PREVALENCE OF CARDIOVASCULAR RISK FACTORS IN TYPE-II DIABETIC PATIENTS WITH IHD

Muhammad Shahid Khan, Shaheen Moin

Combined Military Hospital Gujranwala, Fauji Foundation Hospital Rawalpindi

ABSTRACT

Diabetes mellitus (DM) is more prevalent in Asians as compared to White Caucasians. People with diabetes have a risk of IHD two to five times greater than that in the non-diabetic individuals. There is limited data available in the literature about IHD and its association with the known risk factors in Pakistani diabetic population. A comparative study was carried out in Military Hospital (MH) and Armed Forces Institute of Cardiology-National Institute of Heart Diseases (AFIC-NIHD) Rawalpindi on 132 known diabetics with and without IHD to establish the relative prevalence of hyperglycemia, dyslipidemias, hypertension and smoking among diabetics with IHD as compared to those who did not develop IHD. Data was collected from the patients attending OPDS and detailed scrutiny of hospital records of admitted cases. The patient population was divided into two groups depending upon the presence or absence of IHD i.e., group A (n=67) and B (n=65) respectively. Both the groups were studied independently for various risk factors including glycemic control, lipid profile, hypertension and smoking habits. The results obtained in each group were compared with each other to find out the statistical significance of each risk factor. The mean fasting glucose was 150.92 + 42.47 in group A (DM + IHD) and 131.64 + 46.21 in group B (DM alone). Poor glycemic control in group A was positively correlated with IHD ($p < 0.01$). Serum triglycerides level was higher in group A (DM + IHD) than in group B (DM alone) and the results were statistically significant ($p=0.02$). The value of serum cholesterol level was higher in group A (195. 73 + 46.22) than in group B (183.55 + 40.66) but the results were statistically insignificant ($p > 0.05$). The lower HDL level in group A was positively correlated with IHD ($p=0.01$). Similarly the higher prevalence of smoking and hypertension in group A was positively associated with higher incidence of IHD. ($p= 0.04$ and 0.043 respectively. Overall results have clearly shown that the prevalence of these risk factors is higher in diabetics with IHD as compared to those without IHD. Therefore, it is concluded that the prevalence of conventional cardiovascular risk factors is quite significant in Pakistani diabetic population.

Keywords: Dyslipidemia, hyperglycemia, hypertension, smoking

INTRODUCTION

Diabetes mellitus is 8th health related cause of death all over the world and fourth most common cause of death in the United States. Diabetes mellitus is one of the leading public health problems globally and especially in the industrialized world, and it has a profound effect on the cardiovascular system affecting nearly 100 million cases worldwide [1]. Diabetes mellitus is a chronic hereditary or acquired metabolic disorder characterized by persistent hyperglycemia due to relative or absolute deficiency of insulin. This condition is invariably associated with an altered carbohydrate metabolism leading to secondary alteration of fat, protein, water and electrolyte metabolism.

Ischaemic Heart Disease (IHD) is a syndrome, which remains a major cause of death worldwide. It includes Angina Pectoris, Acute Myocardial Infarction (AMI) and sudden cardiac death. As per WHO report 55/100,000 of American die of IHD and 45.3% of all deaths in USA are due to IHD[2]. However, in UK 25,000

Correspondence: Maj Muhammad Shahid Khan, Combined Military Hospital, Gujranwala Cantt.

patients suffer from AMI annually [3], with an over all mortality three folds greater in diabetics.

The major risk factors that predispose to atherosclerosis and resultant IHD have been identified by means of a number of prospective studies in well established population groups like Framingham study and Multiple Risk Factor Intervention Trial[4], i.e Dyslipidemia (hypercholesterolemia, high level of LDL, hypertriglyceridemia and low level of HDL[5], Hypertension[6], Cigarette smoking[7] and Diabetes Mellitus[8].

Ischemic heart disease (IHD) accounts for as much as 75% of all mortality in type II diabetes [9]. In the United Kingdom prospective diabetes study [3] after 9 years of follow-up, IHD events were 70 times more frequent than other diabetic complications. The annual average mortality rate is double than that in non-diabetic people [9].

The study was designed to investigate the correlation of the most prevalent conventional risk factors in diabetic population of Pakistan i.e. dyslipidemia, hypertension and smoking and to support the theory that DM is a major independent risk factor in the development of IHD among diabetics in terms of hyperglycemia and other risk factors.

MATERIAL AND METHODS

Data Collection

A case control study was carried out at Military Hospital and Armed Forces Institute of Cardiology/National Institute of Heart Diseases Rawalpindi (AFIC-NIHD) from 1999 to 2001. Data was collected from out patient departments as well as hospital records.

Case Selection

Patients with age ranging between 40 to 55 years and diagnosed to have Type II DM with and without IHD, were selected for this study. Those diabetics were preferably selected who had the duration of DM 15 years or less because the longer the duration of the disease, the greater is the incidence of the associated risks and complications.

A total of 132 subjects who met with the following inclusion/Exclusion criteria were selected for further study.

Inclusion Criteria

- Biochemically proved diabetics with or without history of IHD
- Age > 40 years < 55 years
- Patients on oral Hypoglycemic agents

Exclusion Criteria

- Age < 40 and > 55 years
- Type- I DM
- History of Diabetic Ketoacidosis
- Known cases of Hyperlipidemia
- Patients with advanced liver or renal disease or malignancy were excluded from the study.

The selected patients were divided into two age and sex matched groups depending upon the presence or absence of IHD.

Group A (number = 67)

Patients having Type- II DM and IHD

Group B (number = 65)

Patients having Type- II DM but no evidence of IHD.

Study Protocol

The patients were studied through a structured questionnaire proforma and following parameters were recorded for each subject.

Age (Years), sex of the patient , weight in Kilograms (indoor clothes), height in centimeters without shoes, occupation of the patient , duration of DM in years, duration of IHD, history of Hypertension, smoking habits , family history of DM, treatment history, socio economic class, body mass index (weight in Kgs / Height in m2.), blood pressure in mmHg.

Laboratory Parameters

The laboratory parameters used and methods employed for each are given in table-I

Diabetes mellitus is defined as Fasting plasma glucose of 126 mg/dl or greater. Fasting is defined

as no caloric intake for at least 8 hours preceding the measurement. A fasting glucose level of 110 mg/dl but less than 126 mg/dl defines IFG.

Hypertension is defined as systolic BP > 140 mm Hg and/or Diastolic B.P > 90 mmHg.

IHD is evidenced by documented clinical history of angina pectoris or myocardial infarction, or diagnosed on resting ECG with the following criteria:

a. Significant Q waves (> 40 ms) consistent with a prior MI
b. Resting ST segment depression (> 1 mm in limb leads and 2 mm in chest leads),or
c. T wave inversion suggestive of myocardial ischaemia.

The diagnosis of IHD was also supported by positive Exercise Tolerance Test (Bruce Protocol).

Statistical Analysis

The data was computerized and analyzed using SPSS version 7.5. The results are expressed as mean + SD. The difference between the groups was assessed by chi-square test, and student's two tailed test for independent samples.

RESULTS

A total of 132 diabetic patients comprising 94 males (71.2%) and 38 females (28.7%) with the age ranging from 40 to 60 years were studied. One sixth of the patients were overweight. Depending upon the presence or absence of IHD, the selected subjects were divided into two groups i.e.,

- Group A (n= 67) Diabetics with IHD
- Group B (n=65) Diabetics without IHD

Both the groups were studied independently for various risk factors including fasting glucose level, serum cholesterol, serum triglycerides, HDL, hypertension and smoking. The mean values thus obtained were compared with each other in two groups to analyze the statistical significance of each parameter studied.

Significant results were obtained. Mean values of study parameters are shown in Fig.-I. The levels of fasting glucose and triglycerides were significantly higher in group A (DM+IHD) as compared to those in group B (DM alone) i.e., p: 0.01and 0.02 respectively. The level of HDL was significantly lower in group A than in group B (p: 0.01). The mean level of serum cholesterol was higher in group A (mean value 195 .73 + 46.22) than in group B (183.55 + 40.66), though the difference was statistically not significant (p > 0.05).

There were 31 hypertensives in Group A whereas Group B had only 19 hypertensives. There were 33 smokers in Group A and 21 in Group B. The presence of hypertension and smoking was positively correlated with IHD in our study i.e., p: 0.043 & p: 0.04 respectively. Mean values of different parameters and their comparisons are shown in table II.

DISCUSSION

The prevalence of IHD amongst Type II Diabetics has shown variation in different parts of the world. An incidence of 75% has been reported recently from the western countries [9]. Approximately about 15 – 25 % of the patients with heart failure are diabetics [10]. The annual average mortality rate of 5.4% in diabetic adults is double than that in non-diabetic people [8].

National US survey data found a prevalence of both fatal and non-fatal IHD events in adults with type II diabetes of about 2-20 times higher than rates in similarly aged non-diabetic adults [8]. In the Multiple Risk Factor Intervention Trial, men with diabetes alone had an absolute excess risk of IHD death of about 25 per 10,000 person-years; diabetes and any one of hypertension, hypercholesterolemia, or cigarette smoking increased this risk to 47 per 10,000 person-years; and with all of these risk factors the risk was 78 per 10,000 person-years[4]. In a local study 9% of the 500 diabetics had objective evidence of IHD[11]. In our study 50.7% diabetics had evidence of IHD. This prevalence is higher than that reported from Lahore. The possible reason of such higher prevalence of IHD would be that the present study was conducted mostly at AFIC.

Our diabetic patients with IHD showed poor glycemic control (p: <0.05) which is also supported by two other local studies done on Pakistani diabetic population by Raza [11] and Malik [12]. Hyperglycemia contributes to accelerated atherogenesis and to increased clinical IHD events through various mechanisms e.g. glycation of proteins and lipoproteins (LDL, HDL)

etc. Incidence of heart failure is correlated with HbA1C levels as shown by UKPDS and other studies [13,14].

The total cholesterol was significant univariate predictor of coronary mortality in the Paris Prospective Study [15]. Pooling project group [6] has also clearly labeled hypercholestrolemia as a risk factor. However in our study although the mean cholesterol level in group A (DM + IHD) was higher (195.73 + 46.22) than in group B (DM alone) 183.55 + 40.66) but the results were statistically insignificant (p: 0.11). Similar observations were made by Laackso [16]. Poor correlation was observed between serum lipids and glycemic control among Pakistani diabetics in a study from Lahore [11,12]. Several possibilities can be offered to explain the weak association of hypercholestrolemia as a risk factor for IHD in the present study, the most important being the dietary awareness or use of lipid lowering drugs among patients being treated at AFIC. Another possible explanation may be the genetic factors.

The significance of increased plasma triglyceride level as a risk factor for IHD has been controversial. Some studies show direct association of high triglycerides levels with atherogenecity[17]. But other studies show the association of atherogenecity of triglycerides via decreased HDL levels. In our study population Type-II DM patients with IHD had higher levels of total triglycerides (p: 0.02) and lower levels of HDL (p: 0.01) than patients with out IHD. This is in accordance with other international studies [16-19]. The results of local studies are also controversial. In a study published in Pakistan Journal of Medical Research [20], hypertriglyceridemia was found around 42%, where as study by Malik[12] found minimal elevation of cholesterol and modest increase in triglyceride levels among diabetics. Decreased HDL level is also an important risk factor for IHD where as the role of increased triglycerides as an independent risk factor is still being debated[21]. Larger studies in patients with type II DM have also found low HDL cholesterol and higher triglycerides while LDL cholesterol is usually normal [22]. A recent study from Saudi Arabia showed high prevalence of dyslipidemia in type II DM [23].

Hypertension is a well established major risk factor for CVD [24]. It increases risk of both IHD and stroke and contributes to diabetic nephropathy [25]. Hypertension showed significant positive

Table-1: Laboratory parameters and methods used

Parameter	Method	Reference Value (mg/dl)
Fasting plasma Glucose	Hexokinase method	≥126
Fasting Plasma Cholesterol	CHOD –PAP	≥200
Fasting Plasma HDL	Precipitation	≥35
Fasting plasma triglyceride	Kinetic UV (Enzymatic)	≥200

Table-2: Comparison of means in the study groups

Variable	Group A. (n=67)	Group B (n=65)	P. value
Fasting Glucose	150.92 ± 42.47	131.64 ± 46.21	0.01
Triglycerides	203.97 ± 45.87	174.86 ± 119.53	0.02
Cholesterol	195.73 ± 46.22	183.55 ± 40.66	0.11
HDL	42.44 ± 3.91	44.00 ± 3.50	0.01

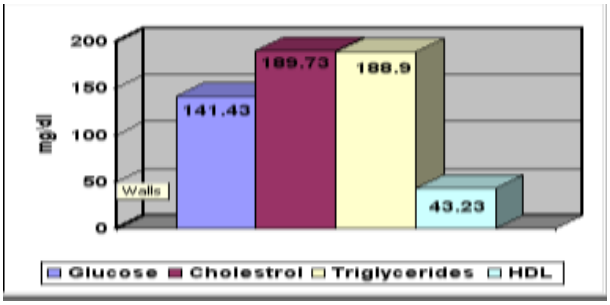

Fig. 1: Mean values of study parameters in study population

corelation with IHD in our study (p: 0.04). Hypertension and DM co-exist more frequently than would be estimated from their relative prevalence in the general population [26,27]. The overall prevalence of hypertension in our diabetics with IHD was 46.2% and diabetics without IHD were found to be 29.2%. The prevalence rate in our study is higher than the study done in Lahore which shows 26.40% diabetics to be hypertensives [28].

Cigarette smoking has been proven as an independent modifiable risk factor for IHD [29].Cigarette smoking appears to be the most important risk factor for IHD in countries where the incidence of IHD is higher [30] even the passive smokers may also be at risk. Our study showed smoking to be positively co-related with IHD p: 0.04. In both the Framingham study and British regional Heart study, the rate of IHD in smokers in about 03 times that of non-smokers [31].

CONCLUSION

Our study showed a clear picture of conventional risk factors i.e. hyperglycemia, dyslipidemia, hypertension and smoking in Pakistani diabetic population. Thus, we can conclude that the higher prevalence of these risk factors was positively correlated with IHD in our study population.

Randomized trials show that control of common modifiable risk factors like hypertension, hypercholesterolemia [32] and smoking reduces the risk of IHD. Because of the strong correlation between hyperglycemia and IHD in type-II diabetes, aggressive control of established IHD risk factors, with particular emphasis on aggressive glycaemic control, is likely to produce the greatest reduction in IHD among these patients. As the contributions of coronary heart disease risk factors specific for type-II diabetes become more clearly defined, additional avenues to reduce the risk of IHD are likely to become available.

RECOMMENDATIONS

On the basis of present study and review of literature on the subject, the following recommendations are made:-

a. After reviewing the literature it was found that a very limited work has been done on the subject in our diabetic population. Countrywide studies are required to determine the prevalence of these risk factors in our diabetic population.

b. Efforts should be made to educate the general public at government level for the primary prevention and modification programs of these risk factors at national level.

REFERENCES

1. Harris M, Hadden, W.C, Knowler W.C, Bennett PIP prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in US population aged 20-74 year **Diabetes. 1987; 36:523-34.**

2. WHO-MONICA project: Myocardial infarction and coronary deaths in the WHO-MONICA project: Registration procedure evens rates and case-fatality rates in 38 populations from 21 countries in four continents **Circulation 1994; 90:583.**

3. Turner R., Gull G Holman R., United Kingdom Prospective Diabetes study, 7 to 9 years update of randomized, controlled Trial on the effect of improved metabolic control on complications in non-insulin dependent diabetes mellitus **Am Inter Med:1996:136-45**

4. Stamler J, Vaccaro O, Neaton J, D Luenther et al , Diabetes other risk factors and 12 year cardiovascular mortality for men screened in the multiple risk factor Intervention trial. **Diabetes Care: 1993. 16. 434-44.**

5. Gordon DJ, Probsfield JL, Garrison RJ, Neaton JD, Castelli W.P et al High Density lipoprotein cholesterol and cardiovascular disease; four prospective American Studies, **Circulation 1989: 79 : 0-15.**

6. Pooling project (final report) relationship of blood pressure, serum cholesterol, relative weight and ECG abnormalities to incidence of major coronay events **J Chronic Dis 1978; 31: 201-306.**

7. Kannel WB, McGee DL. Diabetes and glucose tolerance as risk factors for cardiovascular disease the Framingham study **diabetes care. 1979: 2: 120-26.**

8. Barrentt, Connor E, Ciriqui MH, Khlaumber MR, Hold Brook MJ, Diabetes and hypertension in a community of older adults. **Am J Epidemiol. 1981; 1113: 276-284.**

9. Geiss LS, Herman W.H., Smith P. J. Mortality in non-insulin – dependent diabetes. In Harris M (Ed) Diabetes in America 2nd (Ed) Bethosda: **National Institute of Health, 1995: 233-55.**

10. Ryden L, Armstrong PW, Cleland JG, Horowtz JD, Massie BM, Packer M, Poole-Wilson PA: Efficacy and safety of high-dose lisinopril in chronic heart failure patients at high cardiovascular risk, including those with diabetes mellitus. Results from the ATLAS trial. **Eur Heart J 2000, 21:1967-1978.**

11. Raza Malik. Study of B.P., Serum Lipids, Cholesterol and Triglycerides in diabetic patients. **Pak J Med Res 1995: 34(4).**

12. Mobashir Saeed Malik: Diabetic control and serum lipids in Diabetics attending a Pakistani hospital. The Specialist, **1997; 13(3): 211-17.**
13. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR: Association of glycaemia with macrovascular and microvascular complications of type II diabetes (UKPDS 35): prospective observational study. **BMJ 2000, 321:405-412.**

14. Iribarren C, Karter AJ, Go AS, Ferrara A, Liu JY, Sidney S, Selby JV: Glycemic control and heart failure among adult patients with diabetes. **Circulation 2001, 103:2668-2673.**

15. Fontbonne A, Exchwege E., Cambien F. et al Hypertriglyceridemia as a risk factor of IHD mortality in subject with impaired glucose tolerance or diabetes. **Diabetologia 1989, 32: 300-04.**

16. Laakso M., Letho. S, Penttila I., Pyorola K. Lipid and lipoproteins predicting coronary Heart disease mortality and morbidity in patients with NIDDM **Circulation 1998: 88, 1421-29.**

17. Drexel. H, Franz W, Amann, Berant J, Rentsch K, Candinans. R, Muntwyler Luclhy et al "Plasma TG and the lipoprotein CHO fractions are independent predictors of the extent of coronary atherosclerosis. **Circulation 1994; 90, 2230-35.**

18. Cowie, C.C. Howard B. V., Harris MI "Serum lipoproteins in African, Americans and whites with NIDDM in the US populations **Circulation 1994; 90; 1185-1193.**

19. Stern MP, Haffnar SM, Dyslipidemia in type II diabetes implications for therapeutic intervention. **Diabetes Care 1991: 14144-14159.**

20. Haider Z, Usman.S, Jabeen M, bano KA, Obaid S, and Fayyaz. A Profile of hyperlipidemia in various patient groups and controls.

21. Austin MA, Plasma triglyceride as a risk factor for CHD. The epidemiologic evidence beyond. **Am. J. Epidemiol 1989; 129: 249-59**
22. Brown W V. Lipoprotein disorders in DM. **Med Clinics of North Am, 1994; 31: 126-3.**

23. Mohsin AF, El. Hazmi. Lipids and related parameters in Saudi type II DM patients **Ann Saudi Med .1999; 19 (4) 304-307.**

24. Wilson PW. Diabetes mellitus and coronary heart disease. **Am J Kidney Dis. 1998; 32: S89-S100.**

25. Nelson RG, Pettitt DJ, Baird HR, Charles MA, Liu QZ, Bennett PH, Knowler WC. Pre-diabetic blood pressure predicts urinary albumin excretion after the onset of type II (non-insulin dependent) diabetes mellitus in Pima Indians. **Diabetologia. 1993; 36: 998 – 1001.**

26. Christie L.G. Jr and Conti. CR: Systemic approach to evaluation of angina like chest pain. Pathophysiology and clinical testing with emphasis on objective documentation of myocardial ischemia. **Am Heart J. 102:897, 1981.**

27. Kaplan NM, Lieberman E. Clinical hypertension. 3rd ed. Baltimore: **Williams and Wilkins, 1982:2.**

28. Haider Z, Bano KA, Fayyaz-ud- Din. Hypertension: a clinical study in Lahore 1972-79. Lahore: PMRC research Center, **J Fatima Jinnah Medical College, 1980: 152.**

29. Craig WX, Palmoki GE, Haddow J. Cigarette smoking serum lipid and lipoprotein concentration. An analysis of published data. **Br. Med. J. 1989; 298: 784.88.**

30. Canner PL, Berge KG, Wenger NK et al for the coronary drug projects research group fifteen year mortality in coronary drug project patients. Long term benefits with niacin **J Am Coll Cardiol 1986; 6: 1245.**

31. Shaper AG, Pocock SJ, Walker M, Philips AM, Whitehead TP, Macfarlane PW. Risk factors for ischaemic heart disease: the prospective phase of the British Regional Heart Study. **J Epidemiol Community Health 1985; 39: 197-209.**