
<b>Total</b>	<b>50</b>	<b>100.0</b>

The study showed that hypertension was the most common co-morbid condition which was followed by dyslipidaemia. Stroke and IHD (Ischemic heart disease). Fig. 1 shows the distribution of study cases as per the co-morbid condition.

In the recruited study subjects, intima-media thickness (IMT) was the most common finding comprising of 42%. However, the number of study subjects with normal carotid doppler was

34%. Table 3 represents the data on Carotid Doppler study findings.

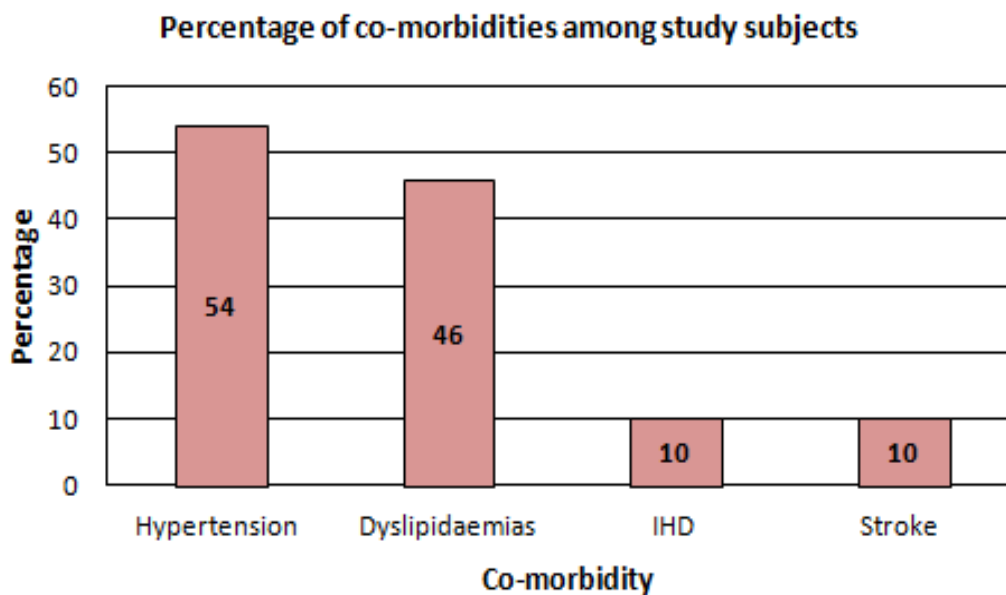
**Table 3. Carotid doppler findings among study subjects**

Carotid doppler	Frequency	Percent
<50% stenosis	8	16.0
>50% Stenosis	4	8.0
IMT	21	42.0
Normal	17	34.0
<b>Total</b>	<b>50</b>	<b>100.0</b>

Among the 50 subjects studied, the duration of diabetes in them and its association with carotid stenosis is evident from the table 4. While, table 5 denotes the association of HsCRP with carotid stenosis. Table 6 represents the data obtained on association of HsCRP with macrovascular complications.

The correlation of HsCRP with age, duration of DM and random Blood Sugar Level (BSL) is chalked out in the Table 7.

The track of exponential growth in the cases of the diabetes mellitus over the last decade is going to be continued in both developed and developing countries. Diabetes has a major socio-economic burden on the health sector, which if not controlled will have an adverse impact in a long run [1,2].



**Fig. 1. Percentage of co-morbidities among study subjects**

The timely treatment and regular follow up along with the screening for the diabetes related complication is meticulous to prevent adverse events in future.

The affirmation of our study is to detect the earlier changes in the carotid bed by using Duplex Carotid Ultrasound and to detect the ongoing slow but continuous inflammation using HsCRP levels [7,8,9].

The said study comprised of 50 subjects (M: F ratio 2.1:1) all being type 2 diabetics, maximum in the age group of 61-70 years with mean age of 60.54 +/- 9.06.

While among the study participants, most common comorbidity found was hypertension (54%) and dyslipidemia (46%) while ten percent each had ischemic heart disease and cerebrovascular accident as shown in Fig 1.

The data from duplex ultra sound substantiated that 16 % had carotid stenosis <50%, while 8% had carotid stenosis >50% and 42 % had intima-media thickness. While among carotid stenosis 87.5% (11/12) subjects were having age above

50 years of age. There was clinically significant association between carotid stenosis and increased age ( $P=0.0001$ ). While in contrast, there was no significant association between carotid stenosis and gender ( $P=0.074$ ).

The data tabulated in Table 4 shows, among diabetics with >10yrs duration 58.8% subjects were having carotid stenosis. There was significant association between carotid stenosis and increased duration of diabetes ( $P=0.0001$ ).

Furthermore, all subjects those were subjected to HsCRP testing, it was found that 26 participants had an elevated level of HsCRP above the normal biological range. While among the subjects who had an elevated HsCRP, 46.2% had carotid stenosis. Hence, there was significant association between carotid stenosis and HsCRP ( $P=0.0001$ ) as depicted in Table 5. On the other front, among ones who had a raised value of HsCRP, 38.5% having macrovascular complications of diabetes. Hence, there was significant association between macrovascular complications and raised HsCRP ( $P=0.014$ ) as shown in a Table 6.

**Table 4. Association of duration of diabetes with carotid stenosis**

Diabetes duration	Carotid stenosis		Total	P value
	Present	Absent		
5-10yrs	2 (6.1%)	31 (93.9%)	33	.0001
>10yrs	10(58.8%)	7(41.2%)	17	
<b>Total</b>	<b>12(24.0%)</b>	<b>38(76.0%)</b>	<b>50</b>	

**Table 5. Association of HsCRP with carotid stenosis**

HsCRP>3	Carotid stenosis		Total	P value
	Present	Absent		
Yes	12 (46.2%)	14 (53.8%)	26	.0001
No	0	24 (100.0%)	24	
<b>Total</b>	<b>12 (24.0%)</b>	<b>38 (76.0%)</b>	<b>50</b>	

**Table 6. Association of HsCRP with macrovascular Complications**

Hs CRP >3	Macrovascular complications		Total	P value
	Present	Absent		
Yes	10 (38.5%)	16 (61.5%)	26	.014
No	2 (8.3%)	22 (91.7%)	24	
<b>Total</b>	<b>12 (24.0%)</b>	<b>38 (36.0%)</b>	<b>50</b>	

**Table 7. Correlation of HsCRP with age, duration, BSL**

HsCRP	Age	Duration of DM	BSL®
Pearson Correlation	0.790	0.919	0.229
P value	0.0001	0.0001	0.109

It was also established that, there was strong correlation of HsCRP with age and duration of diabetes ( $r=0.79$  &  $0.919$ ) and this correlation was statistically significant ( $p=0.0001$ ), but there was mild correlation ( $r=0.229$ ) with BSL and that was not statistically significant ( $p=0.109$ ) as shown in Table 7. Comparing our study with study conducted by S Lehto, T Rönnemaa et al [10] which concluded that positive correlation of dyslipidaemia, addiction, hypertension, age factor, over-weight is responsible for elevated inflammatory markers like HsCRP. While similar outcome was derived in our study too.

Another study conducted in 2019 by T. Doraickannu, T. Sechassayana et al [11] which established the similar fact that 'tight' glycemic control is of paramount importance to cease an ongoing slow inflammatory process. The study has concluded that on HbA1C value on 1<sup>st</sup> day and after 6 months were  $8.088 + 1.219$  and  $7.518 \pm 0.693$  respectively., whereas the values of the HsCRP was  $2.508 + 1.050$  on 1<sup>st</sup> day and  $2.15 + 0.927$  after 6 months. The study substantiates that, there is a significant positive correlation between strict glycemic control and its effect on the current ongoing inflammation, thus being and directly proportional entity. While similar correlation was endorsed in our study where table 6 shows that 24 % had a macrovascular complication of diabetes among the study subject i.e.; 12 subjects. While table no 5 states that those developed carotid stenosis has an elevated HsCRP and having  $P = 0.0001$ . Thus there was a significant association between carotid stenosis and HsCRP.

While comparing our study with Shriram G et al [12] which investigated HsCRP and HbA1c concluded that the mean HsCRP level in type 2 DM was elevated as compared to normal healthy person. Similar positive correlation was also found in our study in about 52% subjects. While according to Deepak et al,[13] HsCRP is an independent marker of cardiovascular diseases (CVD). They found an association between HsCRP and DM, metabolic syndrome and CAD. They found that standardized HsCRP assays with adequate follow up duration are required to derive risk cut-off values for CVD in the Indian perspective. While our study also has similar perspective. Similar out-come was also seen in the study conducted by Asegaonkar S et al.[14] and Mishra DP et al .[15].

The observational cohort study by Wagenknecht LE, Zaccaro D et al [16]; known as The Insulin

Resistance Atherosclerosis Study, concluded that those with greater duration and more impaired glucose intolerance have more tendency to develop carotid intimal thickness. While similar outcome was also noted in our study.

An Intervention project on cerebrovascular diseases and dementia in the district of Ebersberg (INVADE) study by Sander D, Schulze-Horn C et al [17]; concluded that duplex combo of chronic hyperglycemia as suggested by HbA1c and ongoing inflammatory process as evident by pronounced increased in HsCRP levels, elevates the risk of development of CIMT and its progression and new onset of major cardio-cerebrovascular events. Similar conclusion was drawn from our study too.

A study by Van Der Meer IM, De Maat MP et al [18]; also known as Rotterdam study concluded that CRP envisage the progressive atherosclerosis at various arterial tress site. Similar outcome was also noted in our study group.

#### 4. CONCLUSION

From the study data, it is concluded that duration of the diabetes along with the age of subject is an important risk factor for the development of diabetes related complications like ischemic heart disease and cerebrovascular accident etc. Carotid doppler in our study showed high percentage of carotid artery disease (66%) in asymptomatic type 2 diabetes mellitus. While Positive linear correlation between HsCRP, age and duration of diabetes concludes that HsCRP levels are elevated in chronic diabetics warns the risk of future macro and micro vascular complications among diabetics.

#### CONSENT

All authors declare that written informed consent was obtained from all the participants.

#### ETHICAL APPROVAL

All authors hereby declare that the study was approved by the Institutional ethics sub-committee of Dr. D. Y. Patil Medical College, Hospital & Research Centre, Pimpri. (IESC/136/2019).

## ACKNOWLEDGEMENTS

Authors acknowledge the department of Radiology for the support provided for the carotid doppler study.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Alvin C. Power, Kevin D. Niswender. Chapter 396, page no 2850-2882. In: Harrison's Principles of Internal Medicine. 20th edition. Vol 2. New York: McGraw-Hill Education; 2018;2850.
2. Joshi SR Page No 285-420 RSSDI Textbook of Diabetes Mellitus page no. 4<sup>th</sup> Edition; Jaypee Brothers Publication.2020.
3. Fowler MJ. Microvascular and Macrovascular Complications of Diabetes. *Clinical Diabetes Apr* 2008;26 (2):77-82.  
DOI: 10.2337/diaclin.26.2.77
4. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. *JAMA*. 2002;287:2570-2581
5. Boyle PJ. Diabetes mellitus and macrovascular disease: mechanisms and mediators. *Am J Med*. 2000;7120:S12-S17.
6. Heidenreich PA, Trogon JG, Khavjou OA, et al. Forecasting the future of cardiovascular disease in the United States: A policy statement from the American Heart Association. *Circulation*. 2011;123:933–944.  
[PubMed: 21262990]
7. Lima LM, Carvalho M, Soares AL. High-sensitivity C-reactive protein in subjects with type 2 diabetes mellitus and/or high blood pressure. *Arq Bras Endocrinol Metabol*. 2007;51(6):956-60.
8. Duncan BB, Schmidt M, Pankow JS. Low grade systemic inflammation and the development of type 2 diabetes. *Diabetes*. 2003;52(7):1799-805.
9. 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. *J Clin Endocrinol Metab*. 2009 ;94:2123–7.
10. Lehto S, Ronnema T, Pyorala K, Laakso M: Predictors of stroke in middle-aged patients with non-insulin-dependent diabetes. *Stroke*. 1996;27:63-68.
11. Doraickannu T, Sechassayana T, Vithiavathi S, Varisali M. Study of highly sensitive C-reactive protein in type 2 diabetes mellitus and prediction of cardiovascular risk with glycemic status. *Int J Adv Med*. 2019;6:687-90.
12. Shriram G and Keerthika E. Association of high sensitivity C reactive protein and Glycemic status with type 2 Diabetes mellitus. *J. Pharm. Sci. & Res*. Vol. 12(6), 2020, 836-839
13. Deepak Y, Denis X, Alben S. High sensitivity C-reactive protein and cardiovascular disease: An Indian perspective. *Indian J Med Res*. 2015;142:261-8
14. Asegaonkar S, Marathe A, Tekade M, Cherekar L. High-sensitivity C-reactive protein: a novel cardiovascular risk predictor in type 2 diabetics with normal lipid profile. *J Diab Complic*. 2011;25:368-70.
15. Mishra DP, Das S, Sahu P. Prevalence of inflammatory markers (high-sensitivity C-reactive protein, nuclear factor- $\kappa$ B, and adiponectin) in Indian patients with type 2 diabetes mellitus with and without macrovascular complications. *Meta Syndr Relat Dis*. 2012;10:209-13.
16. Wagenknecht LE, Zaccaro D, Espeland MA, Karter AJ, O'Leary DH, Haffner SM. Diabetes and progression of carotid atherosclerosis: the insulin resistance atherosclerosis study. *Arterioscler Thromb Vasc Biol*. 2003;23(6):1035-41.  
DOI:10.1161/01.ATV.0000072273.67342.6D. Epub 2003 Apr 17.  
PMID: 12702517.
17. Sander D, Schulze-Horn C, Bickel H, Gnahn H, Bartels E, Conrad B. Combined effects of hemoglobin A1c and C-reactive protein on the progression of subclinical carotid atherosclerosis: the INVADE study. *Stroke*. 2006;37(2):351-7.  
DOI:10.1161/01.STR.0000199034.26345.bc.  
Epub 2005 Dec 22.  
PMID: 16373634.
18. Van Der Meer IM, De Maat MP, Hak AE, Kiliaan AJ, Del Sol AI, Van Der Kuip DA, Nijhuis RL, Hofman A, Witteman JC. C-reactive protein predicts progression of atherosclerosis measured at various sites

in the arterial tree: the Rotterdam Study.  
Stroke. 2002;33(12):2750-5.

DOI:10.1161/01.str.0000044168.00485.02  
. PMID: 12468765.

---

© 2021 Gokhale et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:*  
<https://www.sdiarticle5.com/review-history/81352>