Zagazig University Medical Journal
www.zumj.journals.ekb.eg

ORIGINAL ARTICLE

# Contribution of Non Traditional Cardiovascular Risk Factors to the Cardiovascular Disease in Patient with Type 2 Diabetes

**Mohamed Hossam El-Shaer [1], Mohamed Mostafa El-Daydamony[1)], Alaa El-Sayed Salama[1] and Huda Abdelrhman Ammar Al Trabulsi[2*]**

[1] *Cardiology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt*
[2] *Cardiology Department, Faculty of Medicine, Benghazi University, Benghazi, Libya*

***:** Huda Abdelrhman Ammar Al Trabulsi
*Department of Cardiology, Faculty of Medicine, Benghazi University, Libya*
hudaeltrabelsi@gmail.com

| | |
|---|---|
| Submit Date | 2019-05-27 |
| Revise Date | 2019-07-16 |
| Accept Date | 2019-07-17 |

## ABSTRACT

**Background:** T2DM is a major risk factor for heart failure, peripheral arterial insufficiency and microvascular complications, affecting life quality and expectancy. Diabetes also increases coronary death rates conferring the patient a worst prognosis after having the first CHD event. The mortality rate in non-diabetic patients was less compared to diabetic patients who experienced CHD. The objective was to study the association of nontraditional risk factors with incidence of coronary heart disease in Patient with Type 2 Diabetes. **Methods:** Our study had been carried out in cardiology department, Zagazig University from April 2017 to December 2017. The study included 105 patients divided into 3 groups; they were young and middle aged subjects selected conveniently according to specified groups (normal control group, diabetic control group without history of coronary artery disease and ischemic heart disease group with history of coronary artery disease. History and physical examinations were recorded and laboratory tests were performed for all patients. **Results:** showed that there ws a statistical significant difference regarding Diastolic dysfunction, Ventricular hypertrophy, Uric acid, Serum hsCRP, Serum fibrinogen and Homocystein in T2DM patients group. **Conclusions:** Cardiovascular risk factors were higher in subjects with diabetes compared to subjects without diabetes, Non-traditional cardiovascular risk factors may be related independently to incident coronary heart disease in T2DM patients.

**Keywords:** Cardiovascular disease; Type 2 Diabetes; Risk Factors

## INTRODUCTION

Cardiovascular disease (CVD) is the major cause of morbidity and mortality for individuals with diabetes and is the largest contributor to the direct and indirect cost of diabetes. Risks of incidence from CAD or fatal CAD are two to fourfold higher in people with DM than in those without. Furthermore, long-term prognosis after a coronary event is significantly worse among people with DM than those without [1].

Diabetes mellitus is associated with a markedly increased risk of cardiovascular mortality compared with the risk in people without diabetes, and CVD is a major cause of death. Thus control of CVD risk factors is an important priority that must be considered in diabetes health programs [2].

It has been reported that patients with type 2 diabetes and no previous history of CAD have the same risk for cardiac events as patients with a prior myocardial infarction, due to the association between type 2 diabetes with cardiovascular risk factors (CRFs) [3].

Duration of diabetes is a key determinant of cardiovascular and CHD risk in diabetes. Patients with diabetes duration longer

than 10 years can be considered in particular increased risk [4]

However, recently in the study of Evans et al. [5], a cross-sectional and cohort study using routinely collected datasets, patients with type 2 diabetes were at lower risk of cardiovascular outcomes than patients with established coronary heart disease.

Reduction of cardiovascular risk in T2DM is thus paramount. Evidence suggests that in patients with T2DM, treatment of cardiovascular risk factors is very important in reducing the risk of cardiovascular disease (CVD). The poor control of risk factors observed in the diabetic population supports the need for more aggressive treatment of modifiable cardiovascular risk factors, especially in patients with previous CVD **[6]**.

## METHODS

This study was carried out on patients attending outpatient clinic and the 105 inpatient department of Cardiology of Zagazig University Hospitals along the duration between April 2017 and the end of 2017. This study included 105 patients, Data were collected with review of records and interview for selected individuals in cardiology department

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Patients were divided into 3 groups:**

**Normal control group:** individuals selected from general population without diabetes or history of coronary artery disease.

**Diabetic control group:** diabetic individuals selected without history of coronary artery disease.

**Ischemic heart disease group:** diabetic individuals selected with history of coronary artery disease.

**Exclusion criteria :**

We excluded from the study patients with Type –I DM, History of diabetic ketoacidosis. Patients with advanced liver or renal disease or malignancy were excluded from the study.

**Clinical examinations**

A complete history was taken for duration of DM, family history of CVD and personal history of hypertension and hyperlipidaemia and treatments used. Clinical examinations included weight, height, blood pressure, fundoscopy and peripheral pulse assessment. A 12-lead resting electrocardiogram (ECG) was taken from all patients. Patients with baseline ECG changes suggestive of CHD, previous history of myocardial infarction, angina, coronary artery bypass graft, angioplasty, treatment for CVD, cerebrovascular accident, transient ischaemic attack, carotid surgery and peripheral vascular disease or absence of peripheral pulse were defined as symptomatic CVD.

**Characteristics of diabetes:** Include duration of diabetes, insulin treatment, oral hypoglycemic agents, glycated hemoglobin (HbA1c%) and fasting blood glucose level (FBG).

**Variables of the study:**

Non traditional risk factors: include Diastolic dysfunction, Ventricular hypertrophy, high sensitivity C-reactive protein (HsCRP), homocysteine (Hcy), serum fibrinogen and microalbumin in urine.

**Data collection, processing:**

Data were collected manually according to variables of the study mentioned above in a hard data sheet, then data entry was made according to a unified code. The source of data were obtained from the hospital records and the patients file.

**Statistical Analysis:**

Data were collected, tabulated and analyzed by SPSS 20, software for Windows. The significance level was set at $P < 0.05$.

## RESULTS

Table (1), showed that the rate of diastolic dysfunction was highest among cases of IHD (62.9%) and lowest among cases without IHD. There was statistically significant

relation between dystolic dysfunction and IHD. P (0.001). Table (2), showed that the ventricular hypertrophy rate was highest among cases of IHD (60%) and zero among controls. There was statistically significant relation between ventricular hyperatrophy and IHD. Table (3), showed that the FBG were significantly different between diabetic without IHD and patients with IHD (132 and 167 mg/dl) p (0.27) and Rates of FBG>110 mg/dl were the same between the two groups. Table (4), showed that the HsCRP are higher in the diabetics with IHD compared to the controls and diabetics without IHD. However the levels of HsCRP are significantly between three group (p<0.001). Table (5), showed that the homocysteine are significantly higher in the diabetics with IHD compared with other group . were significantly different between two group (diabetic with IHD and diabetic without IHD) (p>0.001). Table (6), showed that the median of the Fibrinogen level are higher in the diabetics with IHD compared to the controls and diabetics without IHD. However the levels of Fibrinogen are significantly between three group (p<0.001). Table (7), showed that the microalbumin level are higher in the diabetics with IHD compared to the controls and diabetics without IHD. However the levels of Microalbamin are significantly between three group (p<0.001).

**Table (1).** Diastolic dysfunction across the study groups

| Study group | Diastolic dysfunction | | Total | χ2 (*P*) |
|---|---|---|---|---|
| | Yes | No | | |
| Controls | 0 | 35 | 35 | 29.432 (0.001) Significant |
| | 0.0% | 100.0% | 100.0% | |
| Diabetics | 10 | 25 | 35 | |
| | 28.6% | 71.4% | 100.0% | |
| Diabetics with IHD | 22 | 13 | 35 | |
| | 62.9% | 37.1% | 100.0% | |

**Table (2).** Ventricular hypertrophy across study groups

| Study group | Ventricular hypertrophy | | Total | χ2 (*P*) |
|---|---|---|---|---|
| | Yes | No | | |
| Controls | 0 | 35 | 35 | 35.0 (0.001) Significant |
| | 0.0% | 100.0% | 100.0% | |
| Diabetics | 6 | 29 | 35 | |
| | 17.1% | 82.9% | 100.0% | |
| Diabetics with IHD | 21 | 14 | 35 | |
| | 60.0% | 40.0% | 100.0% | |

**Table (3).** FBG parameters acrossstudy groups; in mg/dL

| Study group | Min. | Max. | mean | 95% CI | | MW-U (*P*) |
|---|---|---|---|---|---|---|
| | | | | Lower | Upper | |
| Diabetics | 87.0 | 311.0 | 132,54 | 120.0 | 170.0 | 800.5 (0.027) Significant |
| Diabetics with IHD | 93.0 | 345.0 | 167.45 | 147.0 | 233.0 | |

CI = confidence interval for mean, MW-U= Mann-Whitney U test

**Table (4.)** Serum hs CRP parameters across study groups

| Study group | Min. | Max. | mean | 95% CI | | KW (*P*) |
|---|---|---|---|---|---|---|
| | | | | Lower | Upper | |
| Controls | 0.0 | 2.7 | 0.8 | 0.6 | 1.0 | 13.498 (0.001) Significant |
| Diabetics | 0.6 | 3.0 | 1.2 | 1.0 | 1.6 | |
| Diabetics with IHD | 0.0 | 7.6 | 1.3 | 1.0 | 2.0 | |

CI = confidence interval for mean, KW= Kruskal Wallis test.

**Table (5).** Serum homo-cysteine parameters across study groups

| Study group | Min. | Max. | Mean | 95% CI | | KW (*P*) |
|---|---|---|---|---|---|---|
| | | | | Lower | Upper | |
| Controls | 5.6 | 14.3 | 8.3 | 7.1 | 9.0 | 12.766 (0.002) Significant |
| Diabetics | 5.0 | 16.0 | 8.8 | 7.7 | 10.0 | |
| Diabetics with IHD | 6.2 | 24.0 | 10.2 | 9.0 | 12.0 | |

CI = confidence interval for mean, KW= Kruskal Wallis test.

**Table (6).** Serum fibrinogen parameters across study groups; in g/L

| Study group | Min. | Max. | mean | 95% CI | | KW (*P*) |
|---|---|---|---|---|---|---|
| | | | | Lower | Upper | |
| Controls | 2.3 | 4.2 | 3.1 | 2.9 | 3.3 | 19.721 (<0.001) Significant |
| Diabetics | 2.1 | 4.3 | 3.6 | 3.4 | 3.8 | |
| Diabetics with IHD | 2.8 | 6.3 | 3.7 | 3.6 | 4.0 | |

CI = confidence interval for mean, KW= Kruskal Wallis test.

**Table (7).** Urine micro albumin parameters across study groups; in mg/dL

| Study group | Min. | Max. | mean | 95% CI | | KW (*P*) |
|---|---|---|---|---|---|---|
| | | | | Lower | Upper | |
| Controls | 2.1 | 22.1 | 6.5 | 5.8 | 7.2 | 46.906 (<0.001) Significant |
| Diabetics | 5.0 | 123.0 | 17.3 | 13.8 | 22.0 | |
| Diabetics with IHD | 6.0 | 168.0 | 19.2 | 12.0 | 32.0 | |

CI = confidence interval for mean KW= Kruskal Wallis test.

## DISCUSSION

Studies showed that the prevalence of CVD in individuals with diabetes is still higher than their non-diabetic counterparts who have the same prevalence of traditional cardiovascular risk factors, the finding that suggests the presence of another set of yet recognized hidden risk factors warranting further exploration and investigation. Therefore a number of non-traditional cardiovascular risk factors may also contribute to the excess cardiovascular risk in individuals with T2DM [7] .

In our study, there was a statistical significant difference regarding the rate of Diastolic Dysfunction in diabetic patients with IHD, where it was (62.9) while it was (28.6) in diabetic patients without IHD. This finding agrees with the results of the study of Virendra et al. [8]

The current study, showed that there was a statistical significant difference regarding the rate of left ventricular hypertrophy in diabetic patients with IHD where it was (60.0%) while in diabetic patients without IHD it was (17.1%). This finding agrees with the results of the study of Kazuo et al. [9]

In our study, there was a statistical significant difference regarding FBG parameters between diabetic without IHD and

patients with IHD (132 and 167 mg/dl). Rates of FBG>110 mg/dl similar in the two studied groups, which agrees with the results of the study of Kazuo et al. [9]

The current study, showed a statistical significant difference between the three studied groups regarding the median of high sensitive C-reactive protein (HsCRP). This finding was in agreement with the study of Christie et al. [10] which found a statistical significant difference of HsCRP. While our result was disagreement with study of Virendra et al. [8] who reported non statistical significant difference regarding HsCRP in the studied group.

Our study showed a statistical significant difference between the three studied groups regarding homocysreine. This finding was in agreement with the study of Wald et al. [11] who reported an increase in the blood level of homocysteine in men who died early with IHD. This also comes in agreement with study of Ghallager et al. [12] which revealed that the elevated plasma level of the amino acid Hcy is a significant and independent risk factor for the development of coronary heart disease.

In our study there was a statistical significant difference between the three studied groups regarding plasma level of fibrinogen. Our finding was in agreement with the study of Lima et al [13] which revealed a highly significant difference of plasma level of fibrinogen related to coronary artery diseases. This also comes in agreement with the study of Sato et al. [14] which showed that there is significant difference regarding plasma level of fibrinogen and coronary artery diseases.

In our study micro-albuminuria showed statistical significant difference between the three studied groups. This finding agreed with the study of Brownrigg et al. [15] which revealed highly significant difference of microalbuminuria related to coronary artery diseases. This also comes in agreement with the study of Stehouwer and Smulders [16] who showed that there was a statistical significant difference between microalbuminuria and coronary artery diseases.

## CONCLUSION

Cardiovascular risk factors were higher in subjects with diabetes compared to subjects without diabetes, Non-traditional cardiovascular risk factors may be related independently to incident coronary heart disease in T2DM patients.

**Declaration of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

**Funding information**

## REFERENCES

**1-Caro JJ, Ward AJ and O'Brien JA:** Lifetime costs of complications resulting from type 2 diabetes in the U.S. Diabetes Care 2002 ;2 5: 476- 81.

**2-Onat A.:** Risk factors and cardiovascular disease in Turkey. Atherosclerosis. **(2001):** 156(1):1–10.

**3- Haffner SM, Lehto S, Rönnemaa T, Pyörälä K and Laakso M:** Mortality from coronary heart disease in subjects with type2 diabetes and in no diabetic subjects with and without prior myocardial infarction, N Engl J Med 1998; 339: 229-234

**4- Rana JS, Liu JY, Moffet HH, Jaffe M and Karter AJ.** Diabetes and prior coronary heart disease are not necessarily risk equivalent for future coronary heart disease events. J Gen Internal Med. **(2016),** 31 (4):387–93

**5- Evans JM, Wang J and Morris AD.** Comparison of cardiovascular risk between patients with type 2 diabetes and those who had had a myocardial infarction: cross sectional and cohort studies. BMJ 2002;324:939

**6- Mitchell RS, Kumar V, Abbas AK, Fausto N.** Robbins Basic Pathology (8th ed.). Philadelphia: Saunders. pp. 345. **(2007).** ISBN 1-4160-2973-7.

**7-Fonseca VA.** Risk factors for coronary heart disease in diabetes. Ann Intern Med. **(2000):** 133(2):154-6.

**8-Virendra C, Harsha V, Luldeep B, Jay D and Pruthvi S.** Diastolic dysfunction in asymptomatic type 2 diabetes mellitus with normal systolic function **(2011):**. 2(4):213-222.

**9- Kazuo E, Bernadette B, Zhezhen J, Tatjana R, Ralph L., Shunichi H et al.** Association between Diabetes Mellitus and Left Ventricular Hypertrophy in a Multi-Ethnic Population. Am J Cardiol, (2008): 101(12): 1787–1791.

**10- Ballantyne CM, Hoogeveen RC, Bang H, Coresh J, Folsom AR, Heiss G, et al.** Lipoprotein-associated phospholipase A2, high-sensitivity C-reactive protein, and risk for incident coronary heart disease in middle-aged men and women in the Atherosclerosis Risk in Communities (ARIC) study. Circulation, (2004): 109(7), 837-842.

**11- Wald NJ, Watt HC, Law MR, Weir DG, McPartlin J and Scott JM** Homocysteine and ischemic heart disease: results of a prospective study with implications regarding prevention. Archives of internal medicine (1998): 158(8), 862-867.

**12- Gallagher PM, Ward P, Tan S, Naughten E, Kraus JP, Sellar GC et al.** High frequency (71%) of cystathionine β-synthase mutation G307S in Irish homocystinuria patients. Human mutation, **(1995)** 6(2), 177-180.

**13- Lima LM, Carvalho MD and Sousa MD.** Plasminogen and fibrinogen plasma levels in coronary artery disease. Revista brasileira de hematologia e hemoterapia, **(2012):** 34 (4), 298-301.

**14- Sato S, Nakamura M, Iida M, Naito Y, Kitamura A, Okamura T et al.** Plasma fibrinogen and coronary heart disease in urban Japanese. American journal of epidemiology, (2000):152(5), 420-423.

**15- Brownrigg JR, de Lusignan S, McGovern A, Hughes C, Thompson MM, Ray KK et al.** Peripheral neuropathy and the risk of cardiovascular events in type 2 diabetes mellitus. Heart, (2014): 100(23), 1837-1843.

**16- Stehouwer CD and Smulders YM.** Microalbuminuria and risk for cardiovascular disease: analysis of potential mechanisms. Journal of the American Society of Nephrology, (2006): 17(8), 2106-2111.

**To Cite This Article:** Mohamed HE , Mohamed ME, Alaa ES , Huda AA.Contribution of Non Traditional Cardiovascular Risk Factors to the Cardiovascular Disease in Patient with Type 2 Diabetes. ZUMJ 2020;26(1);1-6.DOi: 10.21608/zumj.2019.13277.1233.