ORIGINAL ARTICLE

# PREVALENCE OF DIABETES MELLITUS AMONG OBESE AND NON-OBESE PATIENTS WITH CORONARY ARTERY DISEASE

**Sher Bahadar Khan, Hafiz-ur-Rehman, Lubna Noor*, Hameedullah*, Mohammad Hafeezullah, Adnan Mahmood Gul, Abdul Hadi**

**Department of Cardiology, PGMI, Lady Reading Hospital, *Hayatabad Medical Complex, PGMI, Peshawar, Pakistan**

**Background:** Globally, obesity is now recognised as an epidemic. The degree of obesity is proportional to the rate of development of cardiovascular diseases, hence, resulting in a dramatic increase in morbidity and mortality. Apart from obesity, diabetes mellitus is another well recognised risk factor contributing to coronary artery disease. The precise prevalence of obesity-related diabetes varies with age, race and gender; and is yet unknown in our population. We therefore, carried out this study with the aim to determine the prevalence of diabetes mellitus in obese and non-obese patients with diagnosed coronary artery disease. **Methods:** This hospital based cross-sectional comparative study was conducted in Cardiology Department of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, from 15th March 2005 to 30th May 2006. A total of 200 patients with diagnosed coronary artery disease were enrolled, 100 were classified as obese and 100 as non-obese. **Results:** Among these, 139 patients were male and 61 female. A total of 88 were found to be diabetic, 54 of these were obese and 34 non-obese ($p$=0.004). **Conclusion:** Diabetes mellitus was significantly more frequent among obese patients with coronary artery disease as compared to non obese patients with coronary artery disease.

**Keywords:** Coronary Artery Disease, Body Mass Index, Obesity, Diabetes Mellitus

## INTRODUCTION

Hypertension, diabetes mellitus, hyperlipidemia, smoking and positive family history are established risk factors for coronary artery disease. The prevalence of these risk factors is more in obese patients with coronary artery disease (CAD) as compared to non-obese patients with coronary artery disease.[1–2] Body weight and prevalence of obesity and its complications are rising so rapidly in many countries of the world, that WHO has recognised that there is 'Global epidemic of obesity'[3–4] which is clear from the fact that worldwide more than one billion adults are overweight and at least 30 million are obese.[4] Up to 130 million people throughout the Asia-Pacific region will suffer from obesity by the year 2010.[3] BMI (weight in Kg/height$^2$ in meters) is frequently used as a surrogate measure of fatness in children and adults.[5]

Data from the Fragmington study showed that the degree of obesity is proportional to the rate of development of cardiovascular diseases and that there is dramatic increase of sudden death, among those patients who are 20% overweight as compared to those with normal weight.[6]

Obesity is associated with an increase in circulating inflammatory markers, including C-reactive protein (CRP)[7,8] and cytokines (i.e., interleukin-6 [IL-6], IL-18, and P-selectin).[9,10] Adipose tissue itself is a likely source of these excess cytokines,[9] and IL-6, which stimulates the production of CRP by the liver.[11] The increase in inflammatory markers is associated with insulin resistance[12,13] and is an important predictor of atherosclerotic events.[14–15] It means adipose tissue is a significant source of inflammatory signals by releasing proinflamatory cytokines or hormones leading to diabetes, hypertension and atherosclerosis, which are risk factors for CAD. Also when BMI raises the capacity of body to remove chylomicrons progressively diminishes and these accumulated chylmicrons lead to CAD.[16]

The prevalence of the metabolic syndrome currently exceeds 20% of individuals ≥20 years of age and 40% of the population >40 years of age. Like obesity, the presence of the metabolic syndrome has been associated with risks of developing diabetes[17] and cardiovascular disease. Insulin resistance is believed to play a central pathophysiological role in the metabolic syndrome.[18]

Another study, concluded that obesity which is the component of metabolic syndrome, increases the risk of CAD by 7.3 times in males and 10.2 times in females.[19] It has been shown in a study done at Baqai University that 'measure to control excessive fat deposition in childhood could be an initial step towards prevention of diabetes and heart disease in later life'.[20]

Our study warrants as obese coronary artery disease patients are more diabetic, so preventive measures should be adapted in order to control the epidemic of obesity, which will not only reduce the incidence of diabetes, but will also decrease the incidence of CAD. Such measures need to be integrated in primary healthcare, as secondary and tertiary treatment costs are not affordable to all people of our community.[21]

## MATERIAL AND METHODS

This hospital based cross-sectional comparative study was conducted in Cardiology Department of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, from 15th March 2005 to 30th May 2006. A total of 200 patients who either were admitted with an acute coronary syndrome, or had a positive ETT, or CAD diagnosed by coronary angiogram, were enrolled into the study. Patient with acute coronary syndrome but with cardiogenic shock, and patients with unstable angina and non ST elevation MI with normal previous report of either ETT or coronary angiography were excluded from the study. Informed consent was obtained from all the patients, and approval of the hospital ethical committee sought. A detailed history was obtained, and physical examination was done, especially recording the height, weight, hip circumference and waist circumference. BMI was calculated for all patients as weight in kg divided by height in $m^2$. Fasting and random blood sugar levels were measured. Exercise tolerance test and coronary angiogram was done for patients as indicated according to the current guidelines and recommendations.

On the basis of the calculated BMI , patients were categorized either as 'obese' or 'non-obese'. In accordance with the WHO expert consultation on appropriate BMI for Asian population[5], patients with BMI $\leq$ 24.9 $Kg/m^2$ were classified into the 'non-obese' group, while those with BMI $\geq$ 25 $Kg/m^2$ into 'obese' group. Subjects were declared diabetic according to New WHO diagnostic criteria 1999, which defines diabetes as fasting blood sugar >126 mg/dl or random blood sugar >200 mg/dl, with one abnormal value in symptomatic individuals or two abnormal values in asymptomatic individuals.

Data was analysed using SPSS-13. Quantitative variables were described as Mean±SD and categorical variable as frequencies or percentages, *t*-test was used as significance testing in the case of quantitative variables or *Chi-square* test for categorical variables. A level of 5% was set for all significance testing.

## RESULTS

In this study, a total of 200 patients were enrolled; 100 obese and 100 non-obese. In both groups, there were more males patients 139 (69.5%) as compared to female 61 (30.5%). In non-obese group, the age range was 32 to 95 years (53±12 years), while in the obese group, it was 30 to 80 years (54±10 years). All the baseline characteristics of the patients are shown in Table-1.

In this study, mean BMI in obese was 29.22±3.22 and in non-obese was 22.99±1.38, with significant statistical difference ($p$<0.001). Most of the patients had been diabetic for more than 5 years duration. In both genders, an increasing trend was observed in the prevalence of diabetes with increasing body mass index (Table-2). A total of 88 patients were found to be diabetic. Out of these, 54 were obese while 34 were non-obese ($p$=0.004).

**Table-1: Baseline characteristics of patients**

| Total number of patients n=200 | Obese patients n=100 | Non-obese patients n=100 | *p* |
|---|---|---|---|
| **Gender** | | | |
| **Male** | 66 | 73 | 0.28 |
| **Female** | 34 | 27 | |
| **Age (years)** | 54±10 | 53±12 | |
| **<25** | 00 | 01 | |
| **25–40** | 12 | 15 | 0.31 |
| **41–60** | 70 | 57 | |
| **>60** | 18 | 27 | |
| **Mean waist circumference (inches)** | 38±4 | 33±3 | 0.21 |
| **Mean hip circumference (inches)** | 41±4 | 35±3 | 0.09 |
| **Mean BMI ($Kg/m^{2)}$** | 29.22±3.22 | 22.99±1.38 | 0.04 |
| **Past history of CAD** | 81% | 88% | 0.36 |
| **Positive ETT result** | 82% | 79% | 0.46 |
| **Coronary angiographic findings** | | | 0.27 |
| **Normal coronaries** | 07% | 11% | |
| **One-vessel disease** | 19% | 35% | 0.13 |
| **Two-vessel disease** | 24% | 25% | |
| **Three-vessel disease** | 50% | 29% | |

**Table-2: Diabetes Profile**

| Variables | | Obese n=100 | Non-Obese n=100 | *p* |
|---|---|---|---|---|
| **Diabetes (n=200)** | **Total=88** | **54** | **34** | **0.004*** |
| ****Treatment to control diabetes (n=88)** | Diet+Oral Hypoglycemic | 40 (74 %) | 32 (94%) | 0.023* |
| | Insulin | 7 (13 %) | 3 (9%) | 0.471 |
| | Diet | 7 (13%) | 27 (79%) | <0.001* |
| | Any Other | 0 | 1 (3%) | 0.218 |
| **Duration of diabetes (n=88)** | Mean±SD | 74±57 | 76±62 | 0.868 |
| | Above 1 to 6 months | 3 (6%) | 1 (3%) | |
| | Above 6 to 12 months | 4 (7%) | 6 (18%) | |
| | Above 12 to 60 months | 27 (50%) | 14 (42%) | |
| | Above 60 to 120 months | 13 (24%) | 9 (27%) | |
| | Above 120 months | 7 (13%) | 4 (12%) | |
| **Complication due to diabetes (n=88)** | Neuropathy | 2 (5%) | 2 (6%) | 0.867 |
| | Nephropathy | 0 | 1 (3%) | 0.275 |
| | Retinopathy | 0 | 1 (3%) | 0.275 |
| | Cataract | 0 | 5 (15%) | 0.012* |
| | Diabetic Foot | 1 (2.5%) | 0 | 0.353 |
| | Any Other | 1 (2.5%) | 4 (12%) | 0.114 |

*Significant, **Cumulate percentages are more than 100% because of patients have multiple controls

## DISCUSSION

In Pakistan, 46% of cardiac deaths are due to myocardial infarction. In a country where resource availability is scarce, a better option is prevention. Time, money and efforts spent on this preventive strategy in patients and population are rewarding. It is likely that the 25% increase in the prevalence of diabetes in the last 20 years in the United States[22] is because of the marked increase in the prevalence of obesity. BMI, abdominal fat distribution, and weight gain are important risk factors for type 2 diabetes.[22]

In our study, the mean BMI in obese patients was 29.22±3.22 and in non-obese it was 22.99±1.38, with significant statistical difference. In Pakistan, average BMI of people aged 15 and above is estimated to be 23–24.9 Kg/m$^2$ for females and 18–22.9 for males; in India, 23.24 for females and 18–22.9 for males; in Brazil, 25–26.9 for females and 23–24.9 for males, and in USA and Canada, it is above 27 for both females and males.[23]

In our study, the prevalence of diabetes increases with BMI in both genders, this result correlates well with local studies in which, in both genders, the prevalence of hypertension, diabetes, and hypercholesterolemia was directly proportional to BMI.[1–24] In our study CAD was more prevalent in male (obese patients; male 66, female 34) (non-obese patients; 73 male, 27 female) as compared to female. This result is in agreement with a local study done at Aga Khan Hospital who concluded that CAD has been shown to be more prevalent in male than females.[25] This correlates well also to international studies, i.e., GISSI-2[26], MILLIS[27] and GUSTO[28] trials, where male patients were 70.4%, 72.6% and 75% respectively.

In non-obese group the minimum age was 32 years and maximum 95 years (53±12 year) and obese the minimum age was 30 years and maximum 80 years (54±10 year). This is an accordance to a study done at Sir Ganga Ram Hospital Lahore, where mean age was 52.5±11.95.[29] In comparison in GUSTO trial the mean age was 62 years.[28] In this study age group of 41–60 years was more common in both obese (70%) and non-obese (57%) CAD patients, followed by age above 60 years in both groups, i.e., in obese (18%) and in non-obese (27%), with no statistical difference. The age group 41–60 years was also the most common group in a study done on 813 CAD admitted patients from July 2004 to June 2005 in the same cardiology unit LRH Peshawar.[30] The reason for this trend is clear from Framingham heart study, which has shown that incidence of IHD increases almost linearly with advancing age.[31] Most of the patients in our study had diabetes for more than 5 years of duration. Similar results were seen in previous studies conducted in the population of Peshawar.[30,32]

In our study, a total of 88 (44%) patients were diabetic. Out of these, 54 (61.36%) were obese while 34 (38.63%) were non-obese, with significant statistical differences ($p$=0.004). Our results are similar to results obtained in large study by Frederique Thomas *et al*, who also reported similar results.[2] When compared with subjects with BMI <25 Kg/m$^2$ without associated risk factors, overweight subjects did not have an increased risk of cardiovascular mortality.[2] Another study also is in agreement with our study, where 72.6% of 3,275 diabetic patients were obese.[33] Data from NHANES III indicated that two-thirds of adult men and women in the United States diagnosed with type 2 diabetes have a BMI of 27 Kg/m$^2$ or greater. Moreover, the risk of diabetes increased in a linear relationship with BMI; diabetes prevalence was 2%, 8%, and 13% in those with BMI 25 to 29.9 Kg/m$^2$ (overweight), 30 to 34.9 Kg/m$^2$ (class I obesity), and 35 Kg/m$^2$ (class II/III obesity), respectively.[22] Weight gain and increase in BMI during adulthood also increase the risk of diabetes, even at relatively low levels of BMI in initially normal-weight individuals.[34] Apart from degree of overweight, the distribution of adipose tissue is also strongly associated with diabetes risk; increased abdominal fat mass increases the risk of diabetes at any BMI value.[34,35]

In the long-term United Kingdom Prospective Diabetes Study, treatment of 2,906 newly diagnosed type 2 diabetes patients for 3 months with a reduced-calorie diet resulted in a mean weight loss of 4.5 Kg, which was associated with 3 mille moles (54 mg/dl) reduction in plasma glucose and a 2% decrease in HbA1c from a baseline level of 9%.[36] These findings are consistent with substantial evidence that a small amount of weight loss improves glycemic control. Weight loss of as little as 5% to 10% has been shown to reduce or prevent the development of type 2 diabetes.[37] Since obesity is a major risk factor for cardiovascular disease (CVD), the increasing prevalence and degree of obesity in all developed countries has the potential to significantly offset the current efforts to decrease CVD burden in our population. This small study is in effort in this regard and warrants us to do such like preventive studies on large scale in whole population.

## CONCLUSION

This study concludes that BMI has direct correlation with diabetes, as diabetes mellitus was significantly more common in obese CAD patients as compared to non-obese patients with CAD.

## REFERENCES


1. Abbas S, Abbas S, Riaz A, Malik N. Risk factors for CAD in Pakistan. Pak Armed Forces Med J 2003;53:12–9.
2. Thomas F, Bean K, Pannier B, Oppert JM, Guize L, Benetos A. Cardiovascular mortality in overweight subjects. The key role of associated risk factors. Hypertension 2005;46:654–5.
3. Zahid A. General aspects of human obesity. J Pak Med Assoc 2003;53:564.
4. World Health Organization. WHO world wide health report: Reducing risks promoting healthy life. Geneva: World Health organization; 2002. viii.
5. World Health Organization. WHO Reports 2004, WHO global NCD infobase [Online] 2004 [Cited on August 13, 2006]. Available from: http://www.who.int/ncd_surveillance/infobase
6. Dawber TR. The Fragmington study: the epidemiology of Atherosclerotic disease. Cambridge: Harvard University press; 1980.
7. Liuzzo G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB, *et al*. The prognostic value of C-reactive protein and serum amyloid a protein in severe unstable angina. N Engl J Med 1994;331:417–24.

8. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen,C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA 1998;279:1477–82.
9. Mohamed-Ali V, Goodrick S, Rawesh A, Katz DR, Miles JM, Yudkin JS, *et al*. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. J Clin Endocrinol Metab 1997;82:4196–4200.
10. Esposito K, Pontillo A, Ciotola M, Di Palo C, Grella E, Nicoletti G, *et al*. Weight loss reduces interleukin-18 levels in obese women. J Clin Endocrinol Metab 2002;87:3864–6.
11. Heinrich PC, Castell JV, Andus T. Interleukin-6 and the acute phase response. Biochem J 1990;265:621– 36.
12. McLaughlin T, Abbasi F, Lamendola C, Liang L, Reaven G, Schaaf P, *et al*. Differentiation between obesity and insulin resistance in the association with C-reactive protein. Circulation 2002;106:2908–12.
13. Festa A, D'Agostino R Jr, Howard G, Mykkanen L, Tracy RP, Haffner SM. Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). Circulation 2000;102:42–7.
14. Kuller LH, Tracy RP, Shaten J, Meilahn EN. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study. Multiple Risk Factor Intervention Trial. Am J Epidemiol 1996;144:537–47.
15. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342:836–43.
16. Wise BC. The inflammatory syndrome: The role of adipose tissue cytokine in metabolic disorders linked to obesity. J Am Soc Nephrol 2004;15:2792–800.
17. Laaksonen DE, Lakka HM, Niskanen LK. Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. Am J Epidemiol 2002;156:1070–7.
18. Hanley AJ, Karter AJ, Festa A. Factor analysis of metabolic syndrome using directly measured insulin sensitivity: the insulin resistance atherosclerosis study. Diabetes 2002;51:2642–7.
19. Sjostrom CD,Peltonen M,Sjostrom L. Blood pressure and pulse pressure during long term weight loss in obese: the Swedish obese subjects (SOS) Intervention study.Obese Res 2001;9:188–95.
20. Basit A, Hakeem R, Hydrie MZ, Ahmedani MY, Masood Q. Fatness, lipid, insulin sensitivity, life style of children from high low risk families. J Ayub Med Coll 2003;15:6–9.
21. Nishtar S. Prevention of coronary artery diseases in South Asia. Lancet 2002;360:1015–8.
22. Harris MI, Flegal KM, Cowie CC. Prevalence of diabetes, impaired fasting glucose and impaired glucose tolerance in US adults. The Third National Health and Nutrition Examination Survey, 1988–1994. Diabetes Care 1988;21:518–23.
23. Hanson L. Primary prevention of coronary heart disease: what is left to be done? Medicographia 1998;20:183–6.
24. Aziz-ur-Rahman, Sattar A, Abaidullah S, Hassan M. Evaluation of cardiovascular risk factors in patient with essential hypertension. Ann KE Med Coll 1999;5:134–7.
25. Ishaq M, Beg MS, Ansari SA, Hakeem A, Ali S. Coronary artery disease risk profiles at a specialized tertiary care centre in Pakistan. Pak J Cardiol 2003;14:61–8.
26. Maggioni AP, Franzosi MG, Santoro E, The risk of stroke in patients with acute myocardial infarction after thrombolytic therapy and anti thrombotic treatment: Gruppo Italiano per lo studio della Superavvivenza nell 'Infarcto Micocardico II (GISSI-2) and the international study group. N Eng J Med 1992;327:1–6.
27. Tofler GH, Stone PH, Machure M. Analysis of possible triggers of acute myocardial infarction (The MILLIS study). Am J Cardiol 1990;22:66–7.
28. The GUSTO investigator. An international randomised trial comparing four thrombolytic strategies for acute myocardial infarction. N Eng J Med 1993;329:673–82.
29. Postmenopusal hormone replacement therapy for the primary prevention of chronic condition: recommendations and rationale, US Preventive Services Task Force. Am Fam Physician 2003;67:358–64.
30. Khan H, Hafizullah M, Ihtesham-ul-Haq. A hospital based study on frequency of risk factors of coronary artery disease in Peshawar. J Postgrad Med Inst 2005;19:270–5.
31. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968–77.
32. Hassan M, Awan ZA, Gul AM, Sahibzada WA, Hafizullah M. Prevalence of coronary artery disease in rural areas of Peshawar. J Postgrad Med Inst 2005;19:14–22.
33. Chaudhary GM. Metabolic syndrome X in diabetic patients, Experience in 3275 diabetic patients at Jinnah Hospital, Lahore. J Coll Physicians Surg Pak 2000;10:278–80.
34. Colditz GA, Willett WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med 1995;122:481–6.
35. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care 1994;17:961–9.
36. Turner RC, Holman RR. Lessons from UK prospective diabetes study. Diabetes 1996;45(Suppl 3):S87–S90.
37. Kuulasmaa K, Kunstall-pedoe H, Dobson A, Fortmann S, Sans S, Tolonen H, *et al*. Estimation of contribution of changes in classic risk factors to trends in coronary–event rates across the WHO MONICA project population. Lancet 2000;355:675–87.


## Address for Correspondence:

**Dr. Sher Bahadar Khan,** Department of Cardiology, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, Pakistan. **Cell:** +92-333-9487717
**Email:** docyousafzai@yahoo.com