Cardiovascular disease risk assessment in Nigerian adults with type 2 diabetes and metabolic syndrome using the Framingham’s risk score

Ifeoma Christiana Udenze, Casmir Ezenwa Amadi
Department of Clinical Pathology, College of Medicine, University of Lagos, 1Department of Medicine, Cardiology Unit, College of Medicine, University of Lagos, Lagos, Nigeria

ABSTRACT

Background: Cardiovascular morbidity is a major burden in Nigerian patients with type 2 diabetes mellitus (DM).

Aims and Objectives: The aim of the present study was to compare the cardiovascular risk scores of type 2 diabetics with those of individuals with metabolic syndrome and in healthy controls and examine the impact of glycemic control and lifestyle on cardiovascular risk.

Subjects and Methods: This was a cross-sectional study of adult Nigerians with type 2 diabetes, metabolic syndrome, and age- and sex-matched controls. Written informed consent was obtained from all the participants. The Ethics Committee of the Lagos University Teaching Hospital, Lagos, Nigeria, approved the study protocol.

Statistical Analysis: The data were analyzed using the IBM SPSS software version 20.0 package. Statistical significance was set at \( P < 0.05 \).

Results: There was a statistically significant difference in cardiovascular disease (CVD) risk scores between the group with diabetes (20.41 ± 12.98), metabolic syndrome (10.00 ± 6.35) and the control group (6.79 ± 7.81) (\( P < 0.001 \)), and also in glycated hemoglobin (HbA\(_1c\)) high-density lipoproteins (HDL)-cholesterol, total cholesterol, and triglyceride concentrations between the groups (\( P < 0.05 \)). CVD risk correlated positively and significantly with HbA\(_1c\), body mass index and waist circumference and negatively with the level of education (\( P < 0.05 \)). Only 52.2% of the people with diabetes on treatment achieved HbA\(_1c\) target of <7%.

Conclusion: People with Type 2 diabetes had high CVD risk scores, control of CVD risk factors is not optimum in adult Nigerians. Strategies to achieve better glycemic control, weight reduction, and increase literacy levels will help achieve CVD risk reduction in adult Nigerians.

Keywords: Cardiovascular disease risk score, Framingham’s study, metabolic syndrome, type 2 diabetes

Introduction

The prevalence of type 2 diabetes is increasing globally, and factors such as aging of the population, increasing the prevalence of obesity and sedentary lifestyles have contributed to this trend.\(^1,2\) In 2009, global estimates put the world prevalence of diabetes among adults at 6.4%, affecting 285 million adults, in 2010, and projected to increase to 7.7%, affecting 439 million adults by the year 2030.\(^3\) There was also an estimated 69% increase in numbers of adults with type 2 diabetes in developing countries compared to 20% increase in developed countries between 2010 and 2015.\(^3\) In Nigeria, the estimated prevalence rate for type 2 diabetes was 4.3%,
and over 5 million people are projected to be affected by 2030.[3]

Diabetes is an independent risk factor for cardiovascular disease (CVD).[4,5] Type 2 diabetes is associated with a 2–4-fold increase in the risk of both coronary heart disease and stroke.[6,7] CVDs are listed as the cause of death in approximately 65% of persons with diabetes[8] and strategies to reduce CVD risk are an important part of the management protocol for type 2 DM.[9]

Quantifying the risk of developing CVD in patients with diabetes has important strategic benefits in patient management.[10‑12] CVD risk quantification is useful in ranking individuals and groups according to absolute risk for the purpose of targeting therapy to those at greatest risk to appropriately allocate community and health resources.[13] It also provides prognostic information or accurate estimation of the likely absolute benefit from a therapeutic intervention.[11,12]

Today's lifestyle choices are characterized by increased physical inactivity and consumption of calorie dense foods which fuel the obesity pandemic. Obesity and physical inactivity have been implicated in the development of insulin resistance in individuals who are genetically susceptible.[1,13] Insulin resistance is the first defect in a cascade of metabolic abnormalities leading up to the onset of type 2 diabetes. These dysmetabolic features include cardiovascular risk factors of dyslipidemia, hypertension, inflammatory, and prothrombotic factors.[14] The clustering of these risk factors in a single individual is termed the metabolic syndrome. The metabolic syndrome commonly precedes the development of type 2 diabetes by many years[15] and is also an independent risk factor for CVD. Thus, early detection of the risk factors associated with the metabolic syndrome is needed for the institution of appropriate primary prevention measures in patients at risk for diabetes.

The Framingham’s risk assessment tool which was developed in the general population and validated in people with diabetes is used to estimate a person’s 10-year risk of developing CVD to identify high-risk individuals for primary prevention.[16] An individual’s risk score can aid clinical decision-making on how intensively to intervene in lifestyle modification strategies, when to include drug therapy[10] and also to assess the efficacy of these interventions.

This study compared the cardiovascular risk scores of people with type 2 diabetes on treatment with those of individuals with metabolic syndrome and in healthy controls. It examined the impact of glycemic control and lifestyle on cardiovascular risk reduction in adult Nigerians.

Subjects and Methods

This was a cross-sectional study of 40 adult men and women with type 2 DM, forty adult men and women with metabolic syndrome and 40 age- and sex-matched males and females who were recruited as healthy controls. The Ethical Research and Review Committee of the Lagos University Teaching Hospital (LUTH) approved the study protocol, and informed consent was obtained from the participants.

The study participants were patients attending The Diabetic Clinic and The Obesity and Metabolic Clinic of the LUTH. Adult men and women between the age group of 30 and 70 years who agreed to participate in the study were consecutively recruited. Sociodemographic and clinical data were obtained from the participants using a structured questionnaire. Anthropometric measurements such as weight, height, waist and hip circumference, and blood pressure readings were taken. Lipid profile results were also determined. The diagnosis of type 2 diabetes was based on the WHO criteria,[16] and the diagnosis of the metabolic syndrome was based on the NCEP-ATPIII criteria.[17]

Patients who did not meet the criteria for metabolic syndrome were matched for age and sex with the cases and recruited as controls.

The inclusion criteria included adult males and females between 30 and 70 years of age who had been diagnosed to have diabetes mellitus by the WHO criteria[16] with blood glucose level controlled with diet and hypoglycemic drugs and nondiabetics who had metabolic syndrome described by the presence of any three of the following: abdominal circumference ≥102 cm in males or ≥88 cm in females, high-density lipoproteins (HDL) cholesterol <1.03 mmol/L (<40 mg/dL)(males) or <1.3 mmol/L(<50 mg/dL)(females), triglycerides (TGs) ≥1.7 mmol/L (≥150 mg/dL), blood pressure ≥130/85 mmHg or the patient receiving hypotensive treatment and fasting glycemia >6.1 mmol/L (>110 mg/dL).[17]

Pregnant women were excluded from the study.

The study participants reported on the morning of the study after an overnight (10–12 h) fast. A volume of 5 ml
venous blood was collected from the antecubital vein and transferred into plain tubes for lipid profile assay, into fluoride oxalate tubes for glucose analysis and into ethylenediaminetetraacetic acid tubes for glycated hemoglobin (HbA$_1c$) assay.

Abdominal obesity was determined by measurement of the waist circumference. The measurement was taken, using an inelastic tape, at the end of several consecutive natural breaths, at a level parallel to the floor, the midpoint between the top of the iliac crest, and the lower margin of the last palpable rib in the mid-axillary line.[18] The hip circumference was measured at a level parallel to the floor, at the largest circumference of the buttocks.[18]

The blood pressure was determined using the Accoson’s Mercury Sphygmomanometer (cuff size 15 cm × 43 cm). The participants were seated and rested for 5 min before measurement. The systolic blood pressure was taken at the first Korotkoff sound and diastolic at the fifth Korotkoff sound.[19]

The total, low-density lipoproteins (LDL), HDL cholesterol, and TG were determined on fasting serum samples and glucose concentrations were determined from fasting fluoride oxalate plasma using reagents from Randox Laboratories Limited, Antrim, UK, BT 29 4QY, on semiautomatic biochemistry analyzer BS3000P-Sinnowa Medical Science and Technology Company limited, Nanjing, China (211135). An ion-exchange chromatographic-spectrophotometric method for HbA$_1c$ was used[20] using reagents from Fortress Diagnostics, UK. The Framingham’s risk score was estimated from a CVD risk calculator based on the equation from the Framingham’s heart study.[21]

### Statistical analysis

The data were analyzed using the IBM SPSS version 20.0 (SPSS Inc., Chicago, IL). The Chi-squared test was employed to test the differences in the categorical variables, ANOVA was employed to test the differences in the mean values for the continuous variables. Spearman’s correlation analysis was employed to determine the association between variables. Statistical significance was set at $P < 0.05$.

### Results

Forty individuals with type 2 diabetes and 40 individuals with metabolic syndrome and forty healthy controls participated in the study. Each group consisted of 13 men and 27 women [Table 1].

The study participants did not differ in their sociodemographic characteristics showing that the study participants have been well matched. The same number of men and women participated in all three groups to ensure matching the groups by gender. The three groups of subjects also showed very similar age group distribution. Although 15% compared to 65% of the metabolic syndrome group and 85% of the healthy controls received post secondary education, the educational levels taken together did not show the statistically significant

| Table 1: Sociodemographic characteristics of study participants ($n=40$) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Characteristics | Subjects with type 2 diabetes, $n$ (%) | Subjects with metabolic syndrome, $n$ (%) | Healthy controls, $n$ (%) | $P$ |
| Gender          |                |                |                |                |
| Males           | 13 (32.55)     | 13 (32.55)     | 13 (32.55)     | 1.00           |
| Females         | 27 (67.5)      | 27 (67.5)      | 27 (67.5)      |                |
| Age (years)     |                |                |                |                |
| 30-40           | 5 (12.5)       | 5 (12.5)       | 7 (17.5)       | 0.83           |
| 41-50           | 14 (35)        | 15 (37.5)      | 12 (30)        |                |
| 51-60           | 18 (45)        | 18 (45)        | 19 (47.5)      |                |
| 61-70           | 3 (7.5)        | 2 (5)          | 2 (5)          |                |
| Level of education |            |                |                |                |
| None            | 2 (5)          | 0 (0)          | 1 (2.5)        | 0.075          |
| Primary         | 9 (22.5)       | 3 (7.5)        | 5 (12.5)       |                |
| Secondary       | 13 (32.5)      | 11 (27.5)      | 6 (15)         |                |
| Tertiary        | 6 (15)         | 26 (65)        | 28 (70)        |                |
| Exercise        |                |                |                |                |
| Yes             | 5 (12.5)       | 2 (5)          | 4 (10)         | 0.81           |
| No              | 35 (87.5)      | 38 (95)        | 36 (90)        |                |
| Alcohol         |                |                |                |                |
| Yes             | 11 (27.5)      | 6 (15)         | 6 (15)         | 0.64           |
| No              | 29 (72.5)      | 34 (85)        | 34 (85)        |                |
difference between the three groups. Most of the study participants in all three groups neither exercised nor took alcohol.

Table 2 shows the clinical and laboratory parameters of the study participants.

The differences between the groups were seen in the lipid profile parameters, HbA1c, and in the absolute values of CVD risk. The group with metabolic syndrome had higher TG, total cholesterol (TC), and LDL cholesterol than the control group and the DM group on treatment. From the post hoc analysis, HDL cholesterol levels from all three groups contributed to differences seen between the groups.

A comparison of CVD risk categories among subjects with type 2 diabetes, metabolic syndrome and healthy controls, calculated using the Framingham’s showed that for low-risk category with a Framingham’s score of 10% or less, 72.5% of the controls fell in to this category compared to 55% with metabolic syndrome and 27.5% with type 2 DM. In the high-risk category (Framingham’s score of 20% or more), 52.5% of the participants with type 2 DM compared with 7.5% and 2.5% in the metabolic syndrome and control groups, respectively, were found in the high-risk category \( (P < 0.001) \)

In the study population, we assessed the relationship of CVD risk scores with glycemic control and lifestyle. The correlation between alcohol consumption, smoking, physical activity, obesity, level of education, HbA1c, and CVD risk showed that obesity, level of education, and glycemic control showed statistically significant relationships with CVD risk \( (P < 0.05) \). Level of education had an inverse relationship with CVD risk.

Table 3 shows the percentage of type 2 diabetics who achieved optimal treatment goals for modifiable cardiovascular risk factors using guidelines from the American Diabetes Association. Standards of diabetic care-2012,\(^{[22]} \) Most of the study population with type 2 diabetes did not attain optimal treatment goals for the modifiable cardiovascular risk factors. Only 16% of the people with diabetes met target treatment values for HDL. 95% of the diabetic population met TG treatment targets. About 50% of the people with diabetes met treatment targets for blood pressure control and glycemic control.

Discussion

This study showed that a statistically significant proportion of the diabetic group belonged to the high CVD risk category compared to the group with metabolic syndrome and the healthy control group despite being on treatment. Diabetes is a major risk factor for CVD\(^{[23]} \) and findings by Haffner et al.,\(^{[24]} \) suggested that patients with type 2 diabetes without previous myocardial infarction have as high a risk of myocardial infarction as nondiabetic patients with previous myocardial infarction, indicating that type 2 diabetes is a coronary heart disease equivalent.\(^{[24,25]} \) A recent meta-analysis by Bulugahapitiya et al.,\(^{[26]} \) however, did not support this hypothesis, asserting that it was not the diabetic status per se but the additional coronary artery disease risk factors which confer the coronary artery disease equivalent state in diabetic subjects. Albeit, more than 70% of patients with type 2 diabetes die of cardiovascular causes.\(^{[27]} \)

Chronic hyperglycemia has been implicated in the microvascular complications of diabetes and more recently too has also been associated with the macrovascular

Table 2: Clinical and laboratory parameters of the study participants \( (n=40) \)

| Parameters          | Subjects with type 2 diabetes, \( n \) (%) | Subjects with metabolic syndrome, \( n \) (%) | Healthy controls, \( n \) (%) | \( P \) |
|---------------------|-------------------------------------------|---------------------------------------------|------------------------------|-------|
| Age (years)         | 50.52±8.70                                | 49.55±7.54                                  | 49.82±8.39                   | 0.832 |
| SBP (mmHg)          | 130.22±19.36                              | 131.92±17.31                                | 126.00±17.30                 | 0.922 |
| DBP (mmHg)          | 78.27±12.03                               | 82.77±11.30                                | 77.67±17.33                  | 0.130 |
| BMI (kg/m\(^2\))    | 29.43±4.39                                | 30.73±4.43                                 | 29.03±5.12                   | 0.073 |
| WC (cm)             | 98.26±13.43                               | 99.75±9.04                                 | 95.22±12.80                  | 0.220 |
| Waist/hip ratio     | 0.93±0.13                                 | 0.88±0.05                                   | 0.88±0.06                    | 0.051 |
| HbA1c (%)           | 8.56±0.47a                                | 4.79±1.04                                  | 4.55±1.76                    | -0.0001* |
| HDL (mmol/L)        | 0.90±0.45a                                | 1.25±0.12*                                 | 1.83±0.62*                   | -0.0001* |
| TG (mmol/L)         | 1.09±0.33                                 | 1.90±0.13*                                 | 1.03±0.52                    | -0.0001* |
| TC (mmol/L)         | 4.16±1.07                                 | 5.03±0.44*                                 | 4.53±0.92                    | -0.0001* |
| LDL (mmol/L)        | 2.78±1.16                                 | 2.91±0.42*                                 | 2.23±1.22                    | 0.045* |
| CVD risk (%)        | 20.41±12.98*                              | 10.00±6.35                                 | 6.79±7.82                    | -0.0001* |

\(^{*}\)Statistically significant, \(^{\text{a}}\)Post hoc analysis showing the group(s) contributing to the observed differences. CVD - Cardiovascular disease, WC - Waist circumference, BMI – Body mass index, SBP - Systolic blood pressure, DBP - Diastolic blood pressure, HbA1c - Glycated haemoglobin, HDL - High-density lipoproteins, LDL - Low-density lipoproteins, TC - Total cholesterol, TG – Triglyceride
The percentage of type 2 diabetics who achieved optimal treatment goals for modifiable cardiovascular risk factors

| Blood pressure < 130/80 mmHg | 50 |
| HbA1c < 7% | 52.5 |
| HDL > 1.56 mmol/L | 16 |
| LDL < 2.6 mmol/L | 40 |
| TC < 5.2 mmol/L | 80 |
| TG < 1.7 mmol/L | 95 |
| Low WC (cm) | 37.5 |

Low WC - Waist circumference < 102 cm in men or < 88 cm in women.
HbA1c - Glycated haemoglobin, HDL - High-density lipoproteins, LDL - Low-density lipoproteins, TC - Total cholesterol, TG - Triglyceride, DM - Diabetes mellitus

A higher proportion of those with metabolic syndrome in this study was in the medium CVD risk category. Metabolic syndrome is an insulin-resistant state and several studies have shown that insulin resistance characterised by impaired glucose tolerance (2-h plasma glucose levels between 7.8 and 11.0 mmol/l) or impaired fasting glucose (plasma glucose between 5.6 and 6.9 mmol/l) have about 2-fold higher risk for CVD events than normoglycemic subjects.[29] HbA1c, a surrogate marker of chronic hyperglycemia has correlated strongly with the microvascular and macrovascular complications of diabetes.[30] HbA1c levels < 6% was the target of the intensive treatment arm of the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications studies which recorded a significant 42% reduction in CVD outcomes and a significant 57% reduction in the risk of nonfatal myocardial infarction, stroke, or CVD death compared with those previously in the standard treatment arm with HbA1c target of 7%–8%.[28]

From our study, only about 50% of people with diabetes achieved an HbA1c target of < 7%[22] and may explain the high proportion of type 2 diabetics in the high CVD risk category.

Chronic hyperglycemia alone cannot explain the relationship between diabetes and CVD.[30] Findings from the United Kingdom Prospective Diabetes Study group[31] showed that the most important risk factors for coronary heart disease were classic risk factors, particularly dyslipidemia. In this study, the diabetic group also had higher HbA1c values and lower HDL cholesterol values than the nondiabetic groups with and without metabolic syndrome which further explains their increased CVD risk.

This study showed that people with diabetes on treatment had comparable TC, LDL and TG values with the healthy controls; although, only 40% of the people with diabetes met the LDL treatment target of < 2.6 mmoles/L.[22] The group with metabolic syndrome had significantly higher levels of TC, LDL, and TG. Lifestyle modification rather than drug therapy has been the management option for CVD risk factor levels above the cut off for metabolic syndrome.[17] This study shows that a very low percentage of the study population participated in physical exercises, sideling one of the avenues to target weight loss, reduce insulin resistance and effectively control metabolic syndrome and its components.[32]

Correlation analysis in this study identified chronic hyperglycemia, obesity, and level of education as factors associated with CVD risk in this population. Alcohol consumption and smoking were not associated with CVD risk in this population compared to other climes[33] probably because a very low percentage of the study population smoked or used alcohol.

A study by Khaw et al.[24] reported that increasing values of HbA1c > 5% was associated with cardiovascular mortality, and all-cause mortality in diabetic men and HbA1c also appeared to be a continuous risk factor for CVD mortality in the nondiabetic population. Strategies to reduce hyperglycemia in both diabetic and nondiabetic populations including creating awareness on the effectiveness of increased physical activity and weight reduction in reducing insulin resistance and increasing literacy levels will help reduce CVD risk scores in adult Nigerians.

Conclusion

CVD risk factors are high in adult Nigerians with type 2 diabetes. Strategies to control the cardiovascular risk factors of metabolic syndrome, achieve better glycemic control and increase literacy levels will help achieve CVD risk reduction in adult Nigerians.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Chisholm DJ, Campbell LV, Kraegen EW. Pathogenesis of the insulin resistance syndrome (syndrome X). Clin Exp Pharmacol Physiol 1997;24:782-4.
2. Muller DC, Elahi D, Tobin JD, Andres R. The effect of age on insulin resistance and secretion: A review. Semin Nephrol 1996;16:289-98.
3. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of
diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87:4-14.
4. Wilson PW, D’Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB, et al. Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837-47.
5. Wilson PW. Diabetes mellitus and coronary heart disease. Am J Kidney Dis 1998;32:89-100.
6. 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.
7. Ho JE, Paultre F, Mosca L; Women’s Pooling Project. Is diabetes mellitus a cardiovascular disease risk equivalent for fatal stroke in women? Data from the women’s pooling project. Stroke 2003;34:2812-6.
8. Geiss LS, Herman WH, Smith PJ. Mortality in non-insulin dependent diabetes. In: National Diabetes Data Group, editor. Diabetes in America. 2nd ed., Vol. 6. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health; 1995. p. 233-57.
9. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003;348:383-93.
10. Champan P, Simmons RK, Sharp SJ, Griffin SJ, Wareham NJ. Cardiovascular risk assessment scores for people with diabetes: A systematic review. Diabetologia 2009;52:2001-14.
11. UI Haq I, Ramsay LE, Pickin DM, Yeo WW, Jackson PR, Payne JN, et al. Lipid-lowering for prevention of coronary heart disease: What policy now? Clin Sci (Lond) 1996;91:399-413.
12. Collins R, Armitage J, Parish S, Sleigh P, Peto R; Heart Protection Study Collaborative Group. MRC/BHF heart protection study of cholesterol-lowering with simvastatin in 5963 people with diabetes: A randomised placebo-controlled trial. Lancet 2003;361:2005-16.
13. Gerich JE. The genetic basis of type 2 diabetes mellitus: Impaired insulin secretion versus impaired insulin sensitivity. Endoear Rev 1998;19:491-503.
14. Gray RS, Fabsitz RR, Cowan LD, Lee ET, Howard BV, Savage PJ, et al. Risk factor clustering in the insulin resistance syndrome. The strong heart study. Am J Epidemiol 1998;148:869-78.
15. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes? JAMA 1990;263:2893-8.
16. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539-53.
17. Executive Summary of the 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). JAMA 2001;285:2486-97.
18. World Health Organization. Waist circumference and waist-hip ratio: Report of a WHO expert consultation. Circulation 2000;5:349.
19. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part I: Blood pressure measurement in humans: A statement for professionals from the subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Circulation 2005;111:697-716.
20. Maquart FX, Gillery P, Bernard JF, Mante JP, Borel JP. A method for specifically measuring haemoglobin A1c with a disposable commercial ion exchange column. Clin Chem Acta 1980;108:329-32.
21. Payne RA, Webb DJ, Maxwell SR. Assessing cardiovascular risk. Correction and transparency of BNF risk charts. BMJ 2009;338:b2330.
22. American Diabetes Association. Standards of diabetic care-2012. Diabetes Care 2012;35:660-97.
23. Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998;339:229-34.
24. Juutilainen A, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Type 2 diabetes as a “coronary heart disease equivalent”: An 18-year prospective population-based study in Finnish subjects. Diabetes Care 2005;28:2901-7.
25. Schramm TK, Gislason GH, Kaber L, Rasmussen S, Rasmussen JN, Abildstrom SZ, et al. Diabetes patients requiring glucose-lowering therapy and nondiabetics with a prior myocardial infarction carry the same cardiovascular risk: A population study of 3.3 million people. Circulation 2008;117:1945-54.
26. Bulugahapitiya U, Siyambalapitiya S, Sithole J, Idris I. Is diabetes a coronary risk equivalent? Systematic review and meta-analysis. Diabet Med 2009;26:142-8.
27. Laakso M. Cardiovascular disease in type 2 diabetes: Challenge for treatment and prevention. J Intern Med 2001;249:225-35.
28. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group, Nathan DM, Zinman B, Cleary PA, Backlund JY, Gennuth S, et al. Modern-day clinical course of type 1 diabetes mellitus after 30 years’ duration: The diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983-2005). Arch Intern Med 2009;169:1307-16.
29. Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. Diabetes Care 1999;22:233-40.
30. Laakso M. Cardiovascular disease in type 2 diabetes from population to man to mechanisms: The Kelly west award lecture 2008. Diabetes Care 2010;33:442-9.
31. Turner RC, Mills H, Neil HA, Stratton IM, Manley SE, Matthews DR, et al. The United Kingdom Prospective Diabetes Study Group: Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). Br Med J 1998;316:823-8.
32. Udenze IC, Amadi CE, Awolola NA, Makwe CC, Ajie OI. The role of inflammation in the metabolic syndrome. J Clin Sci 2016;13:17-22.
33. Criqui MH, Cowan LD, Tyrorler HA, Bangdiwala S, Heiss G, Wallace RB, et al. Lipoproteins as mediators for the effects of alcohol consumption and cigarette smoking on cardiovascular mortality: Results form the Lipid Research Clinics Follow-up Study. Am J Epidemiol 1987;126:629-37.
34. Khaw KT, Wareham N, Luben R, Bingham S, Oakes S, Welch A, et al. Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk). BMJ 2001;322:15-8.