

SCREENING DIABETES THROUGH GLYCATED HEMOGLOBIN (HbA1c) IN NORTH INDIAN POPULATION

C. Kumar, M. Vijayasimha*, R. P. Jayaswal, A. K. Sah, Meenakshi, R. K. Jha and N. M. Praveen

Department of Medical Laboratory Technology, Amity Medical School, Amity University Haryana.

*Author for Correspondence: M Vijayasimha

Department of Medical laboratory Technology, Amity Medical School, Amity University Haryana.

Article Received on 05/05/2017

Article Revised on 26/05/2017

Article Accepted on 15/06/2017

ABSTRACT

Early diagnosis of diabetes is crucially important in reducing health complications worldwide. In this aspect, Glycosylated hemoglobin (HbA1c) has become an accurate marker for the diagnosis of diabetic severity and estimating complications. In this study, the correlation between HbA1c and fasting blood sugar (FBS) was assessed in diabetic patients. The study consists of 102 samples, of which 63 males and 39 females patients of age groups between 40-50 yrs, 51-60 yrs and above 61 yrs were included in our study. HbA1c along with FBS is very sensitive, specific and have predictive values in detection of complication of diabetes. The association of HbA1c with FBS was found relatively stable particularly in diabetic subjects and proved that these tests are more reliable and acceptable for discriminating diabetics from non-diabetics as well as finding long term glycemic complication.

KEYWORDS: HbA1c; Diabetics; Fasting Blood Sugar.

INTRODUCTION

Diabetes mellitus (DM) is recognized as a chronic metabolic disease that can be differentiated by uncontrolled glucose level and increased risk of micro and macro-vascular complications. Around 415 million adult were suffering from diabetes in 2008, as per International Federation of Diabetes (IFD). According to global standards, diabetic incidence among men and women are 9.8% and 9.2% respectively. In India every 26 per 100,000 persons die due to diabetes.^[1] Diabetes is considered as a group of metabolic disorder which causes uncontrolled hyperglycemia^[2], mainly two groups of diabetes is recognized worldwide- Type 1 diabetes mellitus formally known as insulin dependent diabetes mellitus (IDDM) is caused by destruction of autoimmune response of pancreatic islet of β -cells^[3,4]; Type 2 diabetes mellitus recognized as non-IDDM that is caused due to inadequate insulin binding with the sugar receptors.^[5,6] Oral pharmacologic strategies promote release of insulin in type 2 diabetes which manages hyperglycemia.^[7]

The complication of diabetic cases are directly co-related with mean and higher concentration of glycated hemoglobin (HbA1c). Management of hyperglycemic condition is difficult but with precise treatment may help to reduce related disorders.^[8] Retinopathy due to hyperglycemia may be prevented by hyperglycemia using insulin therapy.^[9] Acute myocardial infarction also correlates with elevated mortality in diabetes which

widely effects on auto-neuropathy through toxic release of catecholamine, corticosteroid and free fatty acids.^[10]

Self-monitoring of hyperglycemic condition may help to improve post glycemic conditions through self-supervision by adhering with the instructions prescribed by the specialist^[11], these may reduce long term complications and improve HbA1c level.^[12] HbA1c also target β N-terminal glycated tetra-peptide of immunoglobulin^[13] that reflects hyperglycemia with multiple complications, increases clinical effectiveness and improve patients to recover from glycaemia.^[14] Hemoglobin variants are pointed out by transformation of one amino acid in protein chain which becomes highly reactive with glucose to become glycated forms. HbA1cis linked with huge family dominance where parent hemoglobin may match with offspring's and among the siblings.^[15]

HbA1c, glycoprotein enhances DM and its measurement is significant to differentiate normal and diabetic patients.^[16] Measurement of advance glycation end products (AGEs) and carboxymethyllysine (CML) concentration is a predictor of HbA1c concentration.^[17]

MATERIALS AND METHODS

The samples were collected from 102 patients who visited a diagnostic lab at, Safdarjung Development Area (SDA) New Delhi during February 2017 to April 2017 for routine investigation. This prospective study was

conducted to identify the occurrence of hyperglycemic condition in both male and female patients.

The provided specimen were analyzed for Glycated hemoglobin (HbA1c) by using Sysmex TOSOH G8 analyzer and fasting blood sugar (FBS) was performed by using Backman Coulter AU 680 with maintaining the high and low controls. The patient's data were collected with the support of laboratory supervisor.

All the analyzed samples were categorized in both male and female into three groups -(40-50 yrs), (51-60 yrs) and (Above 61yrs). Using Microsoft Office excel 2013, the recorded report of HbA1c and FBS were analysed to know the hyperglycemic or hypoglycemic condition in male and female patients.

Table No 1: Total number of male & female patient's

Age Group (Yrs)	Male	Female	Total number of patient's
40-50	15	14	29
51-60	19	9	28
Above 61 +	29	16	45

RESULTS

A total of 102 men and women were randomly assigned in our study. The similar characteristics were seen in two study groups of variant ages (Table 1).

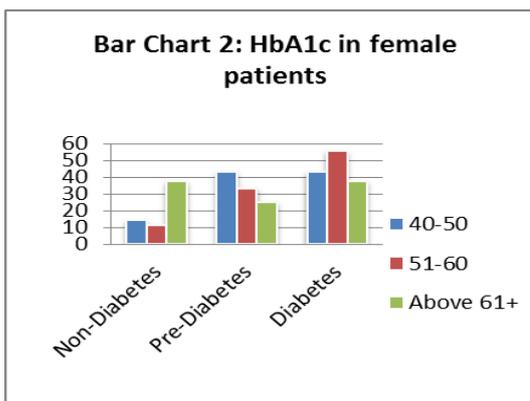
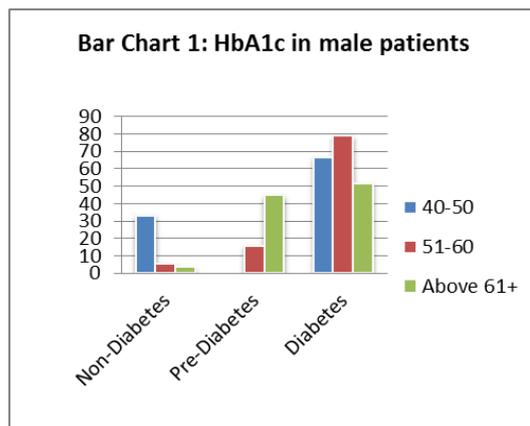
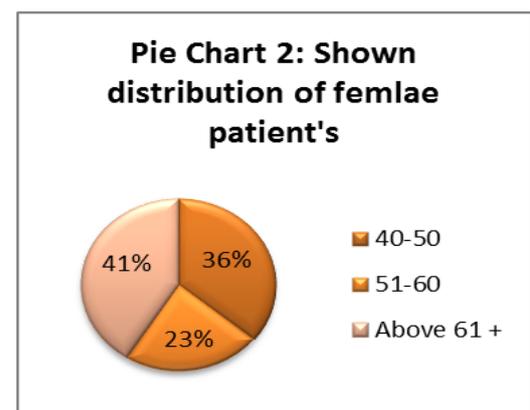
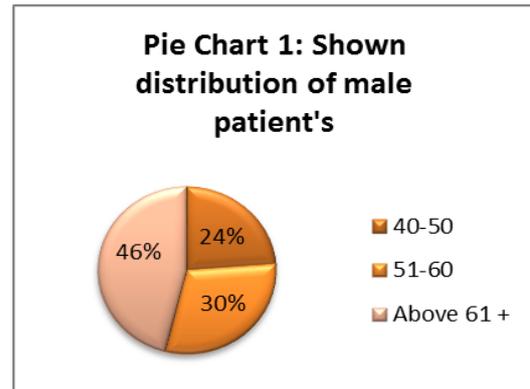
This study included 63 male and 39 female patients of age groups 40-50 yrs, 51-60 yrs and Above 61 yrs were represented accordingly percentage-wise i.e. 24%, 30% and 46% respectively (pie chart 1) in male, 36%, 23% and 41% respectively (pie chart 2) in female patients.

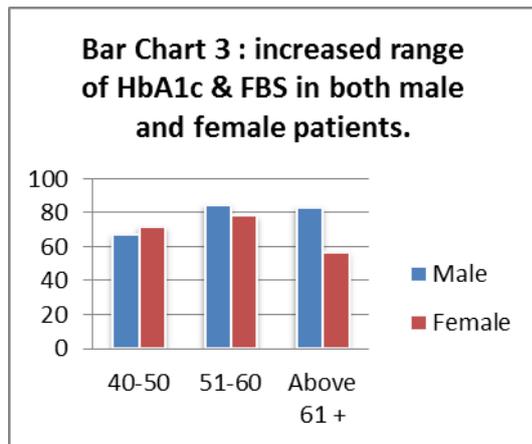
The glycated hemoglobin range below < 5.7 characterizes the non-diabetic cases, the HbA1c levels from 5.8 ± 0.6 revealed pre-diabetes, whereas the range exposed in high peak more than >6.4 bares intensive-therapy group, the patients may require Hypoglycemic agents/insulin supplements to correct the glycated concentration.

The main purpose of this study was to find out the correlation between blood glucose level and glycated hemoglobin (HbA1c). Hyperglycemia plays a vital role in enhancing the complications of atherosclerosis, risk factors for cardiovascular disease like dyslipidemia, hypertension in smokers or obese, nephropathy, retinopathy, nephropathy and foot ulcer.

We assessed fasting glucose and HbA1c level that were correlated with regard to their increasing age. The increased range were observed mainly in male patients, that detailed as 67%, 84% and 83%, in 3 different age group in ascending order respectively whereas in female it was viewed as 71%, 78% and 56% respectively (bar chart 3) accordingly age-wise. It was concluded that the hyperglycemic cases were higher in male patients

compared to female patients which may be due to improper metabolic activity, habit or routine activity, smoking or consumption of alcohol, drugs etc.





DISCUSSION

The study revealed that high HbA1c and FBS values are associated with short and long term complications risk in patients. The collected data revealed that increased hyperglycemic cases were seen in male in comparison to female patients. This study shown that increased level of HbA1c leads to high mortality due to macro-vascular and micro-vascular complication that contribute worsening of kidney function.^[18-20] Hyperglycemia categorized with impaired fasting glucose due to global standardization and threshold with prognostic significance of HbA1c through optimal glucose control may achieved with proper medication, self-management and essential therapy.^[21,22] HbA1c interfere with abnormal hemoglobin traits with alternative clinical circumstances that influence in erythrocyte turnover.^[23,24] Glycated hemoglobin predicts prevalent risk factors of kidney disease and retinopathy due to presence of natural glycemc threshold in the absence of albuminuria and retinopathy which can be compared with fasting blood glucose.^[25,26] Glycemc control extensively observed in adults and adolescents with elevated range of HA1c also incident in hypoglycemic conditions.^[27,28]

Hyperglycemia can occur due to genetic factors, obesity, environmental factors with long term and short term complications by reducing glucose transport to liver, muscle and fat cells.^[29-31] Reduction of glucose concentration may preserve quality of life and adverse side effect observed in cardio vascular disease (CVD) with atherosclerosis, modified lipoprotein activates, it accumulate damage in vascular due to metabolic abnormalities.^[32,33]

Self-management strategy helps in physiological mechanism with excess usage of insulin dose that affect hypoglycemia, hormonal imbalance, and dietary food source manipulate regimen modification in diabetes.^[34,35] Hyperglycemia effects through immune system and inflammatory response that counter through hormones, inflammatory cytokines and oxidative stress leads through dysfunction and cardiovascular complications.^[36,37] Diabetic retinopathy proliferate the microaneurysms and retinal hemorrhage which has an intensive effect during insulin treatment with high

risk^[38,39] characteristic glycemc control stated in retinopathy, nephropathy and neuropathy that can be characterized with type 1 diabetes, long term hyperglycemia associated with lower glycation production in skin collagen.^[40] Physiological factors contribute in wound healing in diabetes that impairs keratinocyte and proliferate through cytokine and growth factors during the production of reactive species in oxidative stress.^[41] The management plan formulate therapeutic drugs, health concern, implementation of proper treatment that responsible for goal plan with diabetes self-management education (DSME) and integral care considering patient's age group, physical activity, dietary source, socio-economic status and cultural factors with medical conditions.^[42]

CONCLUSION

We observed that elevated HbA1c among 51 to 60 years age group in both male and female and clarified that there were no variation among separate gender except two groups. The availability of HbA1c as marker facilitates diabetes care that indexed for long-term hyperglycemia with diagnosis of diabetes, it consider as risk predictor to control glucose level. Long term epidemiological studies highlighted to control hyperglycemia in type 1 and type 2 diabetes mellitus that strongly correlate with HbA1c concentration and complications. The challenge of maintaining consistent blood glucose level in normal range is very difficult with proper diet and modified medications in diabetic patients but monitoring is possible with the help of HbA1c and Fasting Blood Sugar.

REFERENCES

1. Akhtar SN & Dhillon P. Prevalence of diagnosed diabetes and associated risk factors: Evidence from the large-scale surveys in India. *Journal of Social Health and Diabetes*, 2017; 1: 5(1): 28.
2. Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Kirkman MS, Lernmark A, Metzger BE & Nathan DM. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem*, 2011; 57(6): e1-e47.
3. Castano L & Eisenbarth GS. Type-I diabetes: a chronic autoimmune disease of human, mouse, and rat. *Annu Rev Immunol*, 1990; 8: 647-79.
4. Yang W, Lu J, Weng J, Jia W, Ji L, Xiao J, Shan Z, Liu J, Tian H, Ji Q, Zhu D, Ge J, Lin L, Chen L, Guo X, Zhao Z, Li Q, Zhou Z, Shan G, He J; China National Diabetes and Metabolic Disorders Study Group Prevalence of diabetes among men and women in China. *N Engl J Med*, 2010; 25: 362(12): 1090-1001.
5. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*, 1988; 37(12): 1595-607.
6. Sacks DB & McDonald JM. The pathogenesis of type II diabetes mellitus. A polygenic disease. *Am J ClinPathol*, 1996; 105(2): 149-56.

7. Simpson SH, Majumdar SR, Tsuyuki RT, Eurich DT, Johnson JA. Dose-response relation between sulfonylurea drugs and mortality in type 2 diabetes mellitus: a population-based cohort study. *CMAJ*, 2006; 17: 174(2): 169-74.
8. Weykamp C. HbA1c: a review of analytical and clinical aspects. *Ann Lab Med*. 2013; 33(6): 393-400. doi: 10.3343/alm.2013.33.6.393.
9. Brinchmann-Hansen O, Dahl-Jørgensen K, Sandvik L & Hanssen KF. Blood glucose concentrations and progression of diabetic retinopathy: the seven year results of the Oslo study. *BMJ*, 1992; 4: 304(6818): 19-22.
10. Clark RS, English M, McNeill GP & Newton RW. Effect of intravenous infusion of insulin in diabetics with acute myocardial infarction. *Br Med J (Clin Res Ed)*, 1985; 3: 291(6491): 303-5.
11. O'Kane MJ, Bunting B, Copeland M & Coates VE; ESMON study group. Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): randomised controlled trial. *BMJ*. 2008; 24: 336(7654): 1174-7.
12. Simon J, Gray A, Clarke P, Wade A, Neil A & Farmer A; Diabetes Glycaemic Education and Monitoring Trial Group. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. *BMJ*, 2008; 24: 336(7654): 1177-1180.
13. John WG, Mosca A, Weykamp C & Goodall I. HbA1c standardisation: history, science and politics. *Clin Biochem Rev*, 2007; 28(4): 163-168.
14. Lenters-Westra E & Slingerland RJ. Hemoglobin A1c point-of-care assays; a new world with a lot of consequences! *J Diabetes Sci Technol*, 2009; 1: 3(3): 418-23.
15. Weykamp C, John WG & Mosca A. A review of the challenge in measuring hemoglobin A1c. *J Diabetes Sci Technol*. 2009; 1:3(3):439-445.
16. Bunn HF, Haney DN, Kamin S, Gabbay KH & Gallop PM. The biosynthesis of human hemoglobin A1c. Slow glycosylation of hemoglobin in vivo. *J Clin Invest*, 1976; 57(6): 1652-1659.
17. Genuth S, Sun W, Cleary P, Sell DR, Dahms W, Malone J, Sivitz W & Monnier VM; DCCT Skin Collagen Ancillary Study Group. Glycation and carboxymethyllysine levels in skin collagen predict the risk of future 10-year progression of diabetic retinopathy and nephropathy in the diabetes control and complication trial and epidemiology of diabetes interventions and complications participants with type 1 diabetes. *Diabetes*, 2005; 54(11): 3103-11.
18. Gerstein HC, Swedberg K, Carlsson J, McMurray JJ, Michelson EL, Olofsson B, Pfeffer MA. & Yusuf S. The hemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. *Archives of Internal Medicine*, 2008; 168(15): 1699-1704.
19. Khaw KT, Wareham N, Bingham S, Luben R, Welch A & Day N. Preliminary communication: glycated hemoglobin, diabetes, and incident colorectal cancer in men and women: a prospective analysis from the European prospective investigation into cancer–Norfolk study. *Cancer Epidemiology and Prevention Biomarkers*, 2004; 1: 13(6): 915-919.
20. Nicholas J, Charlton J, Dregan A & Gulliford MC. Recent HbA1c values and mortality risk in type 2 diabetes. population-based case-control study. *PLoS One*, 2013; 5: 8(7): e68008.
21. Cowie CC, Rust KF, Byrd-Holt DD, Gregg EW, Ford ES, Geiss LS, Bainbridge KE & Fradkin JE. Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S. population in 1988-2006. *Diabetes Care*, 2010; 33(3): 562-568.
22. American Diabetes Association. Standards of medical care in diabetes—2009. *Diabetes care*, 2009; 1: 32(Supplement 1): S13-61.
23. Bonora E & Tuomilehto J. The pros and cons of diagnosing diabetes with A1C. *Diabetes Care*, 2011; 34(2): S184-190.
24. Riddle MC, Ambrosius WT, Brillon DJ, Buse JB, Byington RP, Cohen RM, Goff DC Jr, Malozowski S, Margolis KL, Probstfield JL, Schnall A & Seaquist ER; Action to Control Cardiovascular Risk in Diabetes Investigators. Epidemiologic relationships between A1C and all-cause mortality during a median 3.4-year follow-up of glycemic treatment in the ACCORD trial. *Diabetes Care*, 2010; 33(5): 983-990.
25. Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. *JAMA*, 2003; 22: 290(16): 2159-2167.
26. Selvin E, Ning Y, Steffes MW, Bash LD, Klein R, Wong TY, Astor BC, Sharrett AR, Brancati FL & Coresh J. Glycated hemoglobin and the risk of kidney disease and retinopathy in adults with and without diabetes. *Diabetes*, 2011; 1: 60(1): 298-305.
27. White NH, Sun W, Cleary PA, Tamborlane WV, Danis RP, Hainsworth DP & Davis MD; DCCT-EDIC Research Group. Effect of prior intensive therapy in type 1 diabetes on 10-year progression of retinopathy in the DCCT/EDIC: comparison of adults and adolescents. *Diabetes*, 2010; 59(5): 1244-1253.
28. Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP Jr & Selby JV. Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. *JAMA*. 2009; 15: 301(15): 1565-1572.
29. Praveen N M, M Vijayasimha, R P Jayaswal, R K Jha, A K Sah, Dhruvi Patel & Pritha Roy. Case

- Study: An emergency case diagnosed with uncontrolled hyperglycemia and glaucomatous was treated as type 2 diabetes. *European J. biomed. Pharm. Sci*, 2017; 4(5): 445-448.
30. Scott LJ, Mohlke KL, Bonnycastle LL, Willer CJ, Li Y, Duren WL, Erdos MR, Stringham HM, Chines PS, Jackson AU, Prokunina-Olsson L, Ding CJ, Swift AJ, Narisu N, Hu T, Pruim R, Xiao R, Li XY, Conneely KN, Riebow NL, Sprau AG, Tong M, White PP, Hetrick KN, Barnhart MW, Bark CW, Goldstein JL, Watkins L, Xiang F, Saramies J, Buchanan TA, Watanabe RM, Valle TT, Kinnunen L, Abecasis GR, Pugh EW, Doheny KF, Bergman RN, Tuomilehto J, Collins FS, Boehnke M. A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants. *Science*, 2007; 1: 316(5829): 1341-1345.
 31. Meigs JB, Shrader P, Sullivan LM, McAteer JB, Fox CS, Dupuis J, Manning AK, Florez JC, Wilson PW, D'Agostino RB Sr & Cupples LA. Genotype score in addition to common risk factors for prediction of type 2 diabetes. *N Engl J Med*, 2008 Nov 20; 359(21): 2208-2219.
 32. Reaven PD, Moritz TE, Schwenke DC, Anderson RJ, Criqui M, Detrano R, Emanuele N, Kayshap M, Marks J, Mudaliar S, Harsha Rao R, Shah JH, Goldman S, Reda DJ, McCarren M, Abaira C & Duckworth W; Veterans Affairs Diabetes Trial. Intensive glucose-lowering therapy reduces cardiovascular disease events in veterans affairs diabetes trial participants with lower calcified coronary atherosclerosis. *Diabetes*, 2009; 58(11): 2642-2648.
 33. Januszkiewicz L. The ACCORD Study Group. Effects of combination lipid therapy in type 2 diabetes mellitus. *Kardiol Pol*, 2010; 68(7): 853-854.
 34. Young-Hyman DL & Davis CL. Disordered eating behavior in individuals with diabetes: importance of context, evaluation, and classification. *Diabetes Care*, 2010; 33(3): 683-689.
 35. Chan JC, So WY, Yeung CY, Ko GT, Lau IT, Tsang MW, Lau KP, Siu SC, Li JK, Yeung VT, Leung WY, Tong PC; SURE Study Group. Effects of structured versus usual care on renal endpoint in type 2 diabetes: the SURE study: a randomized multicenter translational study. *Diabetes Care*, 2009; 32(6): 977-982.
 36. Kitabchi AE, Freire AX, Umpierrez GE. Evidence for strict inpatient blood glucose control: time to revise glycemic goals in hospitalized patients. *Metabolism*, 2008; 31: 57(1): 116-1120.
 37. Umpierrez GE, Smiley D, Zisman A, Prieto LM, Palacio A, Ceron M, Puig A & Mejia R. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). *Diabetes care*, 2007; 1: 30(9): 2181-2186.
 38. American Diabetes Association. Epidemiology of Diabetes Interventions and Complications (EDIC). Design, implementation, and preliminary results of a long-term follow-up of the Diabetes Control and Complications Trial cohort. *Diabetes Care*, 1999; 1: 22(1): 99-111.
 39. Barr CC. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive insulin therapy, by The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. *N. Engl. J. Med*, 2000; 342: 381-389.
 40. Monnier VM, Bautista O, Kenny D, Sell DR, Fogarty J, Dahms W, Cleary PA, Lachin J & Genuth S. Skin collagen glycation, glycoxidation, and crosslinking are lower in subjects with long-term intensive versus conventional therapy of type 1 diabetes: relevance of glycated collagen products versus HbA1c as markers of diabetic complications. DCCT Skin Collagen Ancillary Study Group. *Diabetes Control and Complications Trial. Diabetes*, 1999; 48(4): 870-880.
 41. Christman AL, Selvin E, Margolis DJ, Lazarus GS & Garza LA. Hemoglobin A1c predicts healing rate in diabetic wounds. *Journal of Investigative Dermatology*, 2011; 31: 131(10): 2121-7.
 42. American Diabetes Association. Executive summary: standards of medical care in diabetes-2011. *Diabetes Care*, 2011; 34 (1): S4-10.