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Original Research Article

Sex differences in cardiovascular risk factors among people with type two diabetes

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ABSTRACT

Background: Type 2 Diabetes Mellitus is associated with various risk factors, which accelerates the development of cardiovascular disease (CVD). The increased relative risk for CVD due to diabetes is greater in women than in men. Aims and objectives of this study were to study the prevalence of cardiovascular risk factors among type 2 diabetes patients and to assess the sex differences in the prevalence of cardiovascular risk factors among type 2 diabetes patients.
Methods: A cross-sectional study was performed among the 500 adult (>15 years) patients of type 2 diabetes who attended Department of Medicine, SGRDIMSR, Amritsar and were assessed for the presence of various CVD risk factors and the prevalence of these was compared between both sexes.
Results: The most prevalent CVD risk factor among 500 patients of type 2 DM was high HBA1C levels which was present in 67.2% of the study population. It was followed by obesity (which had prevalence of 66.2%), dyslipidaemia (i.e. high triglyceride levels - 64.8% and low HDL levels - 65.6%) and microalbuminuria along with macroalbuminuria (65.4%). Diabetic males had microalbuminuria (along with macroalbuminuria) as the most prevalent CVD risk factor (69.03%), followed by alcohol consumption (63.18%) and abnormal waist circumference (61%). On the other hand, the most prevalent CVD risk factor among female diabetics was high HBA1C (77.4%) followed by obesity (77.0%) and dyslipidaemia-hypertriglyceridemia (75.1%) and low HDL levels (70.5%).
Conclusions: Cardiovascular risk factors were highly prevalent among patients with type 2 diabetes attending department of medicine, SGRDIMSR, Amritsar with different risk profiles among diabetic male and females. A gender-sensitive approach is required in planning interventions (counselling and treatment) to reduce the risk of cardiovascular disease in diabetes.

Keywords: Cardiovascular disease, Comparison of CVD risk factors among sexes, Gender sensitive approach, Type 2 diabetes mellitus

INTRODUCTION

Cardiovascular disease is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium; it typically occurs when there is an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery (or arteries) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery. Cardiovascular Disease (CVD) has become the leading cause of mortality and morbidity in developing countries with approximately 30% dying of

their first CVD event, emphasizing the need for aggressive preventive strategies.[1] The Indian Asian population accounts for a fifth of all global deaths from CVD. Mortality due to CVD on the Indian subcontinent has doubled since 1990 and is predicted to rise a further 50% by 2030.[2] Reasons underlying the increased CVD mortality among Indian Asians remain unknown. Genetic factors, a high-fat and energy-rich diet, smoking, and a sedentary lifestyle are associated with the emergence of CVD. Obesity, insulin resistance, and type 2 diabetes mellitus are increasing and are powerful risk factors for CVD.[3]

Diabetes mellitus is fast gaining the status of a potential epidemic in India, with more than 62 million diabetic individuals currently diagnosed with the disease. In 2000, India topped the world with the highest number of people with diabetes mellitus with 31.7 million patients affected, followed by China (20.8 million) and the United States (17.7 million) in second and third places, respectively.[4]

Cardiovascular disease is increased in type 2 diabetes mellitus subjects due to a complex combination of various traditional and non-traditional risk factors that have an important role to play in the beginning and the evolution of atherosclerosis over its long natural history from endothelial function to clinical events. The Framingham heart study revealed a marked increase in CVD in DM. The prognosis for individuals with diabetes who have DM is worse than that for non-diabetics. CHD with multiple vessel involvement is common in DM. Type 2 DM increases CVD death rate twofold in men and fourfold in women. AHA has designated DM as "CHD Risk Equivalent". Older age group with long standing type 2 DM has higher CVD risk. Risk factors in diabetes include dyslipidemia, hypertension, obesity, reduced physical activity and cigarette smoking. Additional risk factors more prevalent in diabetic population are microalbuminuria, macroalbuminuria, an elevation of serum creatinine, abnormal platelet function and endothelial dysfunction. The most common pattern of dyslipidemia is hypertriglyceridemia and low levels of HDL. LDL in T2DM are more atherogenic because they are more easily glycated and susceptible to oxidation. Based on guidelines provide by ADA, priorities in treatment of dyslispidemia are to lower LDL (<100), TGs (<150) and increase HDL (>40mg in males and >50mg in females).[5]

Aims and objectives of this study were to study the prevalence of cardiovascular risk factors among type 2 diabetes patients and to assess the sex differences in the prevalence of cardiovascular risk factors among type 2 diabetes patients.

METHODS

A total 500 adult patients with type 2 DM who attended Department of Medicine, SGRDIMSR, Vallah, Sri Amritsar were included in this study and patients with established CVD, pregnancy and lactation were excluded from study.

A structured questionnaire was used to collect information on age, sex, occupation, duration of diabetes, current medication for diabetes, family history of diabetes and personal habits such as current smoking (defined as a history of smoking in the last 3 months) and alcohol consumption (defined as consumption of average daily consumption of 60 ml of alcohol). Occupation was classified as skilled (carpenter, painter, electrician, plumber, etc.), unskilled (farmer, labourer), businessmen, and 'others' for categories such as retired people, homemakers, and unemployed. Socioeconomic status was classified as low (family income <INR 12,000/month), middle (family income INR 12000-24000/month) and high (family income >INR 24000/month).

Anthropometric measurements, including height and weight were measured for calculation of body mass index (BMI). Obesity was defined as BMI ≥25kg/m^2. Waist circumference was measured for assessment of central obesity. Blood pressure was measured of all patients. Hypertension was defined as history of hypertension and receiving anti-hypertensive drugs or systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥90mmHg.

Biochemical parameters such as fasting and postprandial glucose levels and glycosylated haemoglobin (HbA1c) levels were recorded. Lipid Profile was done. Dyslipidemia was defined as history of receiving any lipid lowering drug or the presence of any one lipid abnormality triglycerides ≥150mg/dl or HDL cholesterol <40mg/dl in men and <50mg/dl in women. Microalbumin in urine was defined as values 30-300mg/dl. Thyroid profile was done. Euthyroidism was defined by TSH level between 0.45-4.50mIU/L; clinical hypothyroidism was defined by TSH level >10mIU/L; subclinical hypothyroidism was defined by TSH levels between 4.51-9.99mIU/L; clinical hyperthyroidism was defined by TSH levels <0.1mIU/L and subclinical hyperthyroidism was defined by TSH levels 0.11-0.44mIU/L. CRP was considered abnormal if value is >10mg/L. Fundus examination was done to assess presence of diabetic retinopathy.

RESULTS

In this study, out of 500 type 2 DM patients, 239 patients were male (47.8%) and 261 patients were female (52.2%) with slight female predominance. Mean age of current study population was 56.58±10.65 years, maximum being in the 56-65 years age group (n=169;33.8%). There was no significant difference between the mean age of male and female diabetics (p value = 0.12). 73% of Type 2 DM patients belonged to rural background with almost equal distribution in both genders. Hence, no significant difference was present in demographic profile of male

and female diabetics (p value=0.64). 68.6% of current study population was illiterate out of which female diabetics outnumbered male diabetics. Hence, illiterate female diabetics were significantly more as compared to illiterate male diabetics (p=0.004). Diabetic men were mostly unskilled (farmers) by occupation, whereas diabetic women were mostly homemakers. 40.8% population belonged to low socioeconomic status. Females were significantly less financially affluent than male diabetics (p value=0.004) and had limited access to healthcare facilities.

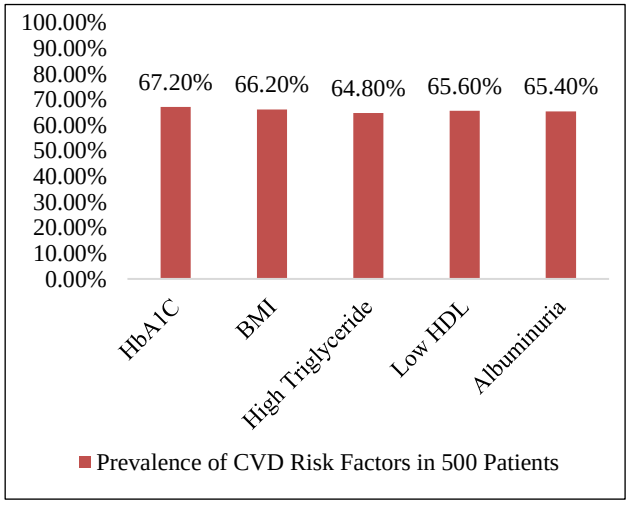

Figure 1: Prevalence of CVD risk factors in 500 patients.

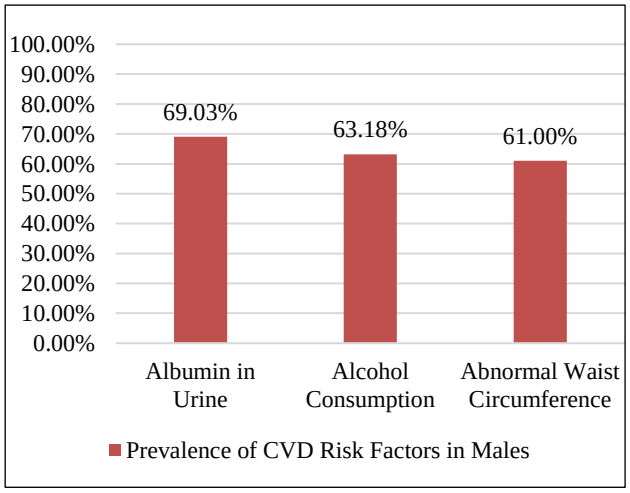

Figure 2: Prevalence of CVD risk factors in males.

Mean duration of T2DM in this study was 6.90±5.95 years. Female diabetics had slightly longer duration of disease and thus had more complications of diabetes at presentation. However, the difference in average duration of diabetes among male and female diabetics was not significant (p value=0.04). Prevalence of oral anti diabetic therapy in this study was extremely high, i.e., 83.4% and very few patients were compliant with insulin therapy. Among both sexes, the female diabetics were using oral anti diabetics significantly more than male counterparts (p value=0.003). On the other hand, insulin usage in females was almost negligible. Positive family history was present in 46.2% of study population and approximately similar distribution was present in male and female diabetics. Hence, no significant difference was present in positive family history of diabetes in male and female diabetics (p value=0.53). The alcohol consumption was present in 30.2% population. It was exclusively present among male diabetics and was non-existent in female diabetics (p value <0.0001).

Obesity was highly prevalent, i.e. 66.2%, in the current study with mean BMI of 26.13±3.13 kg/m^2. The female diabetics were significantly more obese than their male counterparts were (p value <0.002). Prevalence of abnormal waist circumference was 61% in both male and female diabetics, with mean of 95.43±13.95cm and 86.28±13.39cm in male and female diabetics respectively. Hence, no significant difference was present in abnormal waist circumference (p value=0.17). Hypertension was present in 45.2% of study population. There was no significant difference in prevalence of hypertension in male and female diabetics (p value=0.11).

Maximum number of patients (n=190, 38%) had FPG >200mg/dl with mean FPG of 196.41±52.81mg/dl. Mean fasting plasma glucose was significantly more in female diabetics as compared to male diabetics(p<0.0001). Majority of patients (n=149, 29.8%) had PPPG >300mg/dl with mean PPPG of 286.4±56mg/dl. The average post-prandial plasma glucose was significantly higher in women as compared to men (p value<0.001). Prevalence of abnormally high HBA1C levels (>8%) was found in 67.2% of current diabetic population with mean HBA1C level as 8.95±1.57%. Female diabetics had significantly higher levels of HBA1C than male counterparts which indicated poor glycemic control (p<0.0001).

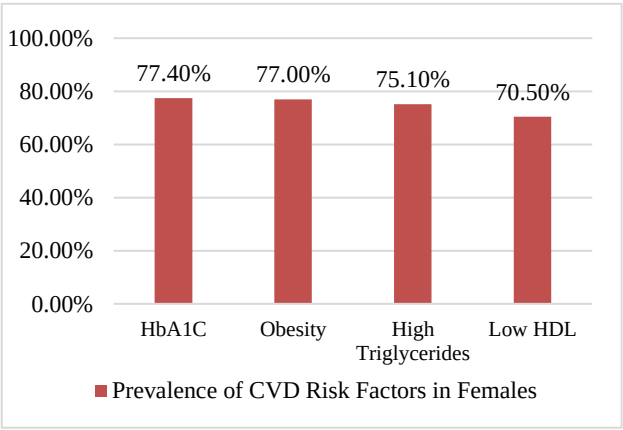

Figure 3: Prevalence of CVD risk factors in females.

Hypertriglyceridemia was present in 64.8% of this study population with mean of 189.96±64 mg/dl. Female

diabetics had significantly more prevalence of abnormally high triglyceride levels than male diabetics did (p<0.0001). 65.6% of study population in present study had abnormally low HDL levels with mean of 37.9±20mg/dl and 41.5±19mg/dl in male and female diabetics, respectively. Hence, the prevalence of abnormal HDL levels in female diabetics was significantly more than in male diabetics (p=0.021).

Combined prevalence of Microalbuminuria and Macroalbuminuria was 65.4% of study population with mean albumin excretion in urine of 136.63±12.29mg/dl. It was significantly more abundant in male diabetics as compared to female diabetics (p<0.0001).

The overall prevalence of thyroid disorders was 33.2% in our study, out of which subclinical hypothyroidism was most prevalent (20.8%). Female diabetics had significantly more associated thyroid disease. Among thyroid disorders, hypothyroidism, both subclinical and clinical, was more prevalent in female diabetics. Also, out of the two hypothyroid states, subclinical hypothyroidism was significantly prevalent in female diabetics (p<0.0001). Abnormal CRP levels were present in 9% of patients of our study with mean of 4.91±4.24mg/dl. There was no significant difference in prevalence of abnormal CRP levels among male and female diabetics (p=0.51). The prevalence of diabetic retinopathy was 54.2% in the current study. Diabetic retinopathy was equally prevalent in male and female diabetics. Hence, no significant difference was present in diabetic retinopathy between both genders (p=0.11).

DISCUSSION

Type 2 diabetes mellitus is associated with the various CVD risks, which are abundant in diabetes. According to Haffner et al, patients with diabetes mellitus but without prior myocardial infarction have a risk of fatal coronary heart disease that is similar to that of patients without diabetes mellitus who have survived a myocardial infarction. Therefore, they concluded that, with regard to cardiovascular risk factors, all patients with diabetes mellitus could be treated as if they had prior coronary heart disease.[6] In a meta-analysis of 37 studies (including 447 T2DM patients), the relative risk (RR 95% CI) for fatal CVD between patients with and without diabetes mellitus was greater among women 3.50 (2.0-4.53), than in men 2.06 (1.81-2.34). Thus, in women with diabetes mellitus, the relative risk for a fatal coronary event is 50% higher than in men. This was probably explained by a less favourable cardiovascular risk profile in women linked to hypertension and hyperlipidemia.[7]

In our cross-sectional study of 500 patients, 239 (47.8%) male and 261 (52.2%) female diabetics were present. The patients were mostly in age group of 56-65 years with the mean age of 56.58±10.65 years. Age difference in male and female diabetics was insignificant. Author also studied the distribution according to demographic profile and we found that most of the patients belonged to rural background, out of which diabetic women were predominantly residing in rural setup. The good glycaemic control depends on education status of the patient hence educational qualification was also enquired. Among the diabetic patients of our study, literacy rate was low and women in comparison to men were mostly illiterate and had less awareness regarding the course of diabetes, its complications and measures to be taken for the maintenance of good glycaemic control.

The diabetic men in current study population were mostly unskilled workers (including farmers) while women were mostly homemakers. The socioeconomic status was also observed, and it was found that majority of population belonged to the middle-income group and when this factor was studied in male and female diabetics, women were found less financially affluent. As women were mostly illiterate and were resident of rural background with low socioeconomic status, they were less aware of their glycaemic status and had little access to healthcare facilities. Thus, women present later in course of illness of Type 2 diabetes mellitus and that too with its established complications. The duration of diabetes plays an important risk factor in development of CVD in diabetes. In most of the patients of the study the duration was <5 years. However, mean duration of diabetes was 6.90±5.95 years. The Framingham heart study states that the duration of diabetes mellitus increases the risk of CVD death independent of coexisting risk factors.[8]

Among the anthropometric measurements linked to cardiovascular risk, BMI and central obesity (in terms of waist circumference) were measured and it was found that BMI >25, i.e., obesity was significantly more prevalent among female diabetics than male diabetics. In a concordant study by Bray GA. et al., diabetic women were found to be more obese than diabetic men.[9] However, waist circumference was approximately equal in both groups.

Current anti diabetic therapy history was documented in detail from all 500 patients. The study results showed that a big chunk of study population was using oral anti diabetic agents. On the other side, administration of insulin was less prevalent due to poor compliance. Usage of oral anti diabetic agents in females was far more than its use among males. The positive family history is an independent risk factor of CVD in diabetes. Its prevalence in our study population was not very high. Hence, no significant difference was found in the prevalence of positive family history among the male and female diabetics. Alcohol consumption is another risk factor of CVD and it was prevalent in 30.2% of patients with its exclusive presence in males. Hypertension complicates the course of diabetes and increases morbidity and mortality. Its co-existence in type 2 diabetes mellitus was associated with 45.2% population. Despite its more prevalence in females, there was no

significant difference in the presence of hypertension in males and females.

Among investigations, both uncontrolled FPG and PPPG have detrimental effect on the cardiovascular system and thus plays an important role in CVD morbidity and mortality. The average FPG and PPPG were extremely high with more prevalence in females. Each milligram per deciliter of fasting plasma glucose increases diabetes mellitus risk by 6% after controlling for other risk factors.[10] Majority of patients had HbA1c >9% with mean HBA1C level as 8.95±1.57% and it was found that most females had deranged HBA1C levels far more than male diabetics. In a similar study by Markku Laakso et al., it was concluded that an increment of 1 unit (%) of glycated hemoglobin increased CVD mortality by 7.5% in type 2 diabetic subjects.[11] Also, dyslipidaemia (an important risk factor of CVD in diabetes) which was assessed by high triglyceride and low HDL levels, was also prevalent in female diabetics. 324 patients (64.8%) had hypertriglyceridemia with mean of 189.96±64mg/dL. The mean HDL level was 37.9±20mg/dL and 41.5±19mg/dL in male and female diabetics respectively. Hence, low HDL levels were more prevalent in females. An important study by Erdogan et al showed Fasting hypertriglyceridemia increases carotid intima–media thickness and impairs coronary microvascular functions in non-obese middle-aged women but not in men.[12] Remarkably, microalbuminuria and macroalbuminuria were more prevalent in diabetic males. 283 patients (56.6%) had microalbuminuria (30-300 mg/dL) and 44 patients (8.8%) had macroalbuminuria (>300 mg/dL) with mean albumin excretion in urine of 136.63±12.29 mg/dL. Hence, majority of patients had microalbuminuria. The mean albumin excretion was 150.97±12.10mg/dL and 123.49±12.35mg/dL in male and female diabetics, respectively. Hence, microalbuminuria was more prevalent in males as compared to females. The similar study by Verhave et al showed that cardiovascular risk factors and urinary albumin excretion rate were significantly correlated only in men (about twofold higher in men). It was the first study demonstrating the effect of gender on the albuminuria-ischemic heart disease relationship in patients with type 2 diabetes mellitus.[13] As hypothyroidism both clinical and sub clinical are well-established risk factors of CVD, thyroid profile was also done and it showed that 33.2% of our study population had some sort of thyroid disorder. The most common out of these was subclinical hypothyroidism. The prevalence of SCH in that study was 4–9% in the general population and 10.2% in T2DM population. Hence, it is necessary to screen thyroid function in patients with T2DM, and appropriate individualized treatments should be given to T2DM patients with SCH as well.[14] In comparison among genders, women were more affected by hypothyroidism than men and that too by SCH as most common thyroid disease presentation. CRP as an inflammatory mediator (a key component of atherosclerosis in diabetes) is also an established CVD risk factor in diabetes. However, our study had little prevalence of raised CRP levels. Also, no significant difference was found in the two sexes in terms of CRP levels.

Fundus examination was also included as an integral part of the study as diabetic retinopathy has been linked to CVD development in various studies. We observed a prevalence of 54.2 % population suffering from diabetic retinopathy. However, we could not find any significant difference in the prevalence of retinopathy in both genders. In a study by N Cheung et al, it was established that diabetic retinopathy was associated with a twofold higher risk of incident CVD events and a threefold higher risk of fatal CVD.[15]

CONCLUSION

Thus, author conclude that the overall most prevalent CVD risk factor among 500 adult patients was poor glycaemic control i.e. high HBA1C levels. It was followed by obesity, dyslipidaemia (i.e. high triglyceride levels and low HDL levels) microalbuminuria and abnormal waist circumference. The most prevalent CVD risk factor in diabetic males was combined microalbuminuria (along with macroalbuminuria), followed by alcohol consumption and central obesity (measured by waist circumference).

On the other hand, the most prevalent CVD risk factor among female diabetics was poor glycemic control (abnormally high HBA1C) followed by obesity (BMI>25) and dyslipidaemia. Hence, gender-based approach is required to manage type 2 DM patients for preventing the risk of future CVD, which includes innovative measures for more aggressive management of glycemic control and comorbidities such as obesity and dyslipidaemia and counselling to quit alcohol consumption.

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Ethical approval: The study was approved by the institutional ethics committee

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