International Research Journal of Biological Sciences _____ ISSN 2278-3202
Vol. **3(3),** 19-22, March **(2014)** *Int. Res. J. Biological Sci.*

Evaluation of Biochemical Parameters in Controlled and Uncontrolled Type-2 Diabetic Patients of Bangladesh

Hasan C.M.M[1], Parial R[1], Islam M.M.[1], Ahmad M.N.U.[2] and Rakhing H.C.[1]
[1]Department of Bio Chemistry and Molecular Biology, University of Chittagong, Chittagong-4331 BANGLADESH
[2]Chittagong Diabetic General Hospital, Chittagong-4000, BANGLADESH

Available online at: www.isca.in, www.isca.me
Received 24th September 2013, revised 10th November 2013, accepted 11th January 2014

Abstract

Type 2 Diabetes mellitus is one of the most serious public health problems, faced by both developed and developing countries. Patients with type 2 diabetes often show an unusual biochemical profile. Glycosylated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetic patients. Therefore the aim of the present study was to investigate the evaluation of biochemical parameters in controlled and uncontrolled type 2 diabetic patients on the basis of glycosylated hemoglobin (HbA1c) level as a control. Venous blood samples collected from 156 subjects (Controlled 45 and Uncontrolled 111) with type 2 diabetes mellitus and serum analyzed for HbA1c, Fasting and after breakfast blood glucose, Total Cholesterol, Triglycerides, HDL, LDL and Electrolytes. All biochemical parameters were measured following standard analytical procedure. The HbA1c and after breakfast glucose level were significantly higher in uncontrolled groups than controlled type 2 diabetic subjects ($p<0.001$ and $p<0.01$respectively). Serum triglyceride level in uncontrolled groups was significantly higher than controlled type 2 diabetic patients ($p<0.009$). Serum Na^+ and Cl^- was significantly higher ($p<0.05$) in the controlled compared to uncontrolled subjects. Total cholesterol and triglycerides showed significant positive correlation with HbA1c ($p<0.00$ and $p<0.01$ respectively). Cl^- is negatively correlated with HbA1c and triglyceride ($p<0.045$ and $p<0.022$ respectively). The present study showed that lipid level is increased and electrolytes level is decreased in uncontrolled type 2 diabetes mellitus and HbA1c may be utilized for early diagnosis of cardiovascular disease and timely intervention with lipid lowering drugs in Type 2 diabetic patients.

Keywords: Type 2 diabetes, HbA1c, lipid profile, electrolytes

Introduction

Diabetes mellitus is a multi factorial complex disease that includes sedentary life style, dietary habits and the genetics. Diabetes mellitus is characterized by absolute or relative deficiencies in insulin secretion and/or insulin action coupled with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism. Long-term vascular complications are a major cause of morbidity and mortality in patients with diabetes mellitus[1]. Patients with type 2 diabetes are at greater risk of developing vascular diseases because of lipid changes due to resistance to insulin, and hyperglycemia, which include decreased high density lipoprotein, increased more small dense low density lipoprotein and high triglycerides[2]. It has been discussed that post meal high blood sugars and high lipid levels are risk factors for vascular diseases[3]. Glycemic control is crucial in diabetes management. As lower level of blood glucose leads to decreased rates of morbidity and mortality, maintaining glucose level is a target for all patients with diabetes[4]. Prospective randomized clinical trials and epidemiological studies have shown that glycemic control is interrelated with reduced rates of retinopathy, nephropathy, neuropathy and cardiovascular diseases. It is therefore considered as the main therapeutic goal for prevention of organ damage and other complications of diabetes[5-8]. Glycosylated hemoglobin (HbA1c) is the most vital target of glycemic control. In this view, desirable value for HbA1c is values below 7.00 [5-7]. HbA1c is a gold standard in analysis of patients' status that indicates the average blood glucose during the past three months which is essential to ensure the optimal care of diabetic patients[9]. One percent change in HbA1c is equivalent to an approximately 35 mg/dl change in mean plasma glucose[10]. Smaller values of HbA1c indicate better glycemic control[11]. The research has shown that with each one percent reduction in the value of HbA1c, the risk of microvascular complications is reduced by 40 percent[10]. Hence the present study was conducted on controlled & uncontrolled diabetic patients in order to observe the effect of abnormal glycemic control on lipid metabolism and electrolytes balance.

Material and Methods

Study subjects: This cross sectional design study was conducted in the Laboratory of Biochemistry and Molecular Biology, Research Division of Chittagong Diabetic General Hospital, Chittagong, Bangladesh. A total of 156 diabetic patients with age range of 30-60 years were included in this study from the Out-Patient Department (OPD). The study

subjects were classified as controlled diabetic group which include 45 patients and uncontrolled diabetic group which contain 111 patients based on their HbA_1C level (individuals with HbA_1C level < 7.00 was considered as controlled diabetic group and with HbA_1C level ≥7.00 was considered as uncontrolled diabetic group)[7]. Among the total subjects, 84 were male and 72 were female. Patients with serious co morbid diseases(infection, stroke, myocardial infarction, major surgery, malabsorption), history of using drugs significantly affecting glucose metabolism (glucocorticoids, oral contraceptives containing levonorgestrel or high-dose estrogen, phenytoin, high-dose thiazide diuretics) were excluded from the study.

Collection of venous blood samples: A fasting sample of blood was drawn after an overnight fast of 10 hours. After that the patient was allowed to take breakfast. After half an hour of breakfast blood was again drawn from the patient. After 10-15 minutes of collection, blood samples were centrifuged for 10 minutes at 3000 rpm to obtain serum.

Laboratory analysis: Glycosylated hemoglobin was analyzed using immunoturbidometricassay[11], fasting and after breakfast glucose level was determined by Glucose oxidase –Peroxidase method[12], cholesterol by Cholesterol Oxidase –Peroxidase method[13] and triglycerides by Trinders Glycerol Phosphate Oxidase-Peroxidase method[14]. HDL by Poly ethylene glycol [PEG] precipitation method[15] and LDL cholesterol was calculated according to Freidewald Formulae[16]. The electrolytes were analyzed on Beckman Coulter DXC auto analyzer.

Statistical analysis: Data analysis was performed using Statistical Package for Social Science (SPSS) for Windows version 17. Student's *t* test was done to compare between groups. P value less than 0.05 was considered as significant.

Results and Discussion

The value of HbA1c was significantly higher in uncontrolled type 2 diabetic subjects compared to controlled type 2 diabetic subjects ($p<0.05$). Fasting serum glucose level in the study between the uncontrolled and controlled type 2 diabetic subjects did not show significant difference. After breakfast (ABF) level of glucose was significantly higher in uncontrolled type 2 diabetic subjects compared to controlled type 2 diabetic subjects ($p <0.05$). Serum Cholesterol, high density lipoprotein (HDL), and low density lipoprotein (LDL) level did not show any significant difference between controlled and uncontrolled type 2 diabetic subjects. Serum triglycerides (TG) level in uncontrolled type 2 diabetic subjects was significantly ($p <0.05$) higher compared to controlled type 2 diabetic subjects (table 1). The value of serum Na^+ and Cl^- were significantly lower in the uncontrolled type 2 diabetic subjects compared to controlled type 2 diabetic subjects ($p <0.05$). Serum Potassium ion (K^+) and bicarbonate (HCO_3^-) level did not show statistically significant difference ($p >0.05$) (table 2). The HbA1c, Cholesterol and LDL showed a significant ($P<0.047$; $P<0.001$ and $p<0.040$ respectively) positive correlation with TG and the HDL and Cl^- showed a significant ($P<0.001$ and $p<0.022$ respectively) negative correlation with TG. The HbA_1c showed a significant negative correlation with Cl^- ($P=0.045$) and Cholesterol and LDL showed a significant positive correlation with HbA1c ($P<0.003$ and $P<0.001$ respectively). The HCO_3^- showed a significant positive correlation with HDL ($P=0.031$). The LDL showed a significant positive correlation with Cholesterol ($P<0.001$) (table 3). Diabetes mellitus is a chronic metabolic disorder which lead to serious cardiovascular, renal, neurologic and retinal complications if untreated[17]. Early detection and management of diabetes to prevent complications is the major challenge of diabetes care. Despite the growing concern about this disease, its natural history and etiopathogenesis are still not completely understood. However several risk factors have been identified which may play an important role to the development of diabetic complication including type and duration of diabetes mellitus, age, gender, glycemic control, hypertension, body mass index, smoking, serum lipids, and electrolyte imbalances. Among these, dyslipidemia is mostly responsible for atherosclerotic coronary heart disease in the type 2 diabetic subjects. However, well controlled diabetic patients were reported to have their blood lipid levels significantly lower in comparison to poor glycemic controlled counterparts with favorable lipoprotein profiles[18-19]. Data of the present study indicated that uncontrolled type 2 diabetic subjects have dyslipidaemia characterized with higher levels of serum cholesterol and TG than controlled type 2 diabetic subjects (table 1). In our study we found significant correlation between serum cholesterol and HbA1c values, which supports the assumption that diabetic hypercholesterolemia is enhanced by poor glycemic control (table 3). The metabolic disturbances and their consequences in diabetes mellitus are well known but still our knowledge on the diabetic disorders in electrolytes and membrane function is limited[19]. It has been reported that sodium and potassium depletion is a common feature of essential hypertension and type 2 diabetes[20]. Our study provided data to show that uncontrolled type 2 diabetic subjects have electrolytes imbalance characterized by depletion in sodium, potassium and chloride ions accompanied with elevation of HCO_3^- compared with their controlled type 2 diabetic individual (table 2). The observed reduction in serum Na^+ and K^+ in our uncontrolled diabetic subjects might be a result of electrolyte loss which arises due to dehydration or a result of kidney dysfunction, diabetic nephropathy. Water is flushed out continuously through the kidney tubules as body tries to flush out excess glucose due to hyperglycemia. This water loss is accompanied by Na^+ and K^+ loss. If the process continues, it could soon bring about depletion of base in the body sufficient to cause dehydration of the tissues which may result in death [21]. This electrolytes imbalance might also occur due to inhibition of the rennin-angiotensin-aldosterone system, which plays a key role in the regulation of fluid and electrolyte balance. This enzyme system has been reported to be affected in many endocrine and cardiovascular diseases particularly diabetes[22].

Table-1
Biochemical status of the study subjects

Biochemical parameter	Controlled type2 diabetic Subjects	Uncontrolled type 2 diabetic subjects	p Value
HbA1c%	6.4467± .46348	9.7455± 2.25849	0.000
FBS	8.1947±10.18441	9.1602±3.49355	0.441
ABF	9.8000±2.14574	14.6241±4.54432	0.000
Cholesterol	195.2444±38.734	200.2364±43.482	.505
HDL	38.1333±3.571	38.7455±6.44	.549
LDL	128.444±35.173	126.9091±38.418	.817
TG	148.7778±75.077	200.8091±123.143	.009

Data are expressed as Mean ±SD. Differences between the groups were calculated using students't'test. HbA1c=Glycosylated Hemoglobin, ABF= after breakfast, FBS= fasting blood sugar, TG= triglycerides, HDL= high density lipoprotein, LDL= low density lipoprotein.

Table-2
Serum electrolytes status of the study subjects

Variable	Controlled type2 diabetic subjects	Uncontrolled type 2 diabetic subjects	P Value
Na^+ (mmol/L)	147.6150±3.82117	145.5767± 2.84322	.036
K^+ (mmol/L)	4.5720±.42117	4.4727±.39459	.400
Cl^- (mmol/L)	108.9550±3.95201	106.0533±3.73997	.012
HCO_3^- (mmol/L)	25.0260±2.18703	25.6177±1.72102	.291

Data are presented as Mean+SD. Differences between the groups were calculated using students't'test.

Table-3
Correlation of some biochemical parameters in type 2 diabetic subjects

		HbA1c	Chol	HDL	LDL	TG	Na^+	K^+	Cl^-	HCO_3^-
HbA1c	Pearson Correlation	1	.237**	.148	.255**	.159*	-.193	-.071	-.282*	.188
	Sig.(2-tailed)		.003	.065	.001	.047	.174	.619	.045	.187
	N	156	156	156	156	156	51	51	51	51
Chol	Pearson Correlation	.237**	1	.011	.928**	.362**	-.102	-.035	-.238	.235
	Sig.(2-tailed)	.003		.889	.000	.000	.476	.805	.093	.096
	N	156	156	156	156	156	51	51	51	51
HDL	Pearson Correlation	.148	.011	1	.157	-.275**	.131	-.152	-.044	.303*
	Sig.(2-tailed)	.065	.889		.051	.001	.360	.288	.759	.031
	N	156	156	156	156	156	51	51	51	51
LDL	Pearson Correlation	.255**	.928**	.157	1	.164*	-.020	-.047	-.124	.135
	Sig.(2-tailed)	.001	.000	.051		.040	.889	.744	.386	.346
	N	156	156	156	156	156	51	51	51	51
TG	Pearson Correlation	.159*	.362**	-.275**	.164*	1	-.228	-.145	-.321*	.169
	Sig.(2-tailed)	.047	.000	.001	.040	-	.107	.309	.022	.237
	N	156	156	156	156	156	51	51	51	51

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed). TG= triglycerides, LDL= low density lipoprotein, HDL= high density lipoprotein, Chol= cholesterol

Conclusion

It may postulate from our study that uncontrolled diabetic subjects are prone to lipid abnormalities and electrolytes imbalance. Further study like microvascular and macrovascular abnormality should observe for better understanding the effect of uncontrolled diabetes mellitus.

References

1. Kannel W.B, McGee D., Diabetes and cardiovascular risk factors: the Framingham study, *Circulatio*n., **59(1)**,8–13(**1979**)

2. Ronald M., Lipid and lipoproteins in type 2 diabetes, *Diabetes Care*., **27(6)**,1496-504 (**2004**)

3. Tushuizen M, Diamant M, Heine R., Postprandial dysmetabolism and cardiovascular disease in type 2 diabetes, *Postgrad Med J.,* **81**,1-6(**2005**)

4. Bevan J.L., Diabetes mellitus: a review of select ADA standards for 2006. *J Nurse Pract,* **2(10)**, 674-679 (**2006**)

5. Middleton J., The effect of case management on glycemic control in patients with type 2 diabetes, *The Case Manager*, **14(6)**, 43-7 (**2003**)

6. Hsin O, La Greca AM, Valenzuela J, Moine C.T. and Delamater A., Adherence and glycemic control among Hispanic youth with type 1 diabetes: Role of family involvement and acculturation, *J Pediatr Psychol*, **35(2)**, 156-166 (**2010**)

7. American Diabetes Association: Standards of medical care in diabetes, *Diabetes Care*, **36(1),** 13-61 (**2013**)

8. Khattab M, Khader Y.S, Al-Khawaldeh A, Ajlouni K., Factors associated with poor glycemic control among patients with type 2 diabetes, *J Diabetes Complications*, **24(2),** 84-89 (**2010**)

9. Roszyk L, Faye B, Sapin V, Somda F, Tauveron I., Glycated haemoglobin (HbA1c) today and tomorrow., *Ann Endocrinol* (Paris), **68(5),** 357-65 (**2007**)

10. Alam T, Weintraub N, Weinreb J., What is the proper use of hemoglobin A1c monitoring in the elderly? *J Am Med Dir Assoc*., **7(3),**60-64(**2006**)

11. Vucic M, Petrovic S, Mesic R, Rocic B., An automated immunoturbidimetric assay for HbA1c determination, *Clin Chem Lab Med*, **37**, (**1999**)

12. Barham D, Trinder P., An improved color reagent for the determination of blood glucose by the oxidase system, *Analyst*, **97(151)**:142-5(**1972**)

13. Allain C.C, Poon L.S, Chan C.S.G, Richmond W, Fu P.C., Enzymatic determination of total serum cholesterol, *Clin Chem*., **20(4),** 470-5 (**1974**)

14. Bucolo G, David H., Quantitative determination of serum triglycerides by the use of enzymes, *Clin Chem*., **19(5),** 476-482 (**1973**)

15. Demacker P.N., Hijmans A.G., Vos-Janssen H.E., Van't Laar A., Jansen A.P., A study of the use of polyethylene glycol in estimating cholesterol in high-density lipoprotein, *Clin Chem*., **26(13),** 1775-1779 (**1980**)

16. Friedewald W.T., Levy R.I., Fredrickson D.S., Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge, *Clin Chem,* **18(6),** 499-502 (**1972**)

17. Rao G.M., Serum electrolytes and osmolality in diabetes mellitus, *Ind J Med Sci*, **46(10),** 301-303 **(1992)**

18. Kendall D.M, Rubin C.J., Mohideen P., Ledeine L.M., Beller R., Gross J., Norwood P., O'Mahony M., Sall K., Sloan G.G., Improvement of glycemic control, triglycerides, and HDL cholesterol levels with muraglitazar, a dual ([alpha]/[gamma]) peroxisome proliferator-activated receptor activator, in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a double-blind, randomized, pioglitazone-comparative study, *Diabetes Care,* **29,** 1016–*1023 (***2006***)*

19. Eckel R.H., Wassef M., Chait A., Prevention Conference VI: Diabetes and Cardiovascular Disease : Writing Group II :pathogenesis of atherosclerosis in diabetes, *Circulation* **105**, 138-143(**2002**)

20. Van Style D.D., Serdroy J., Studies on diabetes and electrolyte equilibrium in blood, *J BiolChem*, **18**: 20-26 (**1928**)

21. Leonard I.K., John M., Physiology and pathophysiology of body water and electrolytes. In: Kaplan and Pesce (Eds.), Clinical Chemistry: Theory, analysis and correlation, The C.V. Mosby Co. St Louis; 313-331 (**1989**)

22. Cowie C.C., Harris M.I., Physical and metabolic characteristics of persons with diabetes, *Diabetes in America,* 2nd ed. National Institutes of Health; 117-164 (**1995**)