Original Article

Association between lipid indices and 10-year cardiovascular risk of a cohort of black Africans living with type 2 diabetes mellitus

Taoreed Adegoke Azeez

Endocrinology Unit, Department of Medicine, University College Hospital, Ibadan, Nigeria

Keywords: Lipid indices, 10-year cardiovascular risk, diabetes, lipids, Black Africans

Abstract

Introduction

Diabetes mellitus is an established cardiovascular risk factor. Diabetes mellitus impairs lipid metabolism and enhances atherosclerosis development. Absolute lipid parameter are inadequate in predicting cardiovascular risk and some lipid indices have been reported to circumvent this deficiency. The objective of the study was to determine the association between these lipid indices and 10-year cardiovascular risk among black Africans with diabetes.

Methods

Seventy individuals (35 males and 35 females) living with diabetes who attended the diabetes clinic of a referral hospital in South-western Nigeria were recruited to the study. Ethical approval and participants' informed consent were duly obtained. Fasting plasma glucose, fasting lipid profile and glycated haemoglobin were done using appropriate laboratory techniques. Atherogenic index of plasma, atherogenic coefficient, Castelli's risk index I, Castelli's risk index II and CHOLindex were calculated using appropriate formulae. QRISK 3 score was obtained using a validated calculator. The association between QRISK 3 and the lipid indices was determined using Pearson's correlation.

Results

The mean age of the participants was 53.34 ± 9.57 years. The mean duration of diabetes mellitus among the participants was 6.29 ± 2.78 years. The mean HbA1c and FPG were 6.98±0.72% and 6.32±0.87 mmol/L respectively. The mean QRISK 3 score was 7.58±4.80. There was a statistically significant and positive correlation between QRISK 3 score and AIP, AC, CR I and CR II. CHOLindex did not significantly correlate with QRISK 3 score.

Conclusion

Among black Africans with diabetes, lipid indices (AIP, AC, CR I and CR II) significantly correlated with QRISK 3 score and therefore may be used as cheap markers of 10-year cardiovascular risk in these individuals.

Introduction

Diabetes mellitus is a metabolic disorder that has been consistently associated with increased cardiovascular morbidity and mortality.[1] This has created an enormous strain on the meagre health budgets of many nations, especially the developing nations in Africa.[2] The presence of diabetes mellitus is often associated with the occurence of other traditional cardiovascular risk factors such as hypertension, dyslipidaemia and obesity.[3] Atherosclerotic coronary artery disease and other cardiovascular diseases contribute the largest proportion to the causes of deaths among people with diabetes.[4] Diabetes mellitus increases the risk of fatal coronary artery disease by 2-4 times.1 A retrospective study has suggested that this cardiovascular burden is associated with reduced life expectancy among individuals with diabetes.[5]

The atherosclerosis mechanisms underlying cardiovascular diseases is a gradual process with varying contribution from both the traditional and the non-traditional cardiovascular risk factors.[6]

*Corresponding Author:
Taoreed Adegoke AZEEZ (MBChB, MSc, MWACP)Endocrinology Unit, Department of Medicine, University College Hospital, Ibadan, Nigeria
Phone number: +2347035728747
Email: adegokegalaxy@yahoo.com
ORCID ID: 0000-0003-3982-5790

Historically, the Framingham study, a landmark prospective study, heralded the concerted efforts at unraveling cardiovascular risks and it culminated into the development of the Framingham risk calculator for quantifying 10-year cardiovascular risk of individuals between 30 and 74 years.[7] The various cardiovascular risk estimators that have been documented in the literature are QRISK 3, Globorisk, ASCVD Risk calculator, Reynolds estimator, ASSIGN-SCORE and PROCAM calculator.[1] Interestingly, all these risk estimators have been validated but they differ in what they are actually estimating and how the estimate could be applied to clinical practice. However, a study done to compare the sensitivity of these risk calculators showed marked variation in their performance.[8] Framingham score was adjudged the best in the general population but it has been found to overestimate cardiovascular risk in individuals with diabetes.[9] In another study, the QRISK Score performed better than the Framingham score and was, in addition, found to be useful in individuals with diabetes.[10]

The QRISK score is a cardiovascular risk equation developed in the United Kingdom and it has been validated in several trials.[10] It has also been compared with other cardiovascular risk estimators and found to be, at least, as good as the other ones. In 2007, the first edition of the QRISK score was made public.[11] A year after, the second edition (QRISK2) was released. Although, QRISK score was primarily designed for the British population, it has been used and validated internationally.[12] The latest edition, QRISK 3, was published in 2017.[13] The QRISK score has been recommended for usage among patients with type 2 diabetes mellitus by the National Institute of Health and Care Excellence (NICE).[14]

Several researches have established a strong association between dyslipidaemia and cardiovascular mortality.[15–17] Clinically, dyslipidaemia is often assessed by determining absolute parameters such as low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), triglycerides and total cholesterol. However, it has been demonstrated that these parameters may be inaccurate in the prediction of cardiovascular risk among individuals with diabetes mellitus.[18,19] Lipid indices such as the atherogenic index of plasma (AIP), atherogenic coefficient (AC), Castelli's risk index I (CR-I), Castelli's risk index II (CR-II) and CHOLindex have been demonstrated to be superior in the prediction of cardiovascular risk compared with the individual parameters of the fasting lipid panel.[20–22] However, there are extremely scanty data on the association between QRISK 3 score and these lipid indices among people living with diabetes in sub-Saharan Africa.

Objective

The objective of the study was to determine the association between certain lipid indices- AIP, AC, C-I, CR-II and CHOLindex and 10-year cardiovascular risk of a cohort of persons living with type 2 diabetes in South-western Nigeria.

Methods

Study design and sample size

The study design was cross-sectional. The sample included 70 individuals living with diabetes who attended the diabetes clinic of a referral hospital in South-western Nigeria. Males and females were equally distributed in the sample.

Ethical consideration

The ethical approval for the study was obtained from the Institute of Advanced Medical Research and Training. The reference number of the ethical body was NHREC/05/01/2008a while the approval number for the study was UI/EC/17/0284. In addition, written informed consent was obtained from the study participants.

Eligibility criteria

Individuals (30 years and above in age) who were previously diagnosed with type 2 diabetes, using the World Health Organization (WHO) criteria,[23] were enrolled into the study while Individuals diagnosed with any acute illness or hospitalized in the preceding 3 months to the study were excluded from the study.

Laboratory analysis and derivation of lipid indices

Participants had venous blood sample collected following an overnight fast of about 8 – 12 hours. Using a fasting plasma sample, high density lipoprotein-cholesterol (HDL-C), total cholesterol and total glycerides were quantified using the enzymatic methods on automated chemistry analyzer LandWind C 100 plus. Friedewald equation was employed in determining the low density lipoprotein-cholesterol (LDL-C) equation provided that the triglyceride was not more than 400mg/dl.[24] The lipid indices were calculated as shown below.

LDL-C = Total cholesterol – HDL-C – total triglycerides/5. (Friedewald equation)

Atherogenic index of plasma (AIP) = Log $\frac{TG}{LDL\text{-}C}$

Atherogenic coefficient (AC) = $\frac{(T\,C - HDL\text{-}C)}{HDL\text{-}C}$

Castelli's risk index I (CR-I) = $\frac{TC}{LDL\text{-}C}$

Castelli's risk index II (CR-II) = $\frac{HDL\text{-}C}{LDL\text{-}C}$

CHOLindex = LDL-C – HDL-C

Glycated haemoglobin (HbA1c) was measured using the high performance liquid chromatography method. Fasting plasma glucose was determined by glucose oxidase enzymatic method on automated chemistry analyzer LandWind C 100 plus. QRISK 3 was determined using an appropriate online calculator.[25]

Data analysis

The obtained clinical and laboratory variables were scrutinized and entered into Microsoft Excel datasheet. The data was later analyzed with the Statistical Package for Social Sciences software, (SPSS) version 22 manufactured by the International Business Machines Corporation (IBM) New York, USA.. Quantitative variables were presented as mean ± standard deviation whereas categorical variables were presented as frequencies and percentages. The association between lipid indices and 10-year cardiovascular risk, using QRISK 3, was determined using Pearson's correlation. p value less than 0.05 was considered to be statistically significant.

Results

The study involved 35 male and 35 female participants. The mean age of the participants was 53.34 ± 9.57 years. The mean duration of diabetes mellitus among the participants was 6.29 ± 2.78 years. Table 1 shows the parameters of the participants. Table 2 shows the association between QRISK 3 and the lipid indices.

Table 1: Parameters of the participants

Parameter	Category	Frequency (N=70)	Percentage	Mean (N=70)	SD
Age category (years)	30-44	14	20.0%		
	45-64	48	68.6%		
	≥ 65	8	11.4%		
Smoking history	Non-smoker	61	87.1%		
	Ex-smoker	9	12.9%		
	Current smoker	0	0.0%		
HDL-C (mg/dl)				50.17	12.16
LDL-C (mg/dl)				127.29	27.63
TG (mg/dl)				101.71	17.16
TC (mg/dl)				193.94	41.88
AIP				-0.13	0.22
AC				3.07	1.30
CR-I				4.06	1.29
CR-II				2.70	0.99
CHOLindex				77.13	29.06
QRISK3				7.58	4.80
HbA1c (%)				6.98	0.72
FPG (mmol/L)				6.32	0.87

Table 2: Association between QRISK 3 and the lipid indices

Lipid index	r	p
Atherogenic index of plasma (AIP)	0.368	0.002**
Atherogenic coefficient (AC)	0.324	0.006**
Castelli's risk index I (CR-I)	0.324	0.006**
Castelli's risk index II (CR-II)	0.354	0.003**
CHOLindex	0.218	0.07

** - statistically significant

r – Pearson's correlation coefficient

Discussion

The majority of the participants (88.6%) were of the middle-age and elderly age groups. Studies have shown that the highest prevalence of type 2 diabetes mellitus is found in the middle-age and elderly age groups.[26–28] The reasons for this observation include increased life expectancy, reduced physical activity with ageing, increased central obesity with ageing and widening adoption of western lifestyles.[26] In addition, the topic of cardiovascular risk is more relevant in this age group because cardiovascular risk is highest in the middle-aged and elderly people.[29]

The bulk of the participants (87.1%) have never smoked cigarette. In a meta-analysis of studies done in Nigeria, Adeloye et al., also concluded that prevalence of smoking in Nigeria is very low when compared with the western world.[30] Poverty and improved public awareness of the detriments of smoking may be responsible for this. Interestingly, this study demonstrated that nobody is presently smoking among the participants. Intensive health education, which is a core component of diabetes care in referral hospitals in Nigeria might have contributed to this finding.[31]

The short term and long term glycaemic control of the participants was averagely good. The mean HbA1c (an indicator of long term glycaemic control) was 6.98% while the mean fasting plasma glucose (an indicator of short term glycaemic control) was 6.32 mmol/L. These values are within the recommended targets of the American Diabetes Association (ADA).[32] In Nigeria, referral health facilities usually have the best expertise and this may explain why glycaemic control among patients with diabetes attending tertiary care facilities tends to be relatively good although a few studies have reported a contrary finding.[33]

The findings of this study showed a statistically significant positive correlation between 10-year cardiovascular risk, using QRISK 3, and atherogenic index of plasma (r=0.368; p=0.002). Bo et al., also reported a significant association between AIP and the presence of cardiovascular risk factors.[34] Li et al., documented a significant association between AIP and the development of chronic complications among individuals living with diabetes.[35] A study done in Cameroon has also found a significant association between AIP and 10-year cardiovascular risk among black Africans but the participants were not diagnosed with diabetes.[36] AIP is a mathematical derivative of HDL-C and triglycerides which have been directly linked with the risk of cardiovascular mortality and this might partly explain the strong association between AIP and 10-year cardiovascular risk.[37]

Furthermore, in the present study, a statistically significant positive correlation was found between atherogenic coefficient (r=0.324; p=0.006) and QRISK 3, a validated 10-year cardiovascular risk estimator. The findings from a previous study also corroborated this observation by demonstrating that atherogenic coefficient could be used in assessing cardiovascular risk in people living with diabetes.[38] Atherogenic coefficient makes use of non-HDL cholesterol, a lipid parameter that has been demonstrated to be a superior predictor of atherosclerosis compared with other conventional lipid values.[39] This might be responsible for the observed association between AC and 10-year cardiovascular risk score.

Moreover, the present study also observed a statistically significant and positive correlation between QRISK 3 and Castelli risk index I (r=0.324; p=0.006) as well as Castelli risk index II (r=0.354; p=0.003). Olamoyegun et al., in their studies, also reported that CR I and CR II could be used in predicting cardiovascular risk among Nigerians.[22] Similarly, Pusapati et al., also posited that CR I and CR II could be used in identifying individuals with higher risk of cardiovascular disease especially when the absolute lipid parameters are not markedly deranged, as found in this study.[40]

The present study, however, did not find a statistically significant association between 10-year cardiovascular risk score and CHOLindex (r = 0.218;p= 0.07). In the study done among Nigerian participants, Olamoyegun et al., also showed that CHOLindex had the lowest performance in predicting cardiovascular risk when com-

pared with other lipid indices.[22] In another study done in Nigeria, Williams demonstrated that the correlation between HDL and lipid indices were statistically significant except for CHOLindex. However, the William's study was done among individuals with hypertension only but the present study was done among individuals with diabetes although a few of them also had hypertension.

Limitations

The sample size was small. A larger study would be more representative. Similarly, it was a hospital-based study and might not reflect what is obtainable in the community.

Conclusion

There was a statistically significant association between QRISK 3 and AIP, AC, CR I as well as CR II among black Africans with type 2 diabetes mellitus. Therefore, these ratios may be used as simple surrogate markers of 10-year cardiovascular risk among individuals with diabetes mellitus in Africa.

Abbreviations

AC - Atherogenic coefficient

ADA – American Diabetes Association

AIP - Atherogenic index of plasma

ASCVD – Atherosclerotic cardiovascular disease

CR I - Castelli's risk index I

CR II - Castelli's risk index II

FPG – Fasting plasma

HbA1c - Glycated haemoglobin

HDL-C - High density lipoprotein-cholesterol

IBM - International Business Machines Corporation

LDL-C - Low density lipoprotein-cholesterol

NICE - National Institute of Health and Care Excellence

p – Statistically significant

PROCAM – Prospective cardiovascular Munster study

SPSS - Statistical Package for Social Sciences software

TC – Total cholesterol

TG – Triglyceride

WHO - World Health Organization

References

1. Kalofoutis C, Piperi C, Kalofoutis A, Harris F, Phoenix D, Singh J. Type II diabetes mellitus and cardiovascular risk factors: Current therapeutic approaches. Vol. 12, Experimental and Clinical Cardiology. Pulsus Group; 2007: p. 17–28.

2. Fasanmade OA, Dagogo-Jack S. Diabetes Care in Nigeria. Vol. 81, Annals of Global Health. Elsevier USA; 2015. p. 821–9.

3. Petrie JR, Guzik TJ, Touyz RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. Vol. 34, Canadian Journal of Cardiology. Elsevier Inc.; 2018: p. 575–84.

4. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: A systematic literature review of scientific evidence from across the world in 2007-2017. Vol. 17, Cardiovascular Diabetology. BioMed Central Ltd.; 2018: p. 83.

5. Salehidoost R, Mansouri A, Amini M, Aminorroaya Yamini S, Aminorroaya A. Diabetes and all-cause mortality, a 18-year follow-up study. Sci Rep. 2020;10(1):3183.

6. Santos P. The Role of Cardiovascular Risk Assessment in Preventive Medicine: A Perspective from Portugal Primary Health-Care Cardiovascular Risk Assessment. Vol. 2020, Journal of Environmental and Public Health. Hindawi Limited; 2020.

7. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: The Framingham heart study. Circulation. 2008;117(6):743–53.

8. Garg N, Muduli SK, Kapoor A, Tewari S, Kumar S, Khanna R, et al. Comparison of different cardiovascular risk score calculators for cardiovascular risk prediction and guideline recommended statin uses. Indian Heart J. 2017 Jul 1;69(4):458–63.

9. Wang L-N. What is QRISK? - The Pharmaceutical Journal. Pharm . 2009;9(6):45.

10. Robson J, Hippisley-Cox J, Coupland C. QRISK or Framingham? Vol. 74, British Journal of Clinical Pharmacology. 2012. p. 545–6.

11. Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, May M, Brindle P. Derivation and validation of QRISK, a new cardiovascular disease risk score for the United Kingdom: Prospective open cohort study. Br Med J. 2007;335(7611):136–41.

12. Pike MM, Decker PA, Larson NB, St. Sauver JL, Takahashi PY, Roger VL, et al. Improvement in Cardiovascular Risk Prediction with Electronic Health Records. J Cardiovasc Transl Res. 2016; 9(3):214–22.

13. Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: Prospective cohort study. BMJ. 2017;357.

14. Overview | Cardiovascular disease: risk assessment and reduction, including lipid modification | Guidance | NICE [cited 2021 May 3]. Available from: https://www.nice.org.uk/Guidance/cg181

15. Nelson RH. Hyperlipidemia as a Risk Factor for Cardiovascular Disease. Vol. 40, Primary Care - Clinics in Office Practice. NIH Public Access; 2013. p. 195–211.

16. Ayoade OG, Umoh I, Amadi C. Dyslipidemia and Associated Risk Factors among Nigerians with Hypertension. Dubai Med J. 2020;3(4):155–61.

17. Hedayatnia M, Asadi Z, Zare-Feyzabadi R, Yaghooti-Khorasani M, Ghazizadeh H, Ghaffarian-Zirak R, et al. Dyslipidemia and cardiovascular disease risk among the MASHAD study

population. Lipids Health Dis. 2020;19(1):42.

18. Hajian-Tilaki K, Heidari B, Bakhtiari A. Triglyceride to high-density lipoprotein cholesterol and low-density lipoprotein cholestrol to high-density lipoprotein cholesterol ratios are predictors of cardiovascular risk in Iranian adults: Evidence from a population-based cross-sectional study. Casp J Intern Med. 2020;11(1):53–61.

19. Wakabayashi I, Daimon T. Comparison of discrimination for cardio-metabolic risk by different cut-off values of the ratio of triglycerides to HDL cholesterol. Lipids Health Dis [Internet]. 2019;18(1):156.

20. Akpinar O, Bozkurt A, Acartürk E, Şeydao/ lu G. A new index (CHOLINDEX) in detecting coronary artery disease risk. Anadolu Kardiyol Derg. 2013;13(4):315–9.

21. Bhardwaj S, Pharm IJ, Sci B, Bhardwaj S, Bhattacharjee J, Bhatnagar MK, et al. Atherogenic Index Of Plasma, Castelli Risk Index And Atherogenic Coefficient-New Parameters In Assessing Cardiovascular Risk. International Journal of Pharmacy and Biological Sciences. [cited 2021 May 3]. Available from: www.diabetes.com.au/pdf/obesity_report.pdf].

22. Olamoyegun M, Oluyombo R, Asaolu S. Evaluation of dyslipidemia, lipid ratios, and atherogenic index as cardiovascular risk factors among semi-urban dwellers in Nigeria. Ann Afr Med. 2016;15(4):194.

23. WHO. Definition and diagnosis of diabetes. [cited 2021 Mar 5]. Available from: https://www.who.int/diabetes/publications/Definition and diagnosis of diabetes_new.pdf

24. Tsai CH, Wu HH, Weng SJ. Comparison of various formulae for estimating low-density lipoprotein cholesterol by a combination of ages and genders in Taiwanese adults. BMC Cardiovasc Disord. 2014;14(1):113.

25. QRISK3 [Internet]. [cited 2021 Mar 6]. Available from: https://qrisk.org/three/

26. Chentli F, Azzoug S, Mahgoun S. Diabetes mellitus in elderly [Internet]. Vol. 19, Indian Journal of Endocrinology and Metabolism. Medknow Publications; 2015 p. 744–52.

27. Banerjee J, Dhas Y, Mishra N. Middle-Aged Indians with Type 2 Diabetes Are at Higher Risk of Biological Ageing with Special Reference to Serum CDKN2A. J Diabetes Res. 2020;2020.

28. Kalyani RR, Golden SH, Cefalu WT. Diabetes and aging: Unique considerations and goals of care. Vol. 40, Diabetes Care. American Diabetes Association Inc.; 2017 p. 440–3.

29. Ejim EC, Okafor CI, Emehel A, Mbah AU, Onyia U, Egwuonwu T, et al. Prevalence of cardiovascular risk factors in the middle-aged and elderly population of a nigerian rural community. J Trop Med. 2011;

30. Adeloye D, Auta A, Fawibe A, Gadanya M, Ezeigwe N, Mpazanje RG, et al. Current prevalence pattern of tobacco smoking in Nigeria: A systematic review and meta-analysis. BMC Public Health. 2019;19(1):1719.

31. Essien O, Otu A, Umoh V, Enang O, Hicks JP, Walley J. Intensive Patient Education Improves Glycaemic Control in Diabetes Compared to Conventional Education: A Randomised Controlled Trial in a Nigerian Tertiary Care Hospital. Atkin SL, editor. PLoS One. 2017;12(1):e0168835.

32. Association AD. Glycemic targets: Standards of medical care in diabetes-2020. Diabetes Care. 2020;43(Supplement 1):S66–76. 33.

33. Adamu Y, Garba KM, YAU S, Ya'u J. Glycemic Control and its Predictors among Diabetic Patients Attending a Tertiary Hospital in Nigeria: A Retrospective Observational Study. J Biomed Anal. 2020;3(1):13–25.

34. Bo MS, Cheah WL, Lwin S, Moe Nwe T, Win TT, Aung M. Understanding the Relationship between Atherogenic Index of Plasma and Cardiovascular Disease Risk Factors among Staff of an University in Malaysia. J Nutr Metab. 2018;2018.

35. Li Z, Huang Q, Sun L, Bao T, Dai Z. Atherogenic index in type 2 diabetes and its relationship with chronic microvascular complications. Int J Endocrinol. 2018;2018.

36. Noumegni SR, Nansseu JR, Bigna JJ, Jocelyne V, Moor A, Assah FK, et al. Atherogenic index of plasma and 10-year risk of cardiovascular disease in adult Africans living with HIV infection: A cross-sectional study from Yaoundé , Cameroon. [cited 2021 May 4]; Available from: https://us.sagepub.com/en-us/nam/open-access-at-sage

37. Wu TT, Gao Y, Zheng YY, Ma YT, Xie X. Atherogenic index of plasma (AIP): A novel predictive indicator for the coronary artery disease in postmenopausal women. Lipids Health Dis. 2018;17(1):197.

38. Nimmanapalli H, Kasi A, Devapatla P, Nuttakki V. Lipid ratios, atherogenic coefficient and atherogenic index of plasma as parameters in assessing cardiovascular risk in type 2 diabetes mellitus. Int J Res Med Sci. 2016;4(7):2863–9.

39. Orakzai SH, Nasir K, Blaha M, Blumenthal RS, Raggi P. Non-HDL cholesterol is strongly associated with coronary artery calcification in asymptomatic individuals. Atherosclerosis. 2009;202(1):289–95.

40. Pusapati MR, Ramesh BP, Girijasankar G. Estimation Of Lipid Profile And Assessment Of Cardiovascular Risk In Smokers By Using New Atherogenic Indices | Asian J Pharm Clin Res. 2015;8(3):55–7.