

Study the association of the cardiac risk indices and high sensitive C-reactive protein for Type 2 diabetes patients in tertiary care hospital, Puducherry



Suresh Pichandi¹, Janakiraman P², Muraliswaran P³, Prabhu G⁴

¹Associate Professor, ³Professor and Head, Department of Biochemistry, Sri Venkateshwaraa Medical College and Research Center, Puducherry, India, ²Tutor in Statistics, Department of Community Medicine, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India, ⁴Professor, Department of General Medicine, Sri Venkateshwaraa Medical College and Research Center, Puducherry, India

Submission: 14-02-2022

Revision: 26-06-2022

Publication: 01-08-2022

ABSTRACT

Background: Diabetes mellitus (DM) is a metabolic disorder with hyperglycemia. Dyslipidemia associated with DM patient and contributing to atherosclerotic events and increases the likelihood of cardiovascular disease (CVD) in future. Measurement of inflammatory marker like hs-CRP will improve the prediction of the risk of these events. This study aimed to assess the cardiac risk indices and determine their association with hs-CRP in diabetic patients. **Aims and Objectives:** This study is aimed to assess the association of the cardiac risk indices and hs-CRP in diabetic patients. **Materials and Methods:** This study included each 125 subjects of Type 2 diabetic patients and healthy control. The anthropometric parameters (BMI and WHR) and blood parameters such as fasting glucose, glycosylated hemoglobin (HbA1c), lipid profile (total cholesterol, TGL, HDL, and LDL), hs-CRP, and microalbumin were measured. Cardiac risk indices calculated from lipid profile. **Results:** High cardiac risk indices were observed in diabetic subjects. The cardiac risk indices were showed that significant positive correlation with BMI, fasting sugar, HbA1c, total cholesterol, TGL, LDL and HDL shows negative correlation. Furthermore, hs-CRP and microalbumin showed significant positive correlation with cardiac risk indices in Type 2 DM patients. **Conclusion:** The increased in values of cardiac risk indices in diabetic patients shows increasing the susceptibility of CVD in these patients in future. The correlation of indices values with hs-CRP (inflammatory marker) shows the direct association of inflammation with CVD risks in Type 2 DM patients. Screening of these indices among diabetic patients will help the propensity of future development of CVD which can be arrested by encouragement of healthy lifestyle.

Keywords: Diabetes mellitus; Cardiac risk indices; High-sensitive C-reactive protein; Cardiovascular disease; Dyslipidemia

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v13i8.43138

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2022 Asian Journal of Medical Sciences



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia with disturbances of metabolism of carbohydrate, protein, lipid, and resulting of defects in pancreatic insulin secretion, insulin action, or both.¹ The most common form of diabetes is Type 2 DM. The Type 2 DM prevalence is increasing in all populations worldwide.

It is a major risk factor for various nonfatal complications and death.

DM worldwide prevalence is 9.2% in 2020 and Indian prevalence is 8.9.² India is one of the seven countries of the Indian Diabetic Federation South East Asian (IDF SEA) region. A total of 463 million people have diabetes in the world and 88 million people in the SEA Region; by 2045,

Address for Correspondence:

Dr. Suresh Pichandi, Associate Professor, Department of Biochemistry, Sri Venkateshwaraa Medical College Hospital and Research Centre and Research Centre, Puducherry - 605 102, India. **Mobile:** +91-9894421782. **E-mail:** suresh.chanth82@gmail.com

this will rise to 153 million.² India will be diabetic capital due to diabetes incidence is surging rapidly.³

Dyslipidemia condition is associates with diabetes patient. It is contributing to atherosclerotic events and increases the likelihood of cardiovascular disease (CVD) in future.⁴ Diabetes and pre-diabetes act as major risk factors for CVDs. Diabetes patients CVD mortality is 70% and the risk of CVD mortality increases by 2–4 times for diabetic patients when compare with healthy controls.⁵

Inflammation plays a role in the pathogenesis of cardiovascular events and measurement of inflammatory markers will improve the prediction of the risk of these events. High-sensitive C-reactive protein is the most reliable marker of cardiovascular inflammation.⁶ To improve cardiovascular health in diabetic patients and reduce the rate of mortality, new and easily approachable techniques are identified. To optimize the predictive capability of CV risks, the various cardiac risk indices have been made from the parameters of lipid profile.⁷

The names of cardiac risk indices are atherogenic index (AI) which is LDL-to-HDL ratio, cardiac risk ratio (CRR) which is the ratio of total cholesterol to HDL, atherogenic coefficient (AC) that is a ratio of non HDL cholesterol to HDL, and AI of plasma (AIP) which is log of ratio of TG to HDL.⁸ In diabetes patient, inflammation is the main cause which leads to hyperglycemia and associated complications. Indian scenario results show that there is a paucity of studies on association of atherogenic indices with inflammatory markers. Thus, in this study, it is aimed to assess the cardiac risk indices and determine their association with hs-CRP in diabetic patients.

Aims and objectives

This study is aimed to assess the association of the cardiac risk indices and high-sensitive CRP in diabetic patients of tertiary care hospital, Puducherry. This study will help the Puducherry specific DM patients cardiac risk indices range and more useful for the treatment of DM patients attend in our hospital, especially company worker with DM.

MATERIALS AND METHODS

In this study, the samples were collected from the patients attending in medicine OPD and diabetic clinic in Sri Venkateshwaraa Medical College Hospital and Research Centre, Ariyur, Puducherry.

Inclusion criteria

The patients with Type 2 diabetes included in this study probably on above age of 30 years diabetes patients.

Exclusion criteria

Patients with Type 1 diabetes, cardiac diseases, pulmonary diseases, renal diseases, hepatic diseases, malignancies, and any other conditions that may alter the levels of inflammatory markers will be excluded from the study.

Study design

A case–control study and purposive sampling (hospital based) method used with random sampling technique.

Sample size calculation

Sample size calculated based on previous article DM prevalence 8.9%.

DM – 125 patients and control – 125 age- and sex-matched healthy people,

sample size calculated based on the formula

$$n = Z^2 X p(1-p) / d^2$$

(Diabetes prevalence: 8.9% [2], confidence interval: 95%, margin of error: 5%)

This study got approved by the Institutional Ethics Committee. We have used total 250 samples that include 125 Type 2 DM patients and 125 age-matched normal adults based on our sample size calculation. Basic details of each participant (age, gender, and BMI) will be recorded. Fasting blood sample (FBS) will collected for quantification of fasting sugar, glycosylated hemoglobin (HbA1c), lipid profile (cholesterol, HDL, and triglyceride [TG]), hs-CRP, and urine microalbumin.

Serum after separation will stored at –20°C till analysis. HbA1c is assayed in the whole blood. Biochemical parameters measured by Siemens Dimension EXL 200 fully autoanalyzer. Standard kit-based methods will be used for the estimation of biochemical parameters as follows:

- FBS: Hexokinase method
- HbA1c: Immunoturbidimetric method
- Cholesterol (CHO): Cholesterol oxidase-peroxidase method
- HDL: Direct method
- LDL cholesterol: Direct method
- TG: GPO-PAP method
- hs-CRP: Immunoturbidimetric method
- Microalbumin: Immunoturbidimetric method

Calculation of cardiac risk indices/atherogenic indices will be done as follows:⁹

- CRR = Total cholesterol/HDL
- AI = LDL/HDL
- AC = (Total cholesterol – HDL)/HDL
- AIP = Log (TG/HDL).

Statistical analysis

The data will be collected, recorded and analyzed statistically to determine the significance of different parameters using SPSS package for Windows version 23.0. Quantitative characteristics will be summarized by arithmetic mean and standard deviation. The differences in the anthropometric and biochemical parameters are compared using t-test. The association will be determined by Pearson’s correlation coefficient. The difference in level and association is considered statistically significant if $P < 0.05$.

RESULTS

The diabetic subject age was 49.50 ± 10.60 that significantly higher than the control group age (40.17 ± 7.76) (Table 1). The BMI and WHR for diabetic subjects result show significantly high values compare with the control group (Table 1). The FBS and HbA1c values were high in the diabetes group compared to the control group and analysis shows statistical significance (Table 2). Similarly, diabetic patients had significantly high cholesterol and LDL values compared to the control group. Further HDL, the values were significantly low in the diabetic group compared to control. The TG value was significantly high in diabetic patients compared to control (Table 2).

Diabetic patients had significantly high cardiac risk indices compared to controls (Table 3). Further, hs-CRP and microalbumin values were significantly high in diabetic individuals compared with the control group (Table 3). The correlation result is shown in Table 4 of cardiac indices (CRR, AI, AC, and AIP) with basic parameters and hs-CRP, microalbumin of diabetic individuals. There was positive correlation between cardiac risk indices; basic parameters such as BMI, fasting sugar, HbA1c, cholesterol, HDL,

TGL, and LDL were observed but HDL result shows negative correlation for diabetic group. Similarly, hs-CRP and microalbumin also shown positive correlation for diabetic patients (Table 4).

DISCUSSION

DM always leads to lipid abnormalities. DM patients are associated with CVD risks and that further aggregated by the presence of dyslipidemia and inflammatory pathophysiological alterations. CVD is the main cause of mortality in DM patients. Early management of dyslipidemia and improvement in dearranged inflammatory state aid will prevent the atherogenic cardiovascular complications and mortality rate in DM patients.

Therefore, earlier detection of cardiovascular risk in diabetic patients can reduce the CVD associated mortality rate. There were several techniques have been developed to predict the cardiovascular risk in diabetic patients. The cardiac risk indices, namely, CRR, AI, AC, and AIP are economically reliable and most authentic technique measures with high predictive capabilities. This study was started to determine the possible link between cardiac risk indices, hs-CRP, and microalbumin and their role in the development of CVD in patients with DM.

The cardiac risk indices were elevated significantly in diabetic patients compared to the control group. In this study, DM patients indices CRR, AI, AC, and AIP values were 4.55 ± 0.97 , 2.97 ± 0.75 , 3.55 ± 0.97 , and 0.50 ± 0.23 . Similar to our study, Shrestha et al.,¹⁰ reported CRR (4.2), AI (2.7) and AC values (3.3), and AIP (0.4). In this study, significantly high values of cholesterol, TGL, and LDL were observed in the DM patient groups while the level of HDL was significantly low. In this present study, reports show that the presence of dyslipidemia, a major cause of CVD, in the DM patients involved was documented. Our study results were in accordance with the previous study results.^{11,12}

Cardiac risk indices are considered more specific and sensitive marker for the prediction of cardiovascular risk when compared to the individual lipid parameters. Similar

Table 1: Comparison basic parameters in the control and diabetic groups

Parameters	Control	Diabetes	P-value
Age (years)	40.17±7.76	49.50±10.60	<0.001**
BMI	23.52±3.74	26.35±5.46	<0.001**
WHR	0.81±0.12	0.92±0.12	<0.001**

Statistically significant: *→ $P > 0.05$ **→ $P < 0.01$

Table 2: Comparison basic parameters in the control and diabetic groups

Parameters	Control	Diabetes	P-value
FBS	73.25±8.17	195.23±67.82	<0.001**
HbA1c	4.25±0.14	7.89±1.49	<0.001**
Cholesterol	175.27±33.06	190.13±44.42	0.005**
TGL	110.99±62.17	183.46±84.02	<0.001**
LDL-C	115.96±29.69	125.01±36.98	0.041*
HDL-C	45.6±9.15	42.44±8.28	0.013*

Statistically significant: *→ $P > 0.05$ **→ $P < 0.01$

Table 3: Comparison cardiac risk indices parameters in the control and diabetic groups

Parameters	Control	Diabetes	P-value
CRR	3.99±1.07	4.55±0.97	<0.001**
AI	2.65±0.87	2.97±0.75	0.004**
AC	2.99±1.07	3.55±0.97	<0.001**
AIP	0.35±0.25	0.50±0.23	<0.001**
hs-CRP	1.09±0.45	2.99±2.62	<0.001**
Microalbumin	13.20±7.45	49.56±14.45	<0.0001**

Statistically significant: *→ $P > 0.05$ **→ $P < 0.01$

Table 4: Correlation of cardiac risk indices with basic parameters in the diabetic groups

Parameters	Age (r)	BMI (r)	FBS (r)	HbA1c (r)	Cholesterol (r)	TGL (r)	HDL (r)	LDL (r)	hs-CRP (r)	MA
CRR	0.04	0.19*	0.31*	0.29*	0.79**	0.56**	-0.67**	0.54**	0.28*	0.20*
AI	0.03	0.22*	0.28*	0.21*	0.70**	0.35**	-0.57**	0.75**	0.23*	0.19*
AC	0.04	0.24*	0.29*	0.20*	0.59**	0.56**	-0.67**	0.54**	0.22*	0.20*
AIP	0.14*	0.30*	0.27*	0.30*	0.47**	0.89**	-0.61**	0.44**	0.25*	0.23*

Statistically significant: *→P>0.05 **→P<0.01

to this study, Shrestha et al.,¹⁰ also reported high cardiac risk indices diabetic patients suggesting increased CVD risks in future. In DM, patients have both hyperglycemia and associated CVD which are linked with inflammatory mechanisms. Hence, in this study, correlation of cardiac risk indices with inflammatory mediator (hs-CRP) and microalbumin was also assessed. hs-CRP and microalbumin showed significant positive correlation with cardiac risk indices in diabetic patients.

The cardiac risk indices were also significantly correlated with basic parameters. The correlation was negative with HDL and positive with other parameters (BMI, fasting sugar, HbA1c, cholesterol, TG, and LDL).^{13,14} The previous studies have also reported significant positive correlation between CRR, AI, AC, and AIP with age, BMI, fasting sugar, HbA1c, and lipid parameters.^{10,15}

Limitations of the study

This study has some limitation and it is hospital based study and sample size is small. Large sample required community-based assessment. Other inflammatory markers need to be studied with larger sample size in diabetes mellitus.

CONCLUSION

Uncontrolled diabetes always leads to lipid abnormalities. The altered cardiac risk indices and their significant association with inflammatory marker signify the direct association of inflammation with CVD risks. Thus, there is a requirement of novel approaches that can retard inflammatory responses and arrest unwanted cardiac health outcomes. Cardiac risk indices can be generated simply by measuring the level of lipid parameters (total cholesterol, TGL, LDL and HDL). They are the most reliable and economic method for screening compare than other expensive laboratory methods like apolipoproteins estimation. Screening of these indices among diabetic patients will help the propensity of future development of CVD which can be arrested by encouragement of healthy lifestyle.

In this study, we found increased values of cardiac risk indices in diabetic patients and these may increase the susceptibility of CVD of the patients in future. These

indices were also correlating significantly with the inflammatory mediators such as hs-CRP and microalbumin. It is recommended that screening must be conducted among diabetic patients so that through the encouragement of healthy lifestyle or pharmaco therapy, we can prevent the propensity of future development of CVD. It not only improves cardiac risk factors but increase of cardio protective molecules level and also decrease thrives cardiovascular risks.

ACKNOWLEDGMENT

The authors thank faculty and staff members of general medicine unit and department of biochemistry who have helped us for this work.

REFERENCES

- Kahn CR, King GL, Weir GC, Jacobson AM, Moses AC and Smith RJ. Joslins Diabetes Mellitus. 14thed. New York: Lippincott Williams and Wilkins; 2005. p. 331-338.
- Members. Available from: <https://idf.org/our-network/regions-members/south-east-asia/members/94-india.html> [Last accessed on 2020 Apr 29].
- Tandon N, Anjana RM, Mohan V, Kaur T and Afshin A. The increasing burden of diabetes and variations among the states of India: The global burden of disease study. 1990-2016. *Lancet Global Health*. 2018;6(12):e1352-e1362. [https://doi.org/10.1016/S2214-109X\(18\)30387-5](https://doi.org/10.1016/S2214-109X(18)30387-5)
- Kansal S and Kamble TK. Lipid profile in prediabetes. *J Assoc Physicians India*. 2016;64(3):18-21.
- Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies. *Lancet*. 2010;375(9733):2215-2222. [https://doi.org/10.1016/S0140-6736\(10\)60484-9](https://doi.org/10.1016/S0140-6736(10)60484-9)
- Pradhan AD, Manson JE, Rifai N, Buring JE and Ridker PM. C-reactive protein, interleukin 6, and risk of developing Type 2 diabetes mellitus. *JAMA*. 2001;286(3):327-334. <https://doi.org/10.1001/jama.286.3.327>
- Balgi V, Harshavardan L, Sahna E and Thomas SK. Pattern of lipid profile abnormality in subjects with prediabetes. *Int J Sci Study*. 2017;4(11):150-153. <https://doi.org/10.17354/ijss/2017/67>
- Bafna A, Maheshwari RS, Ved RK, Sarkar PD and Batham AR. Study of atherogenic indices in nephritic syndrome. *Int J Biol Med Res*. 2012;3(3):2257-2260.
- Bhardwaj S, Bhattacharjee J, Bhatnagar MK and Tyagi S.

- Atherogenic index of plasma, castelli risk index and atherogenic coefficient-new parameters in assessing cardiovascular risk. *Int J Pharm Bio Sci.* 2013;3(3):359-364.
10. Shrestha S, Sharma P, Kumar P and Prasad M. A study on the lipid ratios and inflammatory markers in pre-diabetic and diabetic patients. *Int J Res Med Sci.* 2019;7(9):3452-3460.
<http://dx.doi.org/10.18203/2320-6012.ijrms20193928>
 11. Farid SM. Gender-related differences in lipid profile and atherogenic indices in patients with Type 2 diabetes mellitus in Jeddah, Saudi Arabia. *Glob J Bio Sci Biotechnol.* 2017;6(3):430-438.
 12. Mahat R, Singh N, Rathore V, Gupta A and Shah R. Relationship between atherogenic indices and carotid intima-media thickness in prediabetes: A cross-sectional study from Central India. *Med Sci.* 2018;6(3):E55.
<https://doi.org/10.3390/medsci6030055>
 13. Nimmanapalli HD. Lipid ratios, atherogenic coefficient and atherogenic index of plasma as parameters in assessing cardiovascular risk in Type 2 diabetes mellitus. *Int. J Res Med Sci.* 2016;4(7):2863-2862.
<http://dx.doi.org/10.18203/2320-6012.ijrms20161966>
 14. Juarez-Perez CA, Madrid GA, Haro-Garcia LC, Gopar NR, Cabello LA, Jimenez RC, et al. Increased cardiovascular risk using atherogenic index measurement among healthcare workers. *Arch Med Res.* 2015;46(3):233-239.
<https://doi.org/10.1016/j.arcmed.2015.03.002>
 15. Akdogan M, Budak YU and Huysal K. The association of hematologic inflammatory markers with atherogenic index in Type 2 diabetic retinopathy patients. *Clin Ophthalmol.* 2016;10(317):1797-1801.
<https://doi.org/10.2147/OPHTH.S110749>

Authors Contribution:

SP– Concept and design of the study, prepared first draft of manuscript; **JP** – Statistical analysis and table preparations; **MP**–Manuscript editing and revision of the manuscript; and **PG**– Patient history and data collection.

Work attributed to:

Sri Venkateshwaraa Medical College and Research Center, Puducherry - 605 102, India

Orcid ID:

Dr. Suresh Pichandi - <https://orcid.org/0000-0002-9254-5774>

Janakiraman P - <https://orcid.org/0000-0002-5802-8861>

Dr. Muraliswaran P - <https://orcid.org/0000-0001-9200-2617>

Dr. Prabhu G - <https://orcid.org/0000-0002-1357-7576>

Source of Funding: Nil, **Conflicts of Interest:** None declared.