



EVALUATION OF ACHIEVEMENT OF CARDIOVASCULAR TARGETS IN PATIENTS OF DIABETES MELLITUS AND FACTORS PREDICTING GOAL ACHIEVEMENT

Nighat Majeed^{a*}, Nausheen Sohail^a, Muhammad Abdul Rehman^b

Abstract

Type 2 diabetes mellitus management requires tight control of hyperglycemia, hyperlipidemia and hypertension. Measuring exposure to these factors helps in risk assessment for patients in primary cardiovascular prevention and achievement of preset targets helps in cardiovascular control.

Patients and Methods. Cross sectional study was performed on three hundred patients attending inpatient and outpatient clinics of services hospital Lahore & khair-un-nisa hospital Lahore from June 1st 2014 to December 31st 2014. Three key parameters HbA1c, systolic blood pressure and LDL-C of all patients were recorded. Patients were divided on the basis of above mentioned goals that is HbA1c $\leq 7\%$, Systolic blood pressure $\leq 140\text{mmHg}$ and LDL-C $\leq 100\text{mg/dl}$ in two groups. Patients achieving all the three goals were compared with no achievers for duration of diabetes mellitus, body mass index, glucose lowering therapy, cardiovascular therapy, and micro and macro vascular complications.

Results. Out of 300 patients only 14 patients achieved all three targets and 102 patients did not achieve any of these targets ($p=.021$). 95.34% patients was non-achievers and only 4.66% patients achieved all three goals. There was no significant difference of micro & macro vascular complications amongst two patients groups ($p=0.48$). No significant difference was found in cardiovascular therapy amongst two groups ($p=0.52$). No significant difference was recorded in duration of diabetes mellitus ($p=0.41$), gender ($p=0.38$), body mass index ($p=0.64$) and duration of diabetes mellitus, type of diabetes mellitus ($P=0.56$) between goal achievers and non-achievers. But there is high prevalence of obesity in study population.

Conclusion. A low proportion of patients of diabetes mellitus meet all recommended goals. Good control of blood pressure, blood glucose and hyperlipidemia is recommended to prevent the complications in patients of diabetes mellitus.

(J Cardiovasc Dis 2013;11(4):101-106)

INTRODUCTION:

Type 2 diabetes mellitus management require tight control of hyperglycemia, hyperlipidemia and hypertension, the three critical quality indicators to prevent cardiovascular complications i.e, Glycosylated hemoglobin(HbA1c)(A),systolic blood pressure(B) and LDL cholesterol(C). Measuring exposure to these factors helps in risk assessment for patients in primary cardiovascular prevention and achievement of preset targets helps in cardiovascular control¹. Severe depression was significantly ($p=0.048$) associated with lower rates of ABC goal attainment(25.4%) compared to those with no depression (5.0%)². The characteristic feature of diabetic dyslipidemia is high plasma triglycerides low HDL concentration and increased LDL cholesterol³. Diabetes mellitus may be complicated with coronary artery disease,stroke,peripheral arte-

rial disease. Patients with diabetes mellitus are at increased risk of developing cardiac diseases, and patients with cardiovascular disease diagnosed to have diabetes mellitus are having poor prognosis⁴. overweight and obesity contributed to the increased prevalence⁵ of diabetes mellitus. Patients having type 2 diabetes are reported to have endothelial dysfunction.Glycometabolic and cardiovascular disorders are inter-related.⁶ Hypoglycemia is a hallmark of diabetes mellitus. It contributes to the myocardial damage after ischemic events. Both prediabetes and metabolic syndrome even in normoglycemic patients increases the risk of diabetes mellitus⁷. There is a strong association between any form of glucometabolic disturbances and heart failure⁸.Hyperglycemia hyperlipidemia, hypertension and microalbuminuria are the main risk factors for increased incidence of coronary artery disease. Controlling the ABC of diabetes mellitus can cut the risk of stroke ischemic heart disease⁹. According to WHO 75% of patients with non-insulin dependent diabetes mellitus die due to vascular events¹⁰.The metabolic syndrome is a cluster of risk factors that is responsible for most of

^a SIMS, Services Hospital, Lahore-Pakistan

^b Sheikh Zayed Hospital, Lahore

* Corresponding author:

Email: dr_nm@hotmail.com



the cardiovascular morbidity amongst persons with type 2 diabetes mellitus. The metabolic syndrome increases the risk for coronary heart disease and stroke by three-fold with a marked increase in cardiovascular mortality, so the diabetes mellitus is considered as vascular disease diagnosed by elevated blood sugar levels¹¹. Abnormal vascular findings associated with atherosclerosis are seen in patients of diabetes mellitus in the form of coronary artery calcification, carotid intima media thickness and vascular endothelial dysfunction are subclinical vascular findings in diabetes mellitus¹². Evidence suggests that LDL-C > 100mg/dl is associated with increased cardiovascular risk¹³. Keeping in view the above mentioned facts we looked for the glycemic control by measuring HbA1c, blood pressure control by measuring systolic blood pressure (SBP) and Lipid control by measuring low density lipoprotein cholesterol (LDL-C) in patients of diabetes mellitus.

AIMS AND OBJECTIVES OF STUDY:

1. To evaluate the of patients of diabetes mellitus patients attaining, LDL-C < 100mg/dl, Systolic blood pressure < 130mmHg and HbA1c < 7%.

2. To compare the goal achievers with non-achievers for factors predicting goal achievement i.e age, sex, body mass index (BMI), glucose lowering drugs micro & macro vascular complications.

Study design.

MATERIAL AND METHODS:

Patients of diabetes mellitus attending in and outpatient clinic of services hospital Lahore & khair-un-nisa hospital Lahore from June 1st 2014 to December 31st 2014 were included in the study.

Patients also having diseases other than diabetes mellitus i.e malignancies, primary renal disease, congenital heart disease, vasculitis were excluded from the study.

Sample size. Sample size was calculated by the given formula

$$n = \frac{2(Z_{\alpha} + Z_{1-\beta})^2 \sigma^2}{\Delta^2}$$

Z_{α} is 1.96. $Z_{1-\beta}$, is 0.8416. The standard deviation (based on the data in the published paper) would be approximately 0.7. Δ the difference in effect of two interventions which is required (estimated effect size) is 15%. Approximate sample size recorded was of 300 patients.

Three hundred patients attending inpatient

and outpatient clinic of services hospital Lahore & khair-un-nisa hospital Lahore from June 1st 2014 to December 31st 2014 were followed. Patient was diagnosed to have diabetes mellitus if fasting plasma glucose (FPG) \geq 126 mg/dl (7.0 mmol/l) or a random plasma glucose \geq 200 mg/dl (11.1 mmol/l) or Plasma glucose \geq 200 mg/dl (11.1 mmol/l) 2 hours after a 75g glucose load or HbA1c \geq 6.5% checked at two occasions. Three key parameters HbA1c, systolic blood pressure and LDL-C of all patients was of all patients were recorded. Patients were divided on the basis of above mentioned goals that is HbA1c \leq 7%, Systolic blood pressure \leq 140mmHg and LDL-C \leq 100mg/dl. Patients who achieved all three goals were included in one group and patients who did not achieve any goal or one to two goals were included in another group. Both groups were compared for duration of diabetes mellitus, body mass index, and glucose lowering therapy, cardiovascular therapy, and micro and macro vascular complications.

The variables recorded were age, type of diabetes mellitus, duration of diabetes mellitus, HbA1c, fasting lipid profile including LDL-Cholesterol (LDL-C), albuminuria, body mass index micro and macro vascular complications, glucose lowering medications including insulin and cardiovascular therapy. Hypertension was defined as systolic blood pressure \geq 140mmHg and diastolic blood pressure \geq than 90mmHg.

Coronary artery disease was diagnosed on the basis of history (myocardial infarction, percutaneous coronary intervention or coronary artery bypass grafting) or on exercise tolerance test or echocardiography. Peripheral arterial disease was defined by history of claudication / evidence of diabetic foot. Peripheral neuropathy was diagnosed on the basis of symptoms of numbness and clinical examination of sensory system. Diabetic retinopathy was diagnosed by doing fundoscopy of patients.

STATISTICAL ANALYSIS:

Frequencies are described as mean and standard deviation. The significance of difference between means was analyzed by chi square test. Difference between results were considered significant or non-significant for $p \leq 0.05$ respectively. Data was analyzed by using SPSS version 20.

RESULTS:

Out of 300 patients, mean age of patients was 51 years. (Figure 1) Mean fasting blood glucose was 173mg/dl, 10% patients were suffering from

type 1 diabetes mellitus and 90% patients were suffering from type 2 diabetes mellitus. 50.7% (152) patients were male while 49.3% (148) patients were female. 70% patients have their HbA1c value more than 7%. 75% patients have their LDL.C > 100mg/

Figure 1: Age of Patients

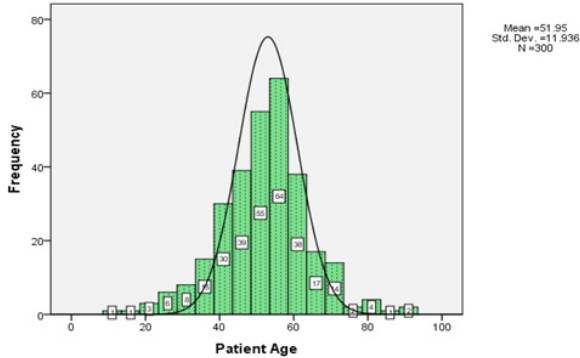


Figure 2 : Duration of diabetes mellitus in patients

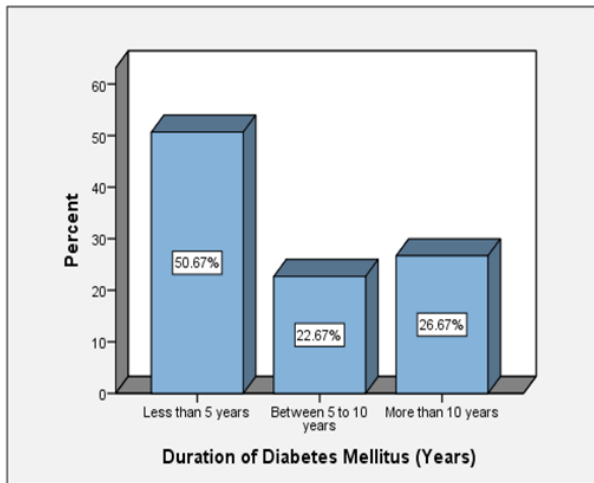


Figure 3: Treatment history of the patients

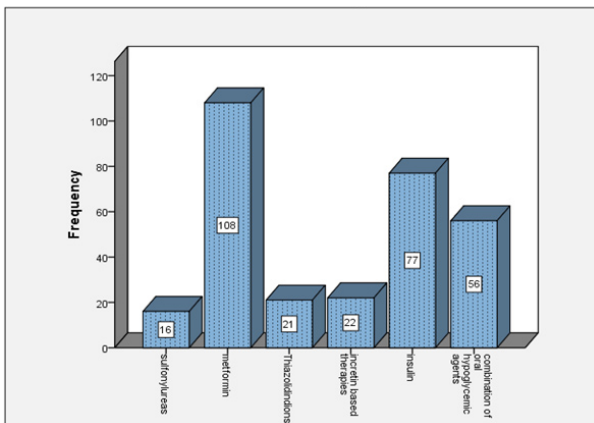


Figure 4: Micro & Macrovascular complications

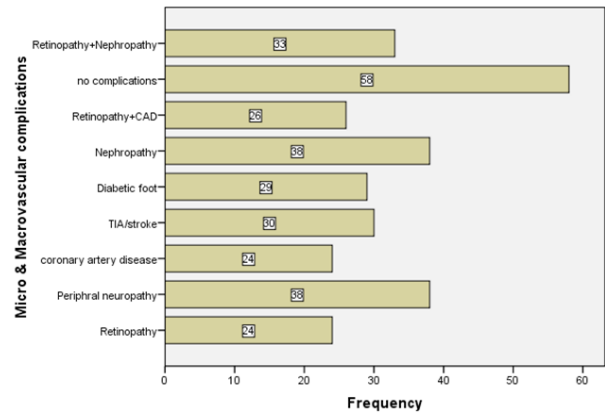


Figure 5: Cardiovascular Therapy

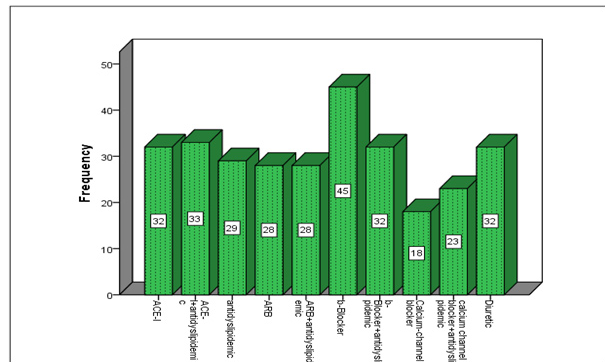


Table 1: Correlation of HB A1c (%) * LDL-c * systolic blood pressure

Systolic Blood Pressure	LDL-c		Total	Significance	
	<100mg/dl	>100mg/dl			
<140mmHg	HB A1c (%) Less or equal 7	14	18	32	.116
	HB A1c (%) More than 7	16	36	52	
	Total	30	54	84	
>140mmHg	HB A1c (%) Less or equal 7	18	41	59	.021
	HB A1c (%) More than 7	26	131	157	
	Total	44	172	216	

Table 2: Body Mass Index

Study population	body mass index		Total
	<30	>30	
Selected(three target achievers)	3	11	14
Not Selected(three target non-achievers)	62	224	286
Total	65	235	300

dl. 72% patients have their systolic blood pressure more than 140mmHg (Table 1). 78% patients have their BMI > 30% (Table 2). 26% patients have more than 10 years duration of diabetes mellitus. (Figure 2).

Out of 300 patients only 14 patients achieved all three targets and 102 patients did not achieved any of these targets ($p = .021$), rest of patients (184)



achieved one or two goals only. 95.34% patients was non-achievers and only 4.66% patients achieved all three goals. 18 patients has their systolic blood pressure less than 140mmHg ($p=.084$) and HbA1c $<7\%$. ($p=.005$). 36% of study population was using metformin, 26% of study population was using insulin and 19% of study population was using combination of oral hypoglycemic agents. (Figure 3). 81%% patients were suffering from micro and macro vascular complications (Figure 4) and only 40% patients were taking cardiovascular therapy. (Figure 5). 8.17% (23) patients were suffering from coronary artery disease and 12.66% (38) patients were suffering from nephropathy.

DISCUSSION:

The aim of the study is to determine the achievement of glycemic control hypertension control and control of hyperlipidemia, the major cardiovascular risk factors in patients of diabetes mellitus. Significant number of patients did not achieve guideline driven goal achievement. Systolic blood pressure was relatively controlled compared to LDL.C. The major prevalent metabolic factor in study population was increased body mass index (BMI) however there was no significant difference between BMI of goal achievers and non-achievers. Using similar cut-offs to document optimal risk factor control in diabetes from the National Health and Nutrition Examination Survey, and the Behavioral Risk Factor Surveillance it was found that triple-target achievement nonsmoking rate raised from 4.6% to 14.3% between 1999 and 2010.¹⁴

No significant difference was recorded between micro and macro vascular complications among the two study groups. 95.34% patients was non-achievers and only 4.66% patients achieved all three goals. More than half of patients were suffering from micro and macro vascular complications. In our study almost half of the patients have more than five years duration of diabetes mellitus though it was not statistically significant. Regarding cardiovascular medications there was no significant difference between goal achievers and no achievers. Chronic hyperglycemia and hypertension synergistically promote micro vascular damage. Increased serum cholesterol has synergistic effect. Most important reason of not achieving normoglycemia, poor control of blood pressure & LDL.C is inappropriate use of medications. Reduction in the burden of cardiovascular disease in diabetes should begin with assessment and treatment of elevated LDL.C. statins are preferred treatment¹⁵. LDL.C is the primary target of lipid lowering therapy

in guidelines both the ADA & NCEP ATP III.^{16,17} The typical lipid disorder in patients with diabetes, the diabetic dyslipidemia is characterized by elevated triglycerides, low HDL cholesterol and increased number of small dense LDL particles.

The implementation of treatment goals for diabetes is challenging and are suboptimal in most of the clinical setting¹⁶. Lowering LDL cholesterol to $<70\text{mg/dl}$ may provide greater cardiovascular targets and latest guidelines recommend $<70\text{mg/dl}$ as an optimum LDL goal in very high risk patients particularly in patients suffering from coronary artery disease^{16,18}.

Macro vascular complications of diabetes starts before the onset of diabetes¹⁹. This phenomenon is explained by increased insulin resistance²⁰. There is a significant increase in risk of cardiovascular death and all cardiovascular events in patients of type 2 diabetic patients with HbA1c levels higher than 7% compared with diabetic subjects with lower HbA1c²¹. Many potential factors associated with failure to achieve critical goals in T2DM represent obstacles or limitations in the management of disease, like statin intolerance etc. Another factor responsible seems to be natural trend for the variables to rise overtime is likely responsible for the disappointing achieving rates of HbA1c (28%) and SBP(30%).²²

The variables defined indicate better target intervention at improving the overall management of major modifiable components of vascular risk. Suitable medications should be prescribed to control blood pressure, blood sugar and lipids including combination of treatment and life style improvement.

There is a growing recognition that diabetes belong to special category of risk factor because of markedly increased risk of cardiovascular disease coexistent metabolic risk factors and hyperglycemic effect on vasculature. Absolute risk of major coronary event is same as of non-diabetic patients with established coronary artery disease.

The ultimate goal of public health and clinical intervention is the prevention of diabetes by reducing obesity and promoting physical activity in general population²¹. Women with diabetes seems to lose their inherent protection against development of cardiovascular disease. Patients with diabetes mellitus has worse prognosis for survival than do coronary artery disease without diabetes mellitus²³.

Most of patients who have micro albuminuria also have hypertension. In these patients control of



hypertension slows decline in glomerular filtration rate²⁴. Hypertension is an established risk factor for cardiovascular disease²⁵.when hypertension coexist with overt diabetes, the risk of cardiovascular disease including nephropathy is doubled. There is a positive association between hypertension and insulin resistance²⁶.

CONCLUSION.

A low proportion of patients of diabetes mellitus meet all recommended major goal. Good control of blood pressure, blood glucose and hyperlipidemia is recommended to prevent the complications in patients of diabetes mellitus. There is high prevalence of obesity, micro and macro vascular complications among the study population and most of the patients were having more than five years duration of diabetes mellitus.

REFERENCES

1. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; 16:434-44
2. Shah BM, Mezzio DJ, Ho J, Ip, EJ, Association of ABC (HbA1c, blood pressure, LDL-cholesterol) goal attainment with depression and health-related quality of life among adults with type 2 diabetes. *J Diabetes Complications*. 2015 Aug;29(6):794-800.
- 3) Mooradian AD, Dyslipidemia in type 2 diabetes mellitus, *Nat Clin Pract Endocrinol Metab*. 2009 Mar;5(3):150-9
- 4) Pedersen CT, Madsen CR, Gustafson I, Gustafson F, Køber L. Diabetes mellitus and cardiovascular risk: just another risk factor?. *Eur Heart J Supplements* (2003) 5 (Supplement F), F26-F32.
5. Must A1, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA*. 1999 Oct 27;282(16):1523-9
6. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in non-diabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998; 339:229-34
7. Muhlestein JB, Anderson JL, Horne BD, Lavasani F, Allen Maycock CA, Bair TL, et al: Effect of fasting glucose levels on mortality rate in patients with and without diabetes mellitus and coronary artery disease undergoing percutaneous coronary intervention. *Am Heart J* 146: 351-358, 2003
8. Thrainsdottir IS, Aspelund T, Thorgeirsson G, Gudnason V, HARDARSON T, et al: The association between glucose abnormalities and heart failure in the population-based Reykjavik Study. *Diabetes Care* 28:612-616, 2005
9. Carneiro AV: Coronary heart disease in diabetes mellitus: risk factors and epidemiology. *Rev Port Cardiol* 2004 Oct; 23(10):1359-66
10. WHO technical report series no 844. prevention of diabetes mellitus: report of WHO study group Geneva: world health organization, 1994
11. Yki-Jarvinen H. Management of type 2 diabetes mellitus and cardiovascular risk: lessons from intervention trials. *Drugs* 2000; 60:975-83
12. Dabelea D1, Kinney G, Snell-Bergeon JK, Hokanson JE, Eckel RH, Ehrlich J, et al. Coronary Artery Calcification in Type 1 Diabetes Study. Effect of type 1 diabetes on the gender difference in coronary artery calcification: a role for insulin resistance? The Coronary Artery Calcification in Type 1 Diabetes (CACTI) Study. *Diabetes*. 2003 Nov;52(11):2833-9.
13. Orchard TJ, Forrest KY, Kuller LH, Becker DJ, Pittsburgh. Epidemiology of Diabetes Complications Study. Lipid and blood pressure treatment goals for type 1 diabetes: 10-year incidence data from the Pittsburgh Epidemiology of Diabetes Complications Study. *Diabetes Care* 2001; 24:1053-1059
14. Stevens RJ, Coleman RL, Adler AI, Stratton IM, Matthews DR, Holman RR. Risk factors for myocardial infarction case fatality and stroke case fatality in type 2 diabetes. *Diabetes Care* 2004; 27:201-7
- 15-. Nesto RW. LDL Cholesterol Lowering in Type 2 Diabetes: What Is the Optimum Approach? *Clinical Diabetes* January 2008 vol. 26 no. 1 8-13
16. American Diabetes Association: Standards of medical care in diabetes: 2007. *Diabetes Care*. 2011 Jan; 34(Suppl 1): S11-S61.
17. The Expert Panel: Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): final report. *Circulation*. 2002 Dec 17;106(25):3143-421.
- 18 . Grundy SM, Cleeman JI, Merz NB, Jr HHH, Clark LT, Hunninghake DB, Pasternak RC et al, for the Coordinating Committee of the National Cholesterol Education Program: Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation*.2004; 110: 227-239
19. Pyorala K, Relationship of glucose tolerance and plasma insulin to the incidence of coronary heart disease: results from two population studies in Finland. *Diabetes Care*, 2 (1979), pp. 131-141
20. Yamagishi S, Matsui T, Ueda S, Fukami K, Okuda S. Clinical utility of acarbose, an alpha-glycosidase inhibitor in cardio metabolic disorders *Curr Drug Metab*,10 (2009),159-163
21. Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, et al. Diabetes and cardiovascular disease: a statement for health professionals from the American Heart Association. *Circulation*. 1999; 100:1134-1146
22. Hermans MP, Amoussou, Guenou KD, Ahn SA, Rousseau MF, Everaert L, Aerts A. The elusive type2 diabetes individual at blood pressure control: phenotypic characterization of goal-achieving patients. *Diabetes Metab Syndr*2010; 4:215-9.
23. Stone PH, Muller JE, Hartwell T, York BJ, Rutherford JD, Parker CB, et al, the MILIS Study Group. The effect of diabetes mellitus on prognosis and serial left ventricular function after acute myocardial infarction: contribution of both coronary disease and diastolic left ventricular dysfunction to the adverse prognosis. *J Am Coll Cardiol*. 1989; 14:49-57.
24. Regan TJ. Congestive heart failure in the diabetic. *Annu*



Rev Med. 1983; 34:161–168.

25. Wilson PW. Diabetes mellitus and coronary heart disease. Am J Kidney Dis. 1998; 32:S89–S100.

26. Reaven GM, Lithell H, Landsberg L. Hypertension and associated metabolic abnormalities: the role of insulin resistance and the sympatho-adrenal system. N Engl J Med. 1996; 334:374–3