GLYCAEMIC CONTROL IN DIABETES MELLITUS

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ABSTRACT

Objective: To evaluate the degree of glycaemic control among diabetic patients.

Methods: The study included 156 diabetic patients (64 with insulin – dependent diabetes mellitus (IDDM) and 92 with non insulin – dependent diabetes mellitus (NIDDM)), and 120 control subject. The parameters measured were fasting blood glucose (FBG) and the level of glycated haemoglobin (Hb A_{1c}).

Results: HbA_{1c} level was significantly higher among diabetic patients (both IDDM and NIDDM) compared to controls ($P<0.001$). Also, 43.8% of IDDM patients and 63.0% of NIDDM patients were in poor glycaemic control.

Conclusion: substantial proportion of diabetic patients are in poor metabolic control , and hence, more prone to early diabetic complications.

Key words: Diabetes mellitus, glycaemic control, HA_{1c}.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease associated with disturbances in the metabolism of glucose, protein and fat resulting from absolute or relative insulin lack[1,2]. Insulin deficiency plays a major role in the metabolic disorders in diabetes, and hyperglycaemia contribute greatly to the complications of diabetes[3].

Diabetes occurs world wide and the prevalence of both type 1 and 2 of Diabetes mellitus is increasing [2-4]. It is estimated that it will affect more than 20 million people by the year 2020[4]. Diabetes mellitus is Diabetes is a major public health problem, especially among older individuals. Individuals with diabetes are at high risk for dyslipidaemia, cardiovascular disease (CVD), and mortality[5-7]. Diabetes mellitus is one of most important modifiable risk factors of coronary heart disease (CHD)[8]. Also, it increases the risk of cardiac, cerebral and peripheral vascular disease 2-7 fold[3].

Glycation of haemoglobin (Hb) refers to a series of stable minor components formed normally between Hb A and glucose or its metabolites. These components are collectively known as Hb A_1. At least 4 Hb A_1 fraction have been identified, and Hb A_{1C} is the most important one accounting for 3-6% of the total Hb in normal people[9]. Measurement of glycated Hb level has been successfully used in monitoring diabetic patients. It is known that Hb A_1c formation depends on the mean blood glucose levels[10,11].

The aim of this study was to evaluate the degree of glycaemic control among diabetic patients by measuring Hb A_1c concentration.

PATIENTS & METHODS

In this prospective study, 156 diabetic patients were included. They were 64 patients with insulin – dependent diabetes mellitus (IDDM), 28 males and 36 females, their age ranged from 8-60 years (mean : 34.5), and 92 patients with non insulin – dependent diabetes mellitus (NIDDM), 43 males and 49 females, their age ranged from 30-70 years (mean: 53.4). They were diagnosed by consultant physicians. In addition, 120 apparently healthy subjects were included as a control group. They were 35 males and 85

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females, 13-76 years of age (mean: 36.7).
Fasting blood glucose (FBG) was carried out using enzymatic kit from bioMeriux, France. Estimation of Hb A_{1c} level was preformed by ion - exchange HPLC using the VARIANT^{TM} program form BIO-RAD . Quatity control sera from bioMerieux were included in each assay batch for all measured parameters. Diabetic patients were considered in poor metabolic control when Hb A_{1c} > 8.0%[12,13].
Statistical analysis was carried out using the analysis of variance (ANOVA). $P<0.05$ was considered statistically significant.

RESULTS

Table 1 summarizes the results. Hb A_{1c} concentration were significantly higher among patients with IDDM and NIDDM compared to control subjects ($p<0.001$).
As shown in Table 2, 56.2% of patients with IDDM were in good glycaemic control and 43.8% in poor metabolic control. The comparative figures in NIDDM were 37.0% and 63.0% respectively.

DISSCUSSION

Glycated Hb is usually used as a supplement to blood glucose estimation to monitor the overall degree of diabetic control. Glycation occurs gradually for about 2-3 months, recurring early in their development and remain constant until their death. That's why Hb A_{1c} has been used in the monitoring of diabetics as an index of long-term glycaemic control for the last 6-8 weeks[2]. Some studies evaluated the glycaemic control depending upon FBG estimation[14]. However, single or serial blood glucose estimations cannot be used for such purpose and only reflect the degree of glycaemia at the moment of sampling.
This study clearly shows that Hb A_{1c} level is markedly elevated among diabetic patients than controls, with the overall mean Hb A_{1c} level among both IDDM and NIDDM patients in the range of poor metabolic control. Such finding indicate that diabetic patients are at exceedingly high risk of cardiovascular complications than normal people. As presented in Table 2, considerable percentage of IDDM and NIDDM patients were in poor glycaemic control. This implies that such patients are at risk of early diabetic complications, accelerated atherosclerotic disease, and also, and increased cardiovascular disease risk. There are sustained racial differences in the nature of diabetes, including vascular risk factors[15]. urban African Americans with diabetes more likely to have suboptimal glycemic control. Differences in age, sex, and insurance type seemed to explain some of the disparities[16]. Differences in glycemic control by race were associated with disease severity, health status, and poorer quality of care[17].
A close correlation has been observed between glycaemic control and serum lipid levels in patients with IDDM[18,19]. Untreated or inadequately treated IDDM patients shows a variety of dyslipidaemia[20]. Therefore, these patients are considerablly prone to accelerated atherosclerotic disease. Adequate treatment results in favorable effects on lipid profile[21,22]. On the other hand, NIDDM is associated with poor glycaemic control and atherogenic changes of lipid profile [23,24]. Type 2 diabetes and elevated plasma lipid levels are important independent risk factors for cardiovascular disease and coronary heart disease[24] .
Diabetes management led to favorable changes in HDL-C and triglyceride levels, but improved glycemic control and weight loss had no independent effect on LDL-C concentration. Initiation of therapy to treat high LDL-C levels should be considered early in the course of diabetes management to reach recommended targets and reduce the risk of cardiovascular complications.[25].
Several therapeutic modalities have been shown to be beneficial in improving atherogenic lipid profile, including metformin, metformin/gluburide, ezetimibe, rosuvastatin, atrovastatin, lovastatin, pravastatin, simvastatin and fenofibrate[24,26-31]. The later is a valuable lipid lowering agent in patients with

atherogenic dyslipidaemia[31].Furthermore, it has been found that combination lipid lowering therapy is more effective than statin monotherapy[28,32]. It has been suggested that pravastatin therapy result in a considerable reduction in the hazard of becoming diabetic. By lowering plasma triglyceride levels, pravastatin therapy may favorably influence the development of diabetes[33]. However, worsening of metabolic control deteriorates lipid and lipoprotein abnormalties and increases cardiovascular complications[34,35].

In conclusion, diabetic patients showed high Hb A_{1c} level with considerable proportion in poor glycaemic control. This necessitates active intervention toward strictly adequate treatment to avoid early and irreversible diabetic complications.

Table 1. FBG and Hb A_{1c} level among diabetic patients and control subjects.

Group		FBG (mg/dl)	Hb A_{1c} (%)
All	IDDM	254.5 (115.9)*	10.9 (4.8)*
	NIDDM	182.4 (86.5)*	8.8 (2.8)*
	Controls	90.3 (15.4)	4.2 (0.94)
Males	IDDM	280.2 (126.4)*	12.8 (6.1)*
	NIDDM	189.5 (69.7)*	9.3 (3.0)*
	Controls	95.1 (25.0)	4.4 (0.97)
Females	IDDM	248.7 (105.3)*	9.9 (3.4)*
	NIDDM	186.0 (64.9)*	8.3 (2.6)*
	Controls	88.2 (12.8)	4.3 (0.94)

Values are expressed as Mean (SD)
*: P< 0.001 (controls vs IDDM and NIDDM)

Table 2. glycaemic control among diabetic patients.

Glycaemic control	IDDM		NIDDM	
	No.	%	No.	%
Good	36	56.2	34	37.0
Poor	28	43.8	58	63.0
Total	64	100.0	92	100.0

REFERENCES

1. World Health Organization. Manual on diabetes in primary health care. Regional office for the Eastern Mediterranean, 1995.
2. Fries BM, Truswell AS, Shepherd J, et al. Diabetes mellitus and nutritional and metabolic disorders. In: Haslett C, Chilvers ER, Hunter JAA, et al, eds. Davidson's Principles and Practice of Medicine. 18th edn, Edinburgh: Churchill Livingstone, 1999: 471-542.
3. Sherwin RS. Diabetes mellitus. In: Goldman L, Bennett JC, eds. Cecil Textbook of Medicine. 23rd edn, Philadelphia: W.B.saunders Company, 2007: 1263-1285.
4. Gale EAM, Anderson JV. Diabetes mellitus and other disorders of metabolism. In: Kumar P, Clark M, eds. Clinical Medicine. 6th edn, Edinburgh: Elsevier Saunders, 2005:1101 – 1151.

5. Brancati FL, Kao WH, Folsom AR, et al. Incident type 2 diabetes mellitus in African-American and white adults: the Atherosclerosis Risk in Communities Study. JAMA 2000; 283:2253–2259.
6. Jencks SF, Cuerdon T, Burwen DR, et al : Quality of medical care delivered to Medicare beneficiaries: a profile at state and national levels. JAMA 2000; 284:1670–1676.
7. American Diabetes Association: Management of dyslipidemia in adults with diabetes. Diabetes Care 2002; 25(Suppl. 1): S74–S77.
8. Visona A, Lusiain L, Bonanome A, et al. Well thickening of common carotid arteries in patients affected by non-insulin dependent diabetes mellitus: relationship to microvascular complications. Angiology 1995; 46: 793-799.
9. Davidson's JK. Clinical diabetes mellitus. A problem oriented approach. New York. Thieme Inc, 1986.
10. Spicer KM, Allen RC, Hallet D, et al. Synthesis of heamoglobin A_{1c} and related minor heamoglobins by erythrocytes. In vivo study of regulation. J Clin Invest 1977; 64: 40-46.
11. Bunn HF, Gabby KH, Gallop PM. The glycosylation of haemoglobin: Relevance to diabetes mellitus. Science 1978; 200: 21-27.
12. Ikeda, T Ochi H, Ohtani I, et al. Serum lipid and lipoprotein levels in non hypertensive lean NIDDM patients, J Intern Med 1991; 230: 131-134.
13. Virtanen SM, Rasanen L, Virtanen M, et al Association of serum lipids with metabolic control and diet in young subjects with insulin dependent diabetes mellitus in Finland. Eur J clin Nutr 1993; 47: 141-149.
14. Azab AS. glycaemic control among diabetic patients. Saudi Med J 2001; 22: 407-409.
15. Davis TM. Ethnic diversity in type 2 diabetes. Diabet Med 2008 ; 25 (Suppl 2) :52-56.
16. Gary TL, McGuire M, McCauley J, et al. Racial comparisons of health care and glycemic control for African American and white diabetic adults in an urban managed care organization. Dis Manag 2004 ;7: 25-34.
17. de Rekeneire N, Rooks RN, Simonsick EM, et al. Racial differences in glycemic control in a well-functioning older diabetic population: findings from the Health, Aging and Body Composition Study. Diabetes Care 2003 ;26:1986-1992.
18. Eckel RH, Albers JJ, Cheung MC, et al. High density lipoprotein composition in insulin dependent diabetes mellitus. Diabetes 1981; 30: 132-138.
19. Lopes-Virella MF, Wohlthann HJ, Mayfield RK, et al. Effect of metabolic control on lipid, lipoprotein and apolipoprotein levels in 55 insulin dependent diabetic patients. A longitudinal study. Diabetes 1983; 32: 20-25.
20. Ginsberg HN. Lipoprotein physiology in non-diabetic and diabetic states. Relationship to atherosclerosis. Diabetes care 1991; 14: 839-855.
21. Brown WV. Lipoprotein disorders in diabetes mellitus. Med J Clin North Am 1994; 78: 143-161.
22. Guerci B, Igau B, Ziegler O, et al. Intraperitoneal insulin infusion improves the depletion in choline containing phospholipids of lipoprotein B particles in type 1 diabetic patients. Metabolism 1996; 45: 430-434.
23. Taskinen MR. Quantitative and qualitative lipoprotein abnormalities in diabetes. Diabetes 1992, 41 (suppl 2): 12-17.
24. Dailey GE , Mohideen P, Fiedorek FT. Lipid effects of glyburide/metformin tablets in patients with type 2 diabetes mellitus with poor glycemic control and dyslipidemia in an open-label extension study. Clin Ther 2002 ;24:1426-1438.
25. Erdman DM, Cook CB, Greenlund KJ, et al. The impact of outpatient diabetes management on serum lipids in urban African-Americans with type 2 diabetes. Diabetes Care 2002; 25: 9 – 15.

26. Robinson AC, Burke J, Robinson S, et al. The effects of metformin on glycemic control and serum lipids in insulin-treated NIDDM patients with suboptimal metabolic control. Diabetes Care 1998 ;21:701-705.
27. Wulffelé MG, Kooy A, de Zeeuw D, et al. The effect of metformin on blood pressure, plasma cholesterol and triglycerides in type 2 diabetes mellitus: a systematic review. J Intern Med 2004 ;256:1-14.
28. Stein EA. Managing dyslipidemia in the high-risk patient. Am J Cardiol 2002 ;89: 50C-57C.
29. Santini E, Madec S, Corretti V, et al. Effect of statins on soluble CD40 ligand in hypercholesterolemic Type 2 diabetic patients. J Endocrinol Invest 2008; 31: 660-665.
30. Harley CR, Gandhi S, Blasetto J, et al. Low-density lipoprotein cholesterol (LDL-C) levels and LDL-C goal attainment among elderly patients treated with rosuvastatin compared with other statins in routine clinical practice. Am J Geriatr Pharmacother 2007 ;5:185-194.
31. Keating GM, Croom KF. Fenofibrate: a review of its use in primary dyslipidaemia, the metabolic syndrome and type 2 diabetes mellitus. Drugs 2007;67:121-153.
32. Tenenbaum A, Fisman EZ, Motro M, Adler Y.Optimal management of combined dyslipidemia: what have we behind statins monotherapy? Adv Cardiol 2008;45:127-53.
33. Freeman DJ, Norrie J, Sattar N, et al. Pravastatin and the Development of Diabetes Mellitus. Evidence for a Protective Treatment Effect in the West of Scotland Coronary Prevention Study. Circulation 2001;103:357-362.
34. Laakso M. Lipids and lipoproteins as risk factors for coronary heart disease in non-insulin dependent diabetes mellitus. Am J Med 1996; 28: 341-343.
35. Iribarren C, MD, Karter AJ, Go AS., MD, et al . Glycemic Control and Heart Failure Among Adult Patients With Diabetes. Circulation 2001;103:2668-2673.

السيطرة الأيضية عند مرضى السكر

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الخلاصة:

الهدف: تقييم مستوى السيطرة الايضية عند مرضى السكر

الطريقة: شملت الدراسة ١٥٦ من مرضى السكر، منهم ٦٤ مريضاً مصابا بالسكر المعتمد على الانسولين و ٩٢ مريضاً بالسكر غير المعتمد على الانسولين ، بالاضافة الى ١٢٠ من الاصحاء كمجموعة ضابطة. تم قياس مستوى السكر في الدم ومستوى خضاب الدم نوع A_{1c} (HbA_{1c}).

النتائج: كان مستوى HbA_{1c} عالياً وبشكل معنوي عند مرضى السكر (في كلا النوعين) مقارنة بالاصحاء ($P<0.001$). وكان ٤٣,٨ % من مرضى السكر المعتمد على الانسولين و ٦٣,٠ % من مرضى السكر غير المعتمد على الانسولين بدرجة سيطرة أيضية سيئة.

الخاتمة: نسبة مهمة من مرضى السكر في درجة سيئة من السيطرة الايضية مما يجعلهم اكثر عرضة للمضاعفات المبكرة للسكري.

مفاتيح الكلمات: داء السكر، السيطرة الايضية، خضاب الدم نوع A_{1c}

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