INCIDENCE OF ISCHEMIC HEART DISEASE IN PATIENTS WITH NON INSULIN DEPENDENT DIABETES MELLITUS

DR. MUHAMMAD HANIF NAGRA
F.C.P.S (Med)
Senior Registrar M-l
Allied Hospital Faisalabad.

DR. MUHAMMAD SHAHID
F.C.P.S (Med)
Medical Unit -l
Allied Hospital Faisalabad.

DR. AHMAD BILAL
F.C.P.S. (Med)
Assistant Professor of Medicine M-l
Allied Hospital Faisalabad.

Dr. Khalid Amin, MBBS FCPS
Assistant Professor Medical unit II
Allied Hospital Faisalabad.

ABSTRACT ... drhanifnagra@hotmail.com **Objective:** To find out the incidence of IHD in patient with NIDDM. To study the pattern of clinical presentation of IHD in diabetic patient. To create awareness in the population that IHD is more prevalent in diabetic patient. **Design:** Prospectus stud**y Setting:** Allied Hospital Faisalabad: **Period:** Apr 2003 to Sep 2003 **Material & Methods:** One hundred with previously diagnosed none insulin dependent diabetes mellitus (NIDDM) investigations of duration of their illness were studies. Among 100 patients , 78 were male and 22 were female. **Results:** Among the 100 patients studied , 17 had evidence of IHD and out these 5 (29.5%) were male and 12 (70.5%) were female. Amongst the patient having IHD, 5 (29.5%) had typical symptoms of angina with or with out ECG change consistent with IHD. Another 6 (35%) had atypical symptoms of IHD with ECG changes. Typical changes of IHD was found in 6 patients. **Conclusion:** The incidence of IHD is higher in diabetic patient as compare to general population. The presentation of IHD is often atypical in diabetic patients.

Key words: Ischemic Heart Disease, Diabetes Mellitus

INTRODUCTION

Patients with diabetes mellitus have a higher prevalence of atherosclerotic heart disease and a higher incidence of myocardial infarction than the general population. Diabetic patients also have several hematologic, rheomatologic and metabolic abnormalities not present in their non-diabetic counterparts that may predispose them to atherosclerotic plaque rupture, intra luminal thrombosis, and consequently may lead to the formation of morphologically complex plaques and the development of acute coronary syndromes like unstable angina and myocardial infarction [1,2,3,17,21,30]

The susceptibility of the diabetic patients to atherosclerosis is due to several factors including[23]

- Dyslipidemia
- Hypertension
- Hyper-insulinemia
- Increased platelet adhesiveness

Diabetic dyslipidemia is characterized by raised serum VLDL Triglycerides and lowered HDL cholesterol[13,14,16,29].

Hypertension is more common in persons with diabetes, being found in over 50% of diabetic patients over 45 year old[1]. The prevalence of hypertension and nephropathy is especially high in diabetic women and is a frequent accompaniment than in general population[9,17,32]. This increase probably is due, atleast in part, to the associated hypertension, which greatly accelerates atherosclerosis.

Hyperinsulinemia, particularly common in patients with NIDDM with insulin resistance, appears to be a risk factor for atherogenesis[12,15]. Diabetic patients have increased platelet adhesiveness and response to aggregating agents. These changes are also likely to favor atherogenesis. The relation of asymptomatic hyperglycemia to cardiovascular risk has been addressed by various studies including the Paris Prospective study, the Tecumseh Study, and the chicago Heart Association Detection Project[20]. Theses studies strongly suggest that asymptomatic hyperglycemia is an independent risk factor for IHD. Occlusive thrombus formation is likely a dynamic process that depends on a balance between those factors that favor clotting and those that oppose it. In diabetes, abnormalities relating to platelet function, coagulation, fibrinolysis, and endothelial function favor intraluminal thrombosis[31]. Platelet aggregation is an essential step in occlusive thrombus formation. Spontaneous and induced platelet aggregation has been shown to be higher in persons with diabetes than in those without diabetes and correlates with an increase in cardiovascular events[3,8,11].

CLINICAL PRESENTATION OF IHD IN DIABETIC PATIENTS

Ischemic heart disease may become manifest in diabetic patients in its usual forms of stable, unstable or variant angina and symptomatic myocardial infarction. However, these patients are more likely than non-diabetic patients to have silent or unrecognized ischemia or infarction or to have atypical symptoms of IHD.

SILENT MYOCARDIAL ISCHEMIA AND INFARCTION

There are two varieties of silent myocardial ischemia:

Type 1:
It occurs in patients with severe coronary artery disease who never experience angina. Even myocardial infarction may be painless in these subject. Both the patient and the physician remain unaware of the presence of IHD until a fatal event ensues or an old infarction is detected on routine ECG.

Type 2 :
Occurs in patients having usual forms of stable, unstable or variant angina. These patients experience angina only during some of the episode of ischemia, the remainder being silent.

Not all cases of apparently silent IHD are truly silent. In various instances the symptoms may be so mild or atypical that they either go un-noticed or Ignored by the patients. These should better be called unrecognized ischemia or infarction.

Silent ischemia is present in about 5% of the asymptomatic population and in about a third of those patients who remain asymptomatic after a mayocardial infarction. Evidence of silent ischemia is also found in about one third of patients having usual forms of angina[6,7.]

Varioys studies have shown that about 30-40% of myocatdial infarctions are silent or clinically unrecognized. In the framingham Study, 25% of the infarctions were silent, half of thee being truly silent

and the other half being unrecognized. The study of the Western Collaborative Group found a 30% rate of unrecognized infarction.

Unrecognized infarction tends to be more common in persons with diabetes. Bradley and Schonfeld reported that 42% diabetic patients have painless infarction compared with 6% non-diabetic patients[4]. Cabin and Robert obtained similar figures in anther study in 1982[5]. In addition to silent infarction, persons with diabetes may also lack angina during ischemia. The incidence of painless ST depression during exercise tolerance tests in diabetic patients is more that double that in non-diabetic patients i.e. 75% vs. 35%[10,12]. Nesto et al. Demonstrated that angina is less common in diabetic that non-diabetic patients during ischemia assessed by exercise thallium scintigraphy[18].

Patients with diabetes who do experience angina become aware of their symptoms later in the course of ischemia that do patients without diabetes. The delay in time from the onset of ST depression to angina may be twice as long in patients with diabetes than in patients without diabetes and correlates with the extent of autonomic nervous dysfunction. Neuropathy of efferent autonomic pathways also may indicate damage to afferent autonomic fibers responsible for the transmission of sensory impulses relating to perception of myocardial ischemia. Both the presence of histological damage to cardiac afferent nerve fibers in persons with diabetes and physiologic evidence of damage to afferent and efferent nerves suggest that neuropathy involving these fibers exist and may play a role in blunting ischemic pain.

ATYPICAL SYMPTOMS OF IHD IN DIABETIC PATIENTS

When diabetic persons seek medical advice because of myocardial infarction, they frequently do so because of atypical symptoms. Accurate diagnosis of infarction based on history may therefore be difficult. Atypical symptoms such as confusion, Dyspnea, fatigue, palpitation, sinking of heart, or nausea and

vomiting may be the presenting complaint in 32-42% of diabetic patients with AMI, as compared with 6-15% of non-diabetic patients[19]. In some cases such symptoms may mimic those associated with either hypo- or hyperglycemia and may lead to diagnostic confusion..

The above-mentioned facts may cause a delay in starting appropriate treatment in patients with myocardial infarction. Therefore, a high index of suspicion of infarction is necessary when diabetic patients present with such atypical symptoms.

AIMS & OBJECTIVES

Diabetes mellitus is one of the major risk factor for the development of ischemic heart disease. Diabetic patients' exhibits more severe involvement of their coronary arteries and are affected at a younger age as compared to general population[24]. Similarly, IHD is more common in diabetic females of reproductive age as compared to their non-diabetic counterparts. Patients with diabetes may not experience typical chest pain during an ischemic event which may be truly silent or asymptomatic, or may produce only mild symptoms and go unrecognized[5].

Diabetic patients may also present with atypical symptoms of IHD such as sinking of heart, dyspnea, palpitations, sweating, and suffocation or unexplained fatigue. It is important to realize that these symptoms may indicate IHD to avoid un-necessary delay in stating appropriate treatment.

The aims of study are:
To find out the incidence of IHD in patients with NIDDM,

To study the pattern of clinical presentation of IHD in diabetic patients i.e.,

1.   With typical symptoms.

2.   With atypical symptoms.
3.   Evidence of silent ischemia, and
4.   Evidence of myocardial infarction.

To create awareness in the population that IHD is more prevalent in diabetic patients. This will help to reduce the morbidity and mortality associated with diabetes as it has been found that by maintaining euglycemic state a diabetic can have normal life.

MATERIALS & METHODS

SET UP
This study was carried out at the diabetic clinic of Allied Hospital, Faisalabad, which is the teaching hospital attached to Punjab Medical College, and drains a large area around apart from the city. The diabetic clinic is situated in the outpatient of this hospital and is run on daily basis from 10.00 am to 2.00pm.

STUDY DESIGN
Consecutive 100 patients with previously with previously diagnosed non-insulin dependent diabetes mellitus (NIDDM), irrespective of the duration of their illness, were studied. These patients were registered between April 2003 & September 2003 at the diabetic clinic.

The study comprised of three steps as follows:

1   A detailed history was taken from all patients.
2   A resting 12- lead ECG of all patients was taken and studied for evidence of IHD.
3   Evidence of IHD was looked for in previous medical record where it was available.

Diagnosis of IHD was based on the following criteria:

1.   History of typical symptoms of angina.
2.   History of atypical symptoms of IHD like sinking of heart, dyspnea, Palpitations, Sweating, suffocation or unexplained fatigue, along with ECG changes consistent with IHD.
3.   Symmetrical T wave inversion in two or more contiguous chest leads or lead aVL, and I or two of the three inferior limb leads i.e. II, III and aVF, in the resting ECG.

ST segment depression > 2mm in chest leads and > 1mm in the limb leads as above.

Pathological Q waves i.e. >0.04 second in duration, or depth > one third of the height of corresponding R waves in two or more contiguous chest leads or lead I and aVL or two of the three inferior limb leads i.e. II, III & aVF.

Documents showing previous admission in hospital with unstable angina or acute myocardial infarction (AMI).

Documents showing previously taken ECGs having changes consistent with IHD as described above. ECGs may or may not have been recorded during chest pain.

Any investigation already done and showing positive evidence of IHD e.g., exercise tolerance test, thallium scan or adenosine perfusion scan, and coronary angiography.

Previous history of coronary angioplasty or coronary artery bypass grafting (CABG).

The relationship between IHD and risk factors other than diabetes mellitus was not studied.

RESULTS

AGE DISTRIBUTION
The 100 patients selected from the study were between 35 & 85 years old. Majority of them belonged to 35-50 year age group (Table I & III).

DURATION OF ILLNESS
Although patients of NIDDM were included in the study irrespective of duration of their illness, the duration was asked from every patient to examine its relationship with the incidence of IHD.

Table-I. Age distribution of patients.	
Age Group (Years)	**% Age**

35-40	24
41-45	14
46-50	24
51-55	6
56-60	13
61-65	9
66-70	6
71-75	2
76-80	1
81-85	1
Total	**100**

The 100 patients included had disease from 1 month to 30 years. (Table II)

Table-II. Duration of illness of 100 NIDDM patients

Duration of Illness (Years)	% of total
<1	23
2-5	40
6-10	28
11-15	5
16-20	3
21-25	0
26-30	1
Total	**100**

SEX DISTRIBUTION
Out of 100 patients, 78 were female and 22 were male (Table III)

INCIDENCE OF IDH IN NIDDM PATIENTS
Amongst the 100 patients studied, 17 had evidence of IHD (Table IV)

Table III. Age and sex distribution of 17 Patient with IHD

Age (Years)	Male	Female	Total	%age
35-40	0	4	4	23.5
46-55	2	6	8	47
56-65	3	2	5	29.5
Total	5	12	17	

Table IV. Incidence of IHD in relation to duration of diabetes mellitus

Duration of Diabetes (Years)	No. Of Diabetic Patients	No. Of Diabetic Patients with IHD %
0-5	63	6(9.5%)
6-10	28	7(25%)
11-15	5	3(60%)
16-20	3	1(33.3%)
21-30	1	0
Total	**100**	**17**

out of these 5 (29.5%) were male and 12 (70.5%) were female. (Table III & IV). Amongst the patients having IHD, 5 (29.5%) had typical symptoms of angina with or without ECG changes consistent with IHD. Out of these, 2 were male and 3 were female. Another 6 (35%) patients had atypical symptoms of IHD with ECG changes Consistent with IHD. Out of these one was male and 5 were female. Two patients (11.7%), 1 male and 1 female, had evidence of myocardial infarction on resting ECG but they did not have any symptoms of IHD. Four (23.5%) patients had previous record showing hospitalization with myocardial infarction. Out of these one was male and 3 were female

Table IV Typical symptoms of IHD were found in 6 patients. Majority of them had more than one symptom and in one patient, dyspnea was the only symptom. Moreover, 5 patients (29.5% of those who had IHD) had dyspnea apart from other atypical symptoms.

The relation of duration of diabetes mellitus and the incidence of IHD is shown in table 7. There is a rise in the incidence with each increment in the duration of diabetes except in the group with the duration above 16 years. This discrepancy may be due smaller number of patients in this group.

Out of 17 patients who had IHD, 15 (88%) had changes in their resting ECG. Nine patients had T wave changes consistent with IHD, while 5 had pathological Q waves. One patients had both T wave and Q waves. Inferior wall ischemia was found in 6 patients. Other 3 patients had anterolateral wall ischemia. Amongst patients who had myocardial infarction (M.I), anterior wall was one frequently involved (4 out of 6) as compared to inferior wall alone (1 out of 6). One patient had inferolateral wall myocardial infarction.

DISCUSSION

Ischemic heart disease (IHD) is found with greater frequency amongst patients with diabetes mellitus as compared to general population. However, its incidence shows variations in different parts of the world. An incidence over 40% was reported from the Western countries in older studies (4). In a study conducted a the diabetic clinic, Mayo hospital, Lahore, from 1987 to 1989, 1786 cases of diabetes of which more than 82% had NIDDM, were analyzed. IHD was found in 14% of these patients[22]..

In another study conducted at the diabetic clinic of Fatima Jinnah Medical College Lahore, from 1972 to 1976, 1000 patients of diabetes were analyzed. IHD was found in 8.5% of these patients[25].

In our study, 17% of the patients with NIDDM had evidence of IHD. Although it is comparable to other local as well as international studies, the incidence may be even higher because of two reasons.

First, there were a few patients who had atypical symptoms of IHD like dyspnea, sinking of heart, palpitations and suffocation etc. but their ECGs were normal. These patients were not considered to have IHD, though the possibility IHD cannot be ruled out

in these patients without further investigation.

Second, there was the marked preponderance of female patients in my study. This was because of the fact that the diabetic clinic is open during morning hours when it is difficult for male patients to attend the clinic. The incidence of IHD increased with increasing duration of diabetes. Unrecognized myocardial infarction tends to be more common in persons with diabetes as compared to general population[5,26,27,28].

In our study 6% of diabetic patients had evidence of myocardial infarction and out of these 33% had unrecognized infarction. Similarly patients with diabetes often present with atypical symptoms of IHD. In this study such patients were considered as cases of IHD only if they had ECG change consistent with IHD. Thus, out of all those diabetes mellitus makes females of reproductive age more likely to develop IHD as compared to their non-diabetic counterparts. In our study 12 females had IHD. Out of these, 8 (66%) belonged to reproductive age group.

CONCLUSION

*   The incidence of IHD is higher in diabetic patients as compared to general population.
*   The presentation of IHD is often atypical in diabetic patients.
*   Unrecognized myocardial infarction occurs more frequently in diabetic patients as compared to general population.
*   The risk of developing IHD increases with an increase in the duration of clinical diabetes mellitus.
*   IHD is more common in diabetic female of reproductive age as compared to their non-diabetic counterparts.

REFERENCES

1.   Assmann G, Schulte H. **The Prospective Cardiovascular Munster (PROCAM) Study: Prevalence of hyperlipidemia in persins with hypertension and / diabetes Mellitus and the relationship to coronary heart disease**. Am Heart J

116:1713, 1998.

2. Adam D T, Anthony W N. **Coronary artery disease. Essentials of Cardiology**, 2nd edition. 5:107, 1993.

3. Breddin HK, Krazywanelc HJ, Althoff, et al. **Platelet aggregation a risk factor in diabetes**.Horm Metab Res Suppl. 15:63, 1985.

4. Bryfogle JW, **Bradley RF Vascular complications of diabetes mellitus. A clinical study.** Diabetes, vol 6:159, 1957.

5. Cabin HS, Roberts WC. **Comparison of patients with symptomatic & silent myocardial infarction**. Am J card. 50:677, 1982.

6. Cohn PF. **Silent myocardial ischemia in patients with a defective anginal warning system.** Am J Card, 45:697, 1980.

7. Epstein SE, Palmer ST, Paterson RE. **Evaluation of patient after acute mayocardial infarction.** N Enkl J Med 307:1487, 1982.

8. Fuster V, Cohen M, Halperin J. **Aspirin in the prevention of coronary disease.** N Engl Med 321:183, 1989.

9. Gomez Marin, et al. **Improvement in long term survival in patients hospitalized with AMI, 1970-1980.** The Minnesota Heart Survey. N Enkl J Med 316:1353, 1987.

10. Griffin BA, Freeman DJ, Tait GW, et al. **Relative contribution of small, dense LDL to coronary heart disease risk.** Atherosclerosis 106:241, 1994.

11. Janet WR, Joan EM, Charles H. **The primary prevention of coronary heart disease in Woman.** N Engl J Med 332:1758-63, 1995.

12. Jean PD, Benoit L, Gilles RD, et al. **Hyperinsulinemia as an independent risk factor for IHD.** N Engl J Med 334:952-55, 1996.

13. Karpe F, Hamsten A. **Postprandial Lipoprotein metabolism and Atherosclerosis.** Curr Opin Lipidology 6:123-29, 1995.

14. Klein R, Klein BEK, Moss Se. **Relation of glcemic control to microvascular complications in diabetes.** Ann Intern Med 124: 90-6, 1996.

15. Lisa H, Jeffrey S. **NIDDM a genetically programmed failure of beta cells to compensate for insulin resistance.** N Engl J Med 334:778-83, 1996.

16. Laakso M, Lheto S. **Lipids and lipoproteins predicting coronary heart disease Mortality and morbidity in patients with NIDDM.** Circulation 88: 1421,1993.

17. Michael JW, Gerard G, Shahid J. **A Guide to angina pectoris:** Management 3:2, 1997.

18. Nexto RW, philips RT, Kett KG, et al. **Angina and exceptional myocardial ischemia in diabetic and non-diabetic patients.** Ann Intern Med 108:1070-5, 1988.

19. Nesto RW, Philips RT, **Asymptomatic myocardial ischemia in diabetic patient.** Am J Med80:40, 1986.

20. Pan WH, Cadres LB, Liu K, et al. **Relationship of clinical diabetic and asymptomatic hyperglycemia to the risk of coronary heat disease mortality in men and women.** Am J Epid 123:504, 1986.

21. Silva JA, Escobar A, Collins TJ et al. **Unstable Angina: A comparison of angiographic findings between diabetic and non-diabetic patients** Circulation 92:1731-36, 1995.

22. Qaisera S, Malik M A. **A study of clinical profile of diabetes in Mayo Hospital, Lahore.** Biomedical 9:1-4, 1993.

23. Stamler J, Vaccaro O, Neaton JP, et al. **Diabetes, other risk factors and 12 year cardiovascular mortality for men screened in MRFIT.** Diabetes Care 16:434, 1993.

24. Waller BF, Palumbo PJ, Robert WC. **Status of coronary arteries at autopsy in diabetic compared with control subject.** Am J Med 69:498, 1980.

25. Haider Z. **Profile of clinical diabetes: and overview of 1000 patients.** Diabetes Mellitus in Pakistan 3- 11, 1984.

26. **Uk prospective Diabetes Study Group Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications with type 2 diabetes.** Lancet 352:837-53, 1998.

27. Inzucchi SE, Maggs DG, Spollett GR et al. **Efficacy and metabolic effect of metformin and**

troglitazone in type 2 diabetes mellitus. New Engl J Med 338:867-72, 1998.

28.   Malmberg K. **Prospective randomized study of intensive insulin treatment on long-term survival after acute myocardial infarction in patients with diabetes mellitus DIGAMI Study Group.** B M J 314:1512-15, 1997.

29.   Laws A, Reaven GM. **Evidence for an independent relationship between insulin resistance and fasting plasma HDL-cholesterol, triglyceride and insulin concentrations.** J Intern Med 1992; 231:2530.

30.   Turner, R C, Millns, H, Neil, H A W, Stratton, I M, S E, Matthews, DR Holman, R R. **Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective diabetes study** (UKPDS:23) BMJ 316:823-828, 1998.

31.   Mudaliar, S. **Intense Management of Diabetes Mellitus: Role of Glucose Control and Antiplatelet Agents.** J Clin Pharmacol 44: 414-422, 2004.

32.   Alderman, M. H., Cohen , H., Madhavan, S. **Diabetes and Cardiovascular Events in Hypertensive Patients.** Hypertension 33: 1130-1134, 1999.