Annals of Health Research

IN THIS ISSUE

- Physical Violence among Secondary School Students
- Plasma Fibrinogen and Hb1Ac in Diabetes Mellitus
- Bronchial Asthma Control in Secondary School Students
- TPTE Expression in Epithelial Ovarian Cancer
- Parents' Knowledge of Childhood Epilepsy
- Tetanus Toxoid Vaccination in Pregnancy
- Sarcoma Botryoides of the Bladder
- Vulva Haematoma following Sexual Assault

VOLUME 8
NO. 2
APR. - JUN. 2022

PUBLISHED BY THE MEDICAL AND DENTAL CONSULTANTS ASSOCIATION OF NIGERIA, OOUTH, SAGAMU, NIGERIA.
www.mdcan.oouth.org.ng
Baseline Plasma Fibrinogen and Glycated Haemoglobin (HbA1c) Levels in Normoglycaemic Offspring of Adults with Type 2 Diabetes Mellitus

Taiwo EO*1, Thanni LOA2, Taiwo OP1

1Department of Physiology, Faculty of Basic Medical Sciences, Olabisi Onabanjo University, Sagamu, Nigeria
2Department of Surgery, Obafemi Awolowo College of Health Sciences, Olabisi Onabanjo University, Sagamu, Nigeria

*Correspondence: Dr EO Taiwo, P. O. Box 901, Sagamu, Nigeria. E-mail: taiwobmc2010@yahoo.com; ORCID – https://orcid.org/0000-0003-4213-0930.

Abstract

Background: Type 2 Diabetes mellitus (T2DM) is known to be preceded by a long pre-diabetic stage. Family studies have confirmed that the incidence of T2DM in the first-degree offspring of T2DM patients is higher than in the non-diabetic population. The levels of plasma fibrinogen and HbA1c in offspring of T2DM patients may be markers of the development of T2DM later in life.

Objectives: To determine the plasma fibrinogen and HbA1c levels of normoglycaemic offspring of T2DM patients.

Methods: This study involved randomly selected 100 offspring of T2DM patients (ODP) and 100 offspring of non-diabetic parents (ONDP) aged between 16 and 40 years. Fasting Blood Glucose (FBG), plasma fibrinogen and HbA1c and height and body weight were measured using standard methods.

Results: The mean age of the ODP and ONDP were similar: 23.3±0.44 years and 23.4±0.40 years, respectively. The mean BMI was 23.83±0.42kg/m² for ODP and 23.20±0.29kg/m² for ONDP. The prevalence of overweight was 13.0% and 25.0% among the ODP and ONDP, respectively. The mean plasma fibrinogen was significantly higher in ODP (322.85 ± 5.15 g/l vs 303.11 ±4.92 g/l; p = 0.006). The mean plasma HbA1c was also significantly higher among OND (5.13±0.03% vs 4.76±0.05; p = 0.000).

Conclusions: The plasma fibrinogen and HbA1c levels are higher among ODP than ONDP. This pattern of variations may serve as a reason for instituting precautionary measures since it predates the development of T2DM.

Key words: Body Mass Index, Diabetes mellitus, Fibrinogen, Glycated haemoglobin, Offspring.

Introduction

Diabetes mellitus (DM) is a disorder of intermediary carbohydrate, protein and lipid metabolism. It is characterised by hyperglycaemia, glucosuria, polydipsia, polyuria, polyphagia and weight loss. It is usually associated with secondary alterations in glucose, fat and protein metabolism, leading to many biochemical disorders. It may be characterised by peripheral insulin resistance, impaired regulation of hepatic glucose production with declining β-cell function and eventually, leading to β-cell failure [1]. DM has a
wide range of prevalence rates across the country. In the rural parts of Nigeria, it affects 2.2% of the population, whereas, in the urban regions, the prevalence may be as high as 10%. A study done by Nwafor and Owahoji in 2001 on selected metropolitan cities revealed a prevalence rate of 23.4% among the higher socioeconomic members of a population of the oil industry staff in the urban city of Port Harcourt. This is higher than 16% among the lower socioeconomic group in the same community. The difference in prevalence rates may be attributed to lifestyle westernisation and progressive rural-urban migrations.

The prevalence of DM is increasing worldwide, and it is projected that by the year 2030, over 500 million adults will be affected by the disease. The projected rise could result from urbanisation and the ageing of the population. The projected increase in prevalence is expected to be higher in Africa and Asia, where there is a rapid epidemiological transition. The prevalence rate of DM is still lower in traditionally rural than urban communities. Previous studies by Bakari et al. found the prevalence rate of 1.6% in a suburban Northern Nigerian city, while Erasmus et al. reported a prevalence of 1.4% in a rural population of North central Nigeria. Most cases of DM in rural and suburban areas remain undiagnosed, and many patients present for the first time with complications.

The modest improvement in living standards witnessed over the past few years in Nigeria has resulted in the ageing of its populace. Insulin resistance tends to worsen with advancing age. This, coupled with decreased physical activity among the aged, increases the risk of Type 2 DM. Of the risk factors for DM reported in many studies, unhealthy dietary habits are the most prevalent; that is not surprising considering the proliferation of fast food outlets in many cities. An unhealthy diet consisting mainly of high-fat, energy-dense foods contributes to the development of obesity and DM.

The American Diabetes Association (ADA) has recently recommended glycated haemoglobin (HbA1c) with a cut-point ≥6.5% for diagnosing DM as an alternative to fasting plasma glucose (FPG ≥7.0 mmol/L)-based criteria. The levels of HbA1c are strongly correlated with FPG. Fasting Blood Glucose (FBG), 2-hour post-glucose load plasma glucose, and oral glucose tolerance tests are recommended for the diagnosis of DM only if HbA1c testing is not possible due to unavailability of the assay or when there are patient factors precluding its interpretations. Glycated Haemoglobin (HbA1c) provides a reliable measure of chronic glycaemia. It correlates well with the risk of long-term DM complications, so it is currently considered the test of choice for monitoring and long-term management of DM. The earliest event associated with atherosclerosis is the accumulation of low-density lipoprotein (LDL) cholesterol and fibrinogen in the affected arterial wall. Therefore, it is essential to understand the mechanisms that govern the endothelial changes.

There is a lack of reports on the level of plasma fibrinogen and HbA1c in first degree relatives of DM patients in this environment. Therefore, this study aimed to determine the levels of plasma fibrinogen and HbA1c in the offspring of T2DM patients. This study will serve as a biomarker of the risk of developing DM when compared with the offspring of non-diabetic parents. This, however, may serve as a basis for advice to the general populace about the risk of developing T2DM in the future.

Methods
This study was designed as a cross-sectional, single-centre, cohort study carried out from March to December 2018. This study involved a random selection of 200 subjects: 100 offspring of T2DM patients (ODP) and 100 offspring of non-diabetic parents (OND). The study was conducted at the State Hospital, Ijebu-ode, Ogun state, a suburban area of southwest Nigeria. The participants were aged between 16 and 40 years and were matched for sex.

**Ethical considerations**

Ethical clearance for the study was obtained from the Health Research Ethics Committee (HREC) of Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu (HREC/OOU/014/2018). All the participants in this study gave informed consent for enrolment.

**Sample size estimation**

This was determined using the formula \((Z_{1-a/2})^2 \times SD^2 / d^2\) where \(Z= \) normal variant, \(d = 3.5\%\), Type 1 error with \(SD = 25\) g/l of fibrinogen from previous study. Additional 5\% was added to the calculated sample size for non-response. Therefore, the minimum sample size was equal to \(1.96^2(25)^2 / (0.035)^2 = 196 + 10 = 206\).

**Inclusion criteria:** Offspring of T2DM patients were randomly selected into the study group, while a similar group of offspring of non-diabetic parents were randomly assigned to the control group.

**Exclusion criteria:** All the participants with cardiovascular and metabolic disorders, smoking habits and clinical pallor were excluded from both arms of the study.

**Clinical procedures**

The body weight was recorded in kilograms (to the nearest 1.0 kg) with the subject in light clothing but without shoes, using a calibrated bathroom weighing scale (Soehnle Waagen GmbH and Co. KG, D 71540 Murrhardt/Germany) positioned on a firm horizontal surface. A stadiometer measured the height (to the nearest 0.1m). The subjects stood erect, without shoes, caps or headgears, on a flat surface with the heels and occiput in contact with the stadiometer (Prestige HM0016D, India). The Body Mass Index (BMI) was subsequently calculated using the formula: weight (kg)/height\(^2\) (metres\(^2\)).

**Biochemical analyses**

Blood samples were drawn from the subjects in the morning after fasting for at least eight hours. The enzymatic hexokinase method was used to determine glucose concentrations. [18] The HBA1c and fibrinogen levels were determined by standard laboratory methods as described below.

Six millilitres of blood samples were drawn from each subject after eight hours of overnight fasting. One millilitre of blood was used to determine the FBG, while three millilitres of blood was centrifuged and the serum analysed for fibrinogen. The remaining two millilitres were transferred into Ethylenediamine tetraacetic acid (EDTA) bottles and analysed immediately for glycated haemoglobin (HbA1c).

**Estimation of Plasma fibrinogen**

A rapid semi-automated method for determining fibrinogen levels in human plasma was used. This method is referred to as the thrombin time method or fibro-meter method, which is based on the principle that when thrombin is added to suitably diluted plasma, the time of clotting is estimated and determined (as described by Dyr and Vodrážka, 1974). [18]

**Estimation of HbA1c**

Plasma was separated from blood cells by centrifugation at 2000 rotation for 10 minutes. Glycated Haemoglobin (HbA1c) was detected using the Fast Ion-Exchange Resin High-Performance Liquid Chromatography
separation method (as used by the Human-Germany Method). [19]

Statistical analysis
The data obtained were analysed using the Statistical Programme for the Social Sciences (SPSS) version 25.0. The Student’s t-test was used to compare variability between the mean values of the test and control groups. A probability value of P less than 0.05 was considered statistically significant.

Results
Table I shows that most of the subjects (48.0% of ODP and 40.0% of ONDP) belonged to the 21-25 years age group. The mean age of the ODP and ONDP were similar: 23.3±0.44 years and 23.44±0.40 years, respectively. The sex ratio was 1:1 in both arms of the subjects, while the mean BMI was 23.83±0.42 kg/m² for ODP and 23.20±0.29 kg/m² for ONDP. The prevalence of overweight was 13.0% and 25.0% among the ODP and ONDP, respectively, whereas 11.0% and 1.0% of ODP and ONDP were obese.

Table I: Distribution of subjects in the ODP and ONDP groups according to age, sex and BMI

| Variable     | Category | ODP n = 100 | ONDP n = 100 | Total n = 100 |
|--------------|----------|-------------|--------------|---------------|
| Sex          | Male     | 50 (50.0)   | 50 (50.0)    | 100 (50.0)    |
|              | Female   | 50 (50.0)   | 50 (50.0)    | 100 (50.0)    |
| Age Range (Years) |          |             |              |               |
| 16-20        |          | 27 (27.0)   | 29 (29.0)    | 56 (28.0)     |
| 21-25        |          | 48 (48.0)   | 40 (40.0)    | 88 (44.0)     |
| 26-30        |          | 15 (15.0)   | 25 (25.0)    | 40 (20.0)     |
| > 30         |          | 10 (10.0)   | 6 (6.0)      | 16 (8.0)      |
| BMI (kg/m²)  | Normal   | 76 (76.0)   | 74 (74.0)    | 150 (75)      |
|              | Overweight| 13 (13.0)   | 25 (25.0)    | 38 (19.0)     |
|              | Obese    | 11 (11.0)   | 1 (1.0)      | 12 (6.0)      |

Figures in parentheses are percentages of the total in the respective column.

The mean plasma fibrinogen level of the ODP group was significantly higher than the levels for ONDP (322.85 ± 5.15 g/l vs 303.11 ±4.92 g/l; p = 0.006). The mean HbA1c of 5.13±0.03% for ODP subjects was significantly higher than 4.76±0.05% for ONDP (p = 0.000), as shown in Table II.

Table III shows that the mean plasma fibrinogen and mean glycated haemoglobin values were higher among ODP than ONDP across ages. In addition, the mean plasma fibrinogen levels progressively increased with age among ODP with statistical significance (p = 0.01). In contrast, the progressive increase in mean values with age among ONDP lacked statistical significance (p = 0.147). The mean Hb1Ac also progressively with age with statistical significance among ODP (p = 0.025), while a similar progressive increase in mean Hb1Ac with age among ONDP was not significant (p = 0.084).

Discussion
In the present study, no significant difference was observed in the BMI of ODP and ONDP. The levels of HbA1c level conform to what is regarded as the threshold for the onset of DM or prediabetes. Generally, the local pattern (Nigerian) of glycated haemoglobin (HbA1c) level can be distinctly higher for the offspring of diabetic patients. It should be taken as such to prevent DM in this environment. In addition, overweight or obesity predisposes to DM or abnormal glycated haemoglobin levels.
Table II: Comparison of the mean values of age, BMI, plasma fibrinogen and glycosylated haemoglobin between ODP and ONDP subjects

| Variables            | ODP n = 100     | ONDP n = 100     | P value |
|----------------------|-----------------|------------------|---------|
| Mean Age (Years)     | 23.30±0.44      | 23.44±0.40       | 0.813   |
| Mean BMI (kg/m²)     | 23.83±0.42      | 23.20±0.29       | 0.211   |
| Mean Fibrinogen (g/l)| 322.85±5.15     | 303.11±4.92      | 0.006   |
| Mean HbA1c (%)       | 5.13±0.03       | 4.76±0.05        | 0.000   |

Table III: Comparison of mean values of plasma fibrinogen and HbA1c among subjects in the ODP and ONDP groups

| Age Group (Years) | Plasma fibrinogen (g/l) | Plasma HbA1c (%) |
|-------------------|-------------------------|-----------------|
|                   | ODP                     | ONDP            |
| 16-20             | 319.15±6.70             | 299.90±6.84     |
| 21-25             | 321.26±10.62            | 301.89±9.15     |
| 26-30             | 325.67±16.41            | 303.26±12.02    |
| >30               | 340.70±15.43            | 319.75±15.54    |
| F-Test            | 3.642                   | 1.828           |
| P value           | 0.010                   | 0.147           |

The study found the HbA1c threshold of 5.1% as highly valuable for detecting undiagnosed DM. This agrees with the 6.3% HbA1c threshold for detecting undiagnosed DM among Shanghai adults with sensitivity and specificity of 63% and 96%, respectively. Other studies in East Asian countries showed the optimal HbA1c cut-off for diagnosing DM as 5.6% in Japan and 5.9% in Korea. Researchers found an HbA1c threshold of 6.4% in a Middle Eastern population. Therefore, it is essential to have HbA1c criteria for diagnosing DM in each population.

The present study shows that plasma fibrinogen concentration was significantly higher among the offspring of patients with DM. This finding may explain the theory that suggests that tissue injury, vascular complications and endothelial dysfunctions may long predate the occurrence of T2DM. The raised concentration of pro-inflammatory cytokines and the resultant acute phase response may underlie much of the metabolic clustering, including glucose tolerance. Therefore, an increase in the acute phase proteins explains the elevation of fibrinogen in T2DM hence, the present study shows that the elevated blood levels of fibrinogen and HbA1c could be an early event that precedes the expression of impaired glucose tolerance or any change in asymptomatic offspring of patients with T2DM.

The involvement of elevated plasma fibrinogen as a risk factor for the development of T2DM remains controversial. Biases in these evaluations may exist due to unmeasured confounding factors such as causality between plasma fibrinogen and endothelial events. The elevated fibrinogen levels may result from an inflammatory state caused by the underlying pathology and, therefore, can predispose to the occurrence of T2DM in the future. Nevertheless, further evidence reinforces the hypothesis that the elevated plasma fibrinogen level may directly influence
endothelial events or progression. Intravenous infusion of human fibrinogen into mice, giving a 1.7-fold increase in plasma fibrinogen, has been observed to lead to resistance to thrombolysis, increased thrombus fibrin content, quicker fibrin formation, greater fibrin network density and increased clot strength and stability. [30]

Fibrinogen may favour atherogenesis when converted to fibrin and its atherogenic degradation products or may trigger lipid deposition and local inflammation resulting in the formation, destabilisation, and rupture of atherosclerotic plaques. The promotion of thrombogenesis is another possible mechanism. Fibrinogen acts as a scaffold for blood clots, enhancing platelet aggregation and fibrin formation, thus making thrombi more resistant to lysis. [31] Furthermore, fibrinogen can interact with red blood cells, mediating erythrocyte sedimentation and blood viscosity while permitting red blood cells to attach to thrombi. Besides contributing to thrombus size, structure, and stability, red blood cells can alter fibrin network organisation, suppress plasmin generation and reduce clot permeability, possibly delaying fibrinolysis and prolonging clot resolution, which may contribute to endothelial changes. [31]

The HbA1c is an accurate and easy-to-administer test with on-the-spot results availability. It can be an effective tool in establishing the diagnosis of DM, especially in low- and middle-income countries and hard-to-reach populations. Even though elevated HbA1c has been recommended for the diagnosis of DM, some testing strategies and cut-off ranges are still being debated. However, the combination of Fasting Glucose Tolerance (FGT) and elevated HbA1c significantly enhances the diagnostic accuracy of these individual tests. [29] The prognostic potential of high HbA1c lies in its unique ability to assess retrospective glycaemic control and predict lipid profile in diabetic patients. As the epidemic of DM increases worldwide, the HbA1c test may continue to be implemented as part of the diagnostic and prognostic tools, leading to better patient care and successful clinical outcomes. [29]

The prevalence of T2DM and its cardiovascular complications has increased significantly worldwide. [30] In China, the prevalence rates of DM and prediabetes Mellitus (pre-DM) are also steadily increasing, with a prevalence rate of DM in adults reaching 10.9% and pre-DM reaching 35.7% in 2013. [31] Chronic, low-grade inflammation is a predisposing factor for DM and also contributes to the genesis of diabetes complications. [32] Fibrinogen, one of the subclinical inflammation biomarkers, increases before the onset of DM [33] and elevates from normal glucose regulation (NGR) over pre-DM to DM. [34] It has been demonstrated that plasma fibrinogen level was significantly associated with glucose metabolism [including fasting blood glucose (FBG) and glycated hemoglobinA1c (HbA1c), a measure of long-term glycaemic control] in patients with acute coronary syndromes (ACS). [35] Nevertheless, few reports have explored the relationship between plasma fibrinogen levels and glucose metabolism in patients with new onset stable Coronary Artery Disease (CAD). Moreover, plasma fibrinogen has also been implicated in the development of macrovascular complications and microvascular disorders in DM. [34, 36, 37] In contrast, there has been no study investigating the pattern of plasma fibrinogen levels in individuals with impaired glucose regulation.

Limitations of the study
A prospective study is desired as the inability to measure HbA1c and plasma fibrinogen levels over a long period in relation to other
underlying health challenges in the subjects may be confounding variables in the present study.

Conclusion

This research has demonstrated that plasma fibrinogen and HbA1c levels are elevated in the offspring of T2DM patients, and this may be a pointer to the risk of T2DM in the population studied. Plasma fibrinogen and Hb1Ac may also serve as baseline parameters to further studies in offspring of T2DM patients. Based on the outcome of this study, people with a family history of T2DM need to reduce their tendency to obesity to improve their metabolic health.

Acknowledgements: The authors thank all the study participants and the adjunct staff who assisted with data processing and manuscript drafting.

Authors’ Contributions: TEO conceived the study while TLO designed the study. Both TEO and TOP did the literature review. TEO did data analysis and drafted the manuscript, while TLO did data interpretation and revised the draft for sound intellectual contents. All the authors read and approved the final version of the manuscript.

Conflict of interest: None.

Funding: Self-funded.

Publication History: Submitted 21 December 2021; Accepted 26 May 2022.

References

1. Sabir A, Ohwovoriole A, Isezuo S, Fasanmade O, Abubakar S, Iwuala S. Type 2 diabetes mellitus and its risk factors among the rural Fulanis of Northern Nigeria. Ann Afr Med 2013; 12: 217-222. https://doi.org/10.4103/1596-3519.122689

2. Enang OE, Otu AA, Essien OE, Okpara H, Fasanmade OA, Ohwovoriole AE, et al. Prevalence of dysglycemia in Calabar: A cross-sectional observational study among residents of Calabar, Nigeria. BMJ Open Diabetes Res Care 2014; 2: e00032. https://dx.doi.org/10.1136/bmjdrcc-2014-00032

3. Nyenwe EA, Oda I, Ihekwanne AE, Ojule A, Babatunde S. Type 2 diabetes in adult Nigerians: A study of its prevalence and risk factors in Port Harcourt, Nigeria. Diabetes Res Clin Pract 2003; 62: 177-185. http://doi.org/10.1016/j.diabres.2003.07.002

4. Nwafor A, Owwoji A. Prevalence of diabetes mellitus among Nigerians in Port Harcourt and correlates with socioeconomic status. J Appl Sci Environ Management 2001; 5: 75e7. https://doi.org/10.4314/jasem.v5i1.54950

5. International Diabetes Foundation. Diabetes Atlas. 6th ed. Brussels: IDF; 2014. Available from: http://www.idf.org/diabetesatlas. Accessed November 2018.

6. Støvring H, Andersen M, Beck-Nielsen H, Green A, Vach W. Rising prevalence of diabetes: Evidence from a Danish pharmaco-epidemiological database. Lancet 2003; 362: 537-538. https://doi.org/10.1016/S0140-6736(03)14116-5

7. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: Prevalence, numerical estimates, and projections. Diabetes Care 1998; 21: 1414-31. https://doi.org/10.2337/diacare.21.9.1414

8. Bakari AG, Onyemelukwe GC, Sani BG. Prevalence of diabetes in suburban Northern Nigeria: Results of a public screening survey. Diabetes Int 1999; 9: 59-60. https://doi.org/10.4236/ojepi.2015.53021

9. Erasmus RT, Ebonyi E, Fakeye T. Prevalence of diabetes mellitus in a rural Nigerian population. Niger Med Pract 1988; 15: 28-38.

10. International Diabetes Federation. Diabetes atlas. 8th Ed. Brussels: International Diabetes
11. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: Estimates and projections to the year 2010. Diabetes Med 1997; 14: S1-85. https://doi.org/10.1002/(SICI)1096-9136(199712)14:5%3CS7::AID-DIA522%3E3.0.CO;2-R.

12. Assah FK, Ekelund U, Brage S, Mbanya JC, Wareham NJ. Urbanisation, physical activity, and metabolic health in sub-Saharan Africa. Diabetes Care 2011; 34: 491-496. https://doi.org/10.2337/dc10-0990

13. Gerch JE. Contributions of insulin-resistance and insulin-secretory defects to the pathogenesis of type 2 diabetes mellitus. Mayo Clin Proc 2003; 78: 447-456. https://doi.org/10.4065/78.4.447

14. Kyari F, Tafida A, Sivasubramaniam S, Murthy GV, Peto T, Nigeria National Blindness and Visual Impairment Study Group. Prevalence and risk factors for diabetes and diabetic retinopathy: results from the Nigeria National Blindness and Visual Impairment survey. BMC Public Health 2014; 18: 1299. http://dx.doi.org/10.1186/1471-2458-14-1299

15. Ekpenyong CE, Akpan UP, Ibu JO, Nyebuk DE. Gender and age specific prevalence and associated risk factors of type 2 diabetes mellitus in Uyo Metropolis, South-Eastern Nigeria. Diabetologia Croatica 2012; 41: 17-23.

16. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. Clin Exp Med 2007; 7: 24-29.

17. Pandey BK, Jabannavar VB, Sonoli SS, Somannavar MS. Serum Sialic acid and Lipid Levels in the Offspring of Type 2 Diabetic Parents. J Krishna Inst Med Sci 2015; 4.

18. Dyr JE, Vodrážka Z. Determination of plasma fibrinogen concentration by the modified clot-weight method. Thrombosis Res 1974; 5: 213-221. https://doi.org/10.1016/0049-3848(74)90069-3

19. Bao Y, Ma X, Li H, Zhou M, Hu C, Wu H, et al. Glycated haemoglobin A1c for diagnosing diabetes in Chinese population: cross sectional epidemiological survey. BMJ 2010; 340. https://doi.org/10.1136/bmj.c2249

20. Nakagami T, Tominaga M, Nishimura R, Yoshiike N, Daimon M, Oizumi T, et al. Is the measurement of glycated hemoglobin A1c alone an efficient screening test for undiagnosed diabetes? Japan National Diabetes Survey. Diabetes Res Clin Pract 2007; 76: 251-256. https://doi.org/10.1016/J.DIABRES.2006.09.015

21. Kim JH, Kim GW, Lee MY, Shin JY, Shin YG, Koh SB, et al. Role of HbA1c in the screening of diabetes mellitus in a Korean rural community. Diabetes Metab J 2012; 36: 37-42. https://doi.org/10.4093%2Fdmj.2012.36.1.37

22. Hajat C, Harrison O, Al Siksek Z. Diagnostic testing for diabetes using HbA1c in the Abu Dhabi population: Weqaya: the Abu Dhabi cardiovascular screening program. Diabetes Care 2011; 34: 2400-2402. https://doi.org/10.2337/dc11-0284

23. Lu J, Bi Y, Wang T, Wang W, Mu Y, Zhao J, et al. The relationship between insulin-sensitive obesity and cardiovascular diseases in a Chinese population: results of the REACTION study. Int J Cardiol 2014; 172: 388-394. https://doi.org/10.1016/j.ijcard.2014.01.073
24. World Health Organization: Definition, Diagnosis and Classification of Diabetes Mellitus and Its Complications: Report of a WHO Consultation. www.staff.ncl.ac.uk/philip.home/who_dmg.pdf; https://apps.who.int/iris/handle/10665/66040

25. Selvin E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in non-diabetic adults. N Engl J Med 2010; 362: 800–811. https://doi.org/10.1056/NEJMoa0908359

26. Gillett MJ. International Expert Committee Report on the role of the Hb1Ac assay in the diagnosis of diabetes. Diabetes Care 2009; 32: 1327-1334. https://doi.org/10.2337/dc09-0033

27. Taiwo EO, Thanni LOA. Effect of Physical Exercise on Glucose Tolerance among University students. Ann Health Res 2020; 5: 224-230. https://doi.org/10.30442/ahr.0604-08-106

28. Taiwo EO, Akindele RA, Adefuye BO, Sofola OA, Fasanmade AA, Oyebola DDO, et al. Insulin Sensitivity in Normoglycemic Offspring of Patients with T2DM on Graded Exercise. Indian J Basic Appl Med Res 2017; 7: 207-215.

29. Herman WH, Fajans SS. Hemoglobin A1c for the diagnosis of diabetes: practical considerations. Pol Arch Med Wewn 2010; 120: 37–40.

30. Machlus KR, Cardenas JC, Church FC. Causal relationship between hyperfibrinogenemia, thrombosis, and resistance to thrombolysis in mice. Blood 2011; 117: 4953-4963. https://doi.org/10.1182/blood-2010-11-316885

31. Wang L, Gao P, Zhang M, Huang Z, Zhang D, Deng Q, et al. Prevalence and ethnic pattern of diabetes and prediabetes in China in 2013. JAMA 2017; 317: 2515-2523. https://doi.org/10.1001/jama.2017.7596

32. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. Nat Rev Immunol 2011; 11: 98–107. https://doi.org/10.1038/nri2925

33. Pietrani NT, Rodrigues KF, Bosco AA, Vieira CM, Perucci LO, Oliveira MC, et al. Peripheral activation of inflammatory intracellular signalling pathways and their correlation with IL6, IL10 and TNFα in obesity and Type 2 diabetes mellitus. Inflammation Cell Signaling 2015; 2. https://doi.org/10.1002/dmrr.2639

34. Grossmann V, Schmitt VH, Zeller T, Panovanoeya M, Schulz A, Laubert-Reh D, et al. Profile of the immune and inflammatory response in individuals with prediabetes and type 2 diabetes. Diabetes Care 2015;38: 1356-1364. https://doi.org/10.2337/dc14-3008

35. Zhang L, Xu C, Liu J, Bai X, Li R, Wang L, et al. Baseline plasma fibrinogen is associated with haemoglobin A1c and 2-year major adverse cardiovascular events following percutaneous coronary intervention in patients with acute coronary syndrome: a single-centre, prospective cohort study. Cardiovascular Diabetol 2019; 18: 1-1. https://doi.org/10.1186/s40635-019-0265

36. Baker NL, Hunt KJ, Stevens DR, Jarai G, Rosen GD, Klein RL, et al. DCCT/EDIC Research Group. Association between inflammatory markers and progression to kidney dysfunction: examining different assessment windows in patients with Type 1 diabetes. Diabetes Care 2018; 41: 128-135. https://doi.org/10.2337/dc17-0867

37. Azad N, Agrawal L, Emanuele NV, Klein R, Bahn GD, McCarren M, et al. VADT Study Group. Association of PAI-1 and fibrinogen

© Annals of Health Research. Volume 8, Issue No. 2, 2022
with diabetic retinopathy in the Veterans Affairs Diabetes Trial (VADT). Diabetes Care 2014; 37: 501-506. https://doi.org/10.2337/dc13-1193

This is an Open Access document licensed for distribution under the terms and conditions of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc/4.0). This permits unrestricted, non-commercial use, reproduction and distribution in any medium, provided the original source is adequately cited and credited.