

A Study of Prevalence of Risk Factors of Coronary Artery Disease in Diabetic Patients and Comparison with Normal Subjects

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ABSTRACT

Introduction: The diabetes mellitus is described as metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbance of carbohydrate, protein and fat metabolism resulting in insulin secretion, insulin action or both. This study was done to check the prevalence of coronary artery disease (CAD) risk factors in diabetic patients and compare with normal subjects.

Material and methods: Sixty diagnosed cases of diabetes and 60 normal subjects from patients attending Diabetic Clinic, Tribhuvan University Teaching Hospital, Kathmandu, Nepal. This was hospital based cross sectional observational study. Diagnosed case of diabetes was taken and non-modifiable and modifiable risk factors of CAD were compared with normal subjects with available data of risk factors CAD.

Results: Mean age of the case group was 48.51 yrs, 46.6% of case group had hypertension, in comparison of control group had only 15%. Study showed overweight (BMI>25 Kg/m²) was observed in 25 (41.6%) diabetic patients in comparison to control which had only 2 (3%) subjects being overweight. About 5% of diabetic cases had family history of CAD. Family history of diabetes was present in 32% of diabetic patients and family history of hypertension was present in 18% of diabetic population.

Conclusion: This study showed the prevalence of risk factor of CAD in diabetic patients was significantly higher compared with normal subjects.

Keywords: Coronary Artery Disease, Diabetic, Risk Factors, Overweight, HbA1c, Lipid Profile

INTRODUCTION

The human burden of diabetes is largely due to its complication, both microvascular and macrovascular complications are the cause of mortality and morbidity.^{1,2} Against the background of increasing prevalence of type 2 diabetes mellitus, determining the prevalence of its complication and risk factors is important for health service planning.³

Increased atherogenesis along with the early endothelial dysfunction and increased advanced glycosylated end product play a vital role in pathogenesis of different micro and macrovascular complications.^{4,5} Macrovascular complications includes coronary artery disease, stroke, and peripheral vascular diseases. Atherosclerosis is the deposition of fatty material along with the other cellular component in the tunica intima of the vessel. In the patient suffering from diabetes premature atherosclerosis is seen.^{6,7}

All manifestations of coronary artery disease is atleast two folds more common in diabetic patients.⁸ According to

UPKDS 23 study 11% of the patients develop myocardial infarction and angina over a median of 8 years follow up. It is also stated in same study that incidence of macrovascular complication in diabetic patients is twice of microvascular complications.⁹ The American Heart Association states that diabetes itself as a major risk factor. The other CVD risk factors are dyslipidemia, cigarette smoking and hypertension act as independent contributors to cardiovascular disease in diabetic patients.¹⁰ The major risks that are amplified in diabetes include (a) alteration in lipoprotein concentration and composition (dyslipidemia), hyperinsulinemia, hypertension, central obesity and genetic components.^{11,12} Risk factors which are modifiable are dyslipidemia, hyperglycemia, hypertension, secondary life style, smoking, obesity, dietary deficiencies of poly unsaturated fatty acids and stress. Nonmodifiable risk factors are sex, age, duration of diabetes, genetic or family history of diabetes and CVD.¹³ In general prevalence of the major risk factors of CAD in the general population is amplified in diabetes. So, this study was expected to know prevalence of coronary risk factors in diabetic patients visited to TUTH and compare the risk factors of CAD in the normal subjects.

MATERIAL AND METHODS

This was a cross-sectional observational study and was undertaken in Tribhuvan University Teaching Hospital (TUTH) from December 2009 to August 2010. Sixty

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consecutive diagnosed diabetic patients were evaluated. Sixty normal subjects were taken from subjects attending patients in different OPD and people from nearby areas of hospital campus.

Inclusion Criteria

1. All diagnosed patients of diabetes according to ADA criteria
2. Age 20 to 70 yrs
3. Obese
4. Smoking and tobacco consumer
5. Diagnosed cases of hypertension by physician
6. HbA1c level $\geq 6.3\%$

Regarding major coronary risk factor emphasis was given to age, sex, cigarette smoking, HTN, history of dyslipidemia and IHD, elevated HbA1c, associated stress factor present and generalised and abdominal obesity. Habits regarding cigarette smoking, pipe or bidi smoking, duration and number of sticks per day was asked to all patients and was calculated in packs/year. Body mass index was used as measurement of generalised obesity.

Categories were established: underweight, normal, overweight, and obese. An individual would be considered to be underweight if his/her BMI was in the range of <18.5 kg/m², normal weight if the BMI was 18.5 to 24.9 kg/m², overweight if the BMI was 25 to 29.9 kg/m², Class I obesity if BMI was 30.0 to 34.9 kg/m², Class II obesity if BMI was 35.0 to 39.9 kg/m² and Class III obesity if BMI ≥ 40 kg/m².¹⁴ Ratio of waist circumference to hip circumference was used as measurement of abdominal obesity. Waist circumference was measured with the help of flexible measuring tape

graded in CMs, in the horizontal plane with the subject standing as minimal circumference between costal margin and iliac crests.¹⁵ Hip circumference was measured in CMs as maximum circumference in horizontal plane over the buttocks. Then waist to hip ratio was calculated by the formula, WHR= waist circumference in CM divided by hip circumference in CM. A waist hip ratio of greater than 0.95 in men and 0.8 in women was regarded as abdominal obesity.¹⁶ On the next morning patient had a lipid profile after 14 hrs fasting. Total and HDL cholesterol was done by enzymatic end point method and TG by GPO-PAP method. Blood sugar fasting blood sample was taken at least 8 hrs fasting and measured by glucose oxidase peroxidase method. Blood sugar PP was taken after 2 hrs of meal and calculated in the same was as fasting blood sugar level. Test was performed by pipetting method by iChroma HbA1c test along with iChroma reader, an immunoassay that measured a ratio of haemoglobin associated with the total haemoglobin.¹⁷ Descriptive statistics of the variables were carried out from both case and control group. The available data of control and case were compared. Statistical tools used for comparison were correlation coefficient, χ^2 test with Fischer exact test student t-test.

RESULTS

Age and Sex Distribution

Age of the patients in this study ranged from 21 to 70 yrs. Mean age of the patient was 48.51 yrs (SD 11.37). Maximum number of the patients and normal subjects were 39 (32%) belonged to the age group of 40-50 yrs followed by age

Age Groups	Cases		Total	Controls		Total
	Male	Female		Male	Female	
<30 yrs	2	5	7	2	1	3
30-40 yrs	3	5	8	3	9	12
40-50 yrs	6	10	16	12	11	23
50-60 yrs	11	4	15	8	10	18
60-70 yrs	9	5	14	4	0	4
Total	31	29	60	29	31	60

Table-1: Age and sex distribution of the cases and controls

		Yes	No	Total
		Smoking	Male	14 (45.2%)
	Female	5 (17.2%)	24 (82.8%)	29
Alcohol	Male	12 (38.7%)	19 (61.3%)	31
	Female	6 (21.4%)	22 (78.6%)	28

Table2: Smoking and alcohol status in our diabetic subjects

Systolic BP				
Group	Mean	Minimum	Maximum	t-test (p-value)
Cases	123.2 \pm 13.10	90	180	0.008
Control	117.85 \pm 8	100	140	
Diastolic BP				
Group	Mean	Minimum	Maximum	t-test (p-value)
Cases	81 \pm 5.21	60	100	0.001
Control	77.5 \pm 6.09	60	90	

Table-3: Systolic and diastolic BP of the cases and controls

Sex	Mean	Minimum	Maximum
Male	96.22±9.29	75	114
Female	93.5±14.04	69	120

Table-4: Waist circumference of the diabetic cases

Value	Fasting sugar		PP sugar	
	<7 mmol/l	>7 mmol/l	<11.1 mmol/l	>11.1 mmol/l
No. of Patients	32	28	21	39

Table-5: Fasting and postprandial blood glucose in diabetic cases

Sex	Mean	Minimum	Maximum
Male	8.63±2.61	1	14.9
Female	7.72±1.43	5.3	11

Table-6: HbA1c levels in diabetic cases

Total Cholesterol	Cases		Controls	
	Frequency	Percentage	Frequency	Percentage
Desirable	53	88.3	53	88.3
Borderline high	7	11.7	5	8.5
High	2	3.3	0	0
Total	60	100	60	100
HDL	Cases		Controls	
	Frequency	Percentage	Frequency	Percentage
Low	39	82.97	23	88.47
High	8	17.03	3	11.53

Table-7: Levels of cholesterol and HDL in cases and controls

group 50-60 yrs which considered of 33 patients (27.5%) collectively. In our study maximum 29 patients were belong to the age group 50-70 yrs. The mean age of females was 44.93 yrs (S.D=13.86) and the mean age of males was 53.71 yrs (S.D=11.62). There were 60 males and 60 females in the study and the male to female ratio was 1:1 [Table 1].

Duration of Diabetes

The duration of diabetes in our cases ranged from 3 months to 27 years. The majority of our patients 33 (55%) had a duration within the range of 1 to 10 yrs followed by 19 patients (32%) who had a duration of less than 1 yr. About 6 (10%) patients had duration of 10 yrs to 20 yrs and 2 (3%) patients had duration of more than 20 yrs.

Physical Activity and Stress Factors

Twenty four patients in our cases (40%) admitted were having adequate physical activities whereas 36 patients (60%) admitted were not having adequate physical activity. Similarly 71% (n=43) of our patients experienced some form of stress and 29% (n=17) did not have stress in life.

Smoking and Alcohol Consumption

A total of 19 patients in our diabetic population smoked which accounted for about 31% of the population. About 45% of the male patients (n=14) smoked and 17% (n=5) of the female patients smoked. About 18 patients (30%) admitted of consuming alcohol out of which 12 (38%) were males and 6 (21%) were females. Mean pack years for smokers was 15.58±8.01 (Range: 5-30 yrs) [Table 2].

Family History of CAD, DM and HTN

Only 5% of our diabetic patients (n=3) had a family history

of CAD and 32% (n=19) had a family history of diabetes, out of which 11 were males and 8 patients were females. About 18% (n=11) of our patients had a family history of hypertension, out of which 5 were males and 6 were females. A total of 28 patients (46.6%) were found to have HTN as opposed to only 15% of the control population (n=9) who had HTN. The mean SBP was 123±13.10 in our cases as opposed to mean SBP of 117.85±8 in the control population. The mean DBP was 81±5.21 in our cases and the mean DBP was 77.5±6.09 in the control group. There is a significant difference between the mean systolic and DBP between cases and controls (p<0.05) [Table 3].

Body Mass Index

In this study BMI and waist circumference was used to assess the degree of obesity, BMI for general obesity and WHR for abdominal obesity. Overweight (BMI>25 kg/m²) was observed in 25 (41.6%) of diabetes cases and 2 control (3%) population. One diabetic and one subject in control population were found to be underweight. Six patients (10%) and 3 patients (5%) in our cases respectively fell under obesity class I and obesity class II respectively as opposed to 1 patient in the control group fell in the obesity class I and no patient in the obesity class II.

The mean waist circumference in males in the diabetic cases 96.22±9.29 cm with a minimum 75 and maximum 114 cm. Similarly the mean waist circumference in the female diabetic cases was 93.5±14.04 (minimum 69 cm and maximum 120).

Blood Glucose and HbA1c levels

The mean fasting sugar was 7.85±3.02 mmol/l in our diabetic

patients (minimum 3.3 mmol/l and maximum 18.10 mmol/l). Similarly the mean post prandial sugar was 12.79 ± 5.32 mmol/l in the diabetic subjects (minimum 4.80 mmol/l and maximum 35.30 mmol/l). Twenty eight patients (46.6%) had a fasting sugar above 7 mmol/l and 39 patients (65%) had a postprandial sugar above 11.1 mmol/l [Table 5].

The mean HbA1c level in male was $8.63 \pm 2.61\%$. The mean HbA1c level in female was $7.72 \pm 1.43\%$ [Table 6].

Lipid Profile

Among them borderline high cholesterol level (5.17-6.18 mmol/l) was seen in 7 cases and high (≥ 6.18 mmol/l) levels was seen in 2 patients. The median total cholesterol was 3.4 mmol/l (S.D 1.24) in the diabetic group and the median level in the control group was 4.2 mmol/l (S.D. 0.63). Mean Whitney test revealed significant difference (p value < 0.01). In the study, low levels of HDL (< 1.03 mmol/l) was seen in 39 of the cases (65%) and high HDL (≥ 1.55 mmol/l) was seen in 8 cases (13.33%) in the diabetic subjects. The median HDL level was 0.98 mmol/l (SD 0.63) in the diabetic group and the median level in the control group was 1.1 mmol/l (SD 0.46). Mann Whitney test revealed significant difference (p value 0.012) [Table 7].

In this study, optimal LDL cholesterol (< 2.58 mmol/l) was seen in 49 cases (81.7%) in the diabetic group as opposed to 35 cases (58.3%) in the control group. the median LDL level was 1.27 mmol/l (S.D 1.01) in the diabetic group and the median level in the control group was 2.4 mmol/l (S.D 0.69). Mann Whitney test revealed significant difference (p value < 0.01). The median triglyceride level was 1.5 mmol/l (SD 0.82) in the diabetic group and the median level in the control group was 1.5 mmol/l (S.D 0.92). Mann Whitney U test revealed no significant difference (p value 0.672).

DISCUSSION

This study showed that the mean age of the case group was 48.51 yrs in both case and control group, 32% patients belonged to age group 40-50 yrs and 27.5% patients belonged to 50-60 yrs collectively in both group. In the diabetic group 16, 15 and 14 patients belonged to 40-50 yrs, 50-60 yrs and 60-70 yrs age group respectively. It showed that with increasing age the prevalence of diabetes increases and this is similar to Abu Lebdeh HS et al study.¹⁸ In this study there was 60 male and 60 female so male female ratio 1:1.

This study showed that 46.6% of case group had hypertension while the control group had only 15% had diagnosed hypertension. Association of diabetes with hypertension was found to be more than three times higher compared to normal subjects. The mean SBP was 123 ± 13.10 in case group in comparison of control group had 117.85 ± 8 . In this study the mean DBP in case group was 81 ± 5.21 and the mean DBP in control group was 77 ± 6.09 , it mean this study showed that the mean systolic and diastolic blood pressure difference were significant. We found in this study that in 28 patients (case) had hypertension in comparison of control group had only 9 subjects this result is similar to Simonson DC et al.¹⁹ In another study done in Skara Health Care Centre, Sweden stated that the percentage of hypertension is greater

with NIDDM. In a comparative study where prevalence of hypertension in type 2 diabetes in referral vs primary care clinic at the Jackson Diabetes Centre and four primary care clinics was done, 78% of referral clinic and 55% of primary care clinics patients had either JNC-V stage 1 or higher hypertension or where on antihypertensive medication. These all studies results were similar to our study result.^{20,21}

In this study overweight (BMI > 25 Kg/m²) was observed in 25 cases that is 41.6% of cases in comparison of control had only 2 subjects and that is 3% of normal population. In our study 10% and 5% diabetic cases had class I obesity and class 2 obesity respectively, in comparison of normal subjects only 1 subject fell in obesity class I and no subject in class 2 obesity. This result indicates that greater BMI or obesity was present in diabetic cases opposed of normal subjects. This result is similar to R. Balamurugan et al²², by Meenu et al²³ and Raal FJ et al.²⁴

In this study we found that only 5% of diabetic cases had family history of CAD, a family history of CAD has been shown to be strong independent risk factor for CAD by the Shea S, et al study.²⁵ This study showed that family history of diabetes was present in 32% diabetic cases and family history of hypertension was present in 18% of diabetic population this result is also similar with the study Slyper and Schectman G et al which showed that increased CAD risk associated with a positive family history may be mediated by genetic effects on other risk factors such as obesity, hypertension, dyslipidemia and diabetes.²⁶

In this study we also evaluated blood sugar fasting and PP level and we found that the mean fasting blood sugar level was 7.85 ± 3.02 mmol/l in our diabetic patient. The mean PP blood sugar level was 12.79 ± 5.32 mmol/l in our case group. The 48% diabetic case group had blood sugar more than 7 and about 65% of case group had increased level of blood sugar PP level more than 11.1 mmol/l. This indicates that majority of diabetic population had uncontrolled blood sugar level thus, majority of diabetic population had increased risk of CAD. Meigs JB, et al²⁷; Mohan V²⁸, Lentzen M et al Euro Heart Survey²⁹ all these study strongly states the strong relation between dyglycaemia and cardiovascular mortality and morbidity.

In this study mean HbA1c level in men was 8.63 ± 2.61 and the mean HbA1c level in female was 7.72 ± 1.43 . In this study we found that only 9 diabetic patients (15%) had HbA1c level less than 6.3% and the majority of 53 patients (51%) had HbA1c level more than 6.3%, maximum up to 14.9%. UKPDS23 states that 1% increases in the HbA1c increases the risk of CAD by 11%, so this study also identified that majority of diabetic population had increased HbA1c level as well as increased level of CAD.¹² In our study we found maximum HbA1c level up to 14.9% that mean the patient had CAD risk increased by 94.6%.

It was observed that 2 diabetic patients (3.3%) had high level of cholesterol in comparison to control group had no subject with high level of cholesterol. Borderline high cholesterol was present in 7 diabetic patients that are about 8.5%. Multiple risk factor interventional trial (MRFIT) and

UKPDS study¹² and Menu Walia et al²³ stated that direct relationship between cardiovascular mortality and morbidity with serum cholesterol level in the diabetic group. So this result also showed our diabetic population at higher risk of CAD. Level of HDL was present in 39 patients (65%) and high level of HDL in 8 patients (13.33%). In this study as opposed to this normal subjects had low level of HDL in about 38.3% and high level of HDL in about 5% subjects. These values showed that in comparison with control group diabetic subjects had approximately double number of low HDL level. Gordon et al³⁰, Romm et al³¹, and Castelli et al³² states low HDL level is indicator of HDL signifies increased level of CAD risk. In our study we found majority of patient in case group with low HDL value in comparison of control, so our cases had greater risk of CAD.

CONCLUSION

The prevalence of non-modifiable risk factors as “age” is higher in diabetic compared with normal group. The prevalence of modifiable risk factor as hypertension is significantly present in diabetes group 46.6% in compared with control group had 15% only. The prevalence of overweight and obesity class I and II is also high with 41.6% in comparison to normal subjects which was only 3-5%. There was also high prevalence of family history of CAD, diabetes and hypertension 5%, 32% and 18% respectively. So, it is recommended for early screening of coronary risk factors in diabetic patients as well as normal subjects who are at increased risk.

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