Assessing cardiovascular status using biomarkers and anthropometry among patients with Type-2 Diabetes in a resource limited setting

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ABSTRACT

Background: Diabetes places extra-burden on those affected with the condition particularly in resource constraint settings. Inaccessibility to affordable diagnostic procedures poses a major challenge to the assessment of cardiovascular status in patients with type-2 diabetes in resource limited settings. The study was aimed at evaluating some easily accessible biochemical markers and anthropometric indices implicated in cardiovascular disease amongst T2DM patients.

Methods: One hundred and sixty (160) type-2 diabetic patients grouped into type-2 diabetes only as group 1, type-2 diabetic patients diagnosed with hypertension as group 2, and eighty (80) age  and sex-matched controls as group 3, were enrolled in a cross-sectional pattern. Biochemical parameters were assayed using standard laboratory methods. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 20.0 with statistical significance considered at p≤0.05.

Results: The values obtained for diabetic groups were: Glycated Hemoglobin (HbA1c) 9.07±1.99, 10.15±4.98, Total Homocysteine (tHcy) 14.85±52.10, 28.35±100.35, high sensitivity C-reactive protein (hs-CRP) 6.72±6.78, 10.00±11.15, Waist Circumference, 92.58±1.55, 93.65±18.91, Hip Circumference, 96.87±9.01, 98.96±20.33, Systolic Blood Pressure, 113.50±12.94, 135.50±22.72, Diastolic Blood Pressure, 70.75±8.57, 75.38±12.62, Body Mass Index, 25.40±4.70, 26.93±6.50 (among patients) and HbA1c 5.81±0.86, tHcy 0.75±1.44, hs-CRP 5.30±6.19, Waist Circumference 83.15±10.69, Hip Circumference 93.50±22.05, Systolic Blood Pressure, 113.50±10.20, Diastolic Blood Pressure, 77.00±7.19, Body Mass Index, 24.84±4.93 (among controls).

Conclusion: The assessment of some cardio metabolic markers and anthropometric indices may provide easy and accessible tools for prediction and assessment of cardiovascular disease in patients with T2DM especially in resource poor settings.

Keywords: non-communicable, anthropometry, Diabetes, heart disease
on individuals, families, healthcare systems and socioeconomic growth cannot be disregarded (WHO, 2017). Cardiovascular disease (CVD) is 2-4 folds more prevalent and the leading cause of early deaths among diabetic patients (Tarkun et al., 2003; Rahman et al., 2009). Type 2 diabetes mellitus (T2DM) has been linked with increased risks of hypertension, myocardial infarction, intermittent claudication and stroke (Giorda et al., 2007; Rahman et al., 2009; Chihia et al., 2012; Martín-Timón et al., 2014). Diabetic patients have been reported to have an increased diagnosis of new heart failure (HF) even in the absence of a baseline heart failure, frequent hospitalization and/or death from HF compared to those without T2DM (Rosano et al., 2017; Kenny and Abel, 2019; Wilkinson et al., 2019). The risk for HF increases 5-fold in women and 2.4-fold in men with diabetes in some climes (Wang et al., 2016).

Type-2 diabetes is characterized by metabolic changes which link hyperglycaemia to other risk factors (Lima et al., 2007) including hypercoagulability, dysglycemia, dyslipidemia, hypertension (Rahman et al., 2009), obesity, overweight (Cheung and Li, 2012), inflammation (Rahman et al., 2017), insulin resistance (Lopez-Candales et al., 2017) and/or elevations in homocysteine concentrations (Malaguarnera et al., 2014; El-Maghraby et al., 2016). Life-style and dietary changes that trigger obesity and overweight have been linked with the T2DM epidemic (Gillies et al., 2007). Improvements of traditional risk factors such as blood pressure, body mass index, total cholesterol and dietary modification have shown to evidently reduce the risk of hypertension in patients with type-2 diabetes (Abdul-Ghani et al., 2017).

Insulin resistance syndrome (IRS) is a key component responsible for increased risk of CVD in T2DM but molecular mechanisms involved directly in the pathogenesis of IR are independent of accompanying metabolic abnormalities linked to T2DM (DeFronzo, 2009). As a result obese non-diabetic individuals with IRS present with increased risk of CVD, impaired glucose tolerance, dyslipidemia and hypertension compared with obese diabetic patients (Eckel et al., 2005; Eddy et al., 2009).

Data from epidemiological studies (Khaw et al., 2004; Gerstein et al., 2005; Elley et al., 2008; Eeg-Olofsson et al., 2010) support the link between cardiovascular disease risk and hyperglycemia. Improved glycemic control associated cardiovascular benefits among diabetic patients (Holman et al., 2008; Hayward et al., 2015) and increased risk of atherosclerotic cardiovascular disease (Selvin et al., 2004) in the presence of coexistent dysglycaemia have also been reported. Contrarily, some studies (Patel et al., 2008; Gerstein et al., 2010) have reliably established that HbA1c reduction in type-2 diabetic patients does not have or have unassertive influence on cardiovascular disease risk worsening (Marso et al., 2016).

Although, there are controversies regarding plasma tHcy levels in T2DM. Prospective studies (Avramoglou et al., 2006; Lorenzo et al., 2013) have shown an independent association between elevated plasma tHcy level, prediction of early cardiovascular events and all-cause mortality amongst diabetics. Plasma tHcy levels in type 2 diabetic patients are reported to be similar to or higher than those in healthy subjects (Drzewoski et al., 1999; El-Maghraby et al., 2016). On the contrary, studies by Bansal et al. (2016) and Smulders et al. (1999) found no significant differences in fasting plasma tHcy levels between type 2 diabetic patients and healthy subjects.

High-sensitivity C-reactive protein (hs-CRP) is considered a stable inflammatory biomarker of arterial wall inflammation, preclinical atherosclerosis and systemic endothelial dysfunction (Tabas et al., 2015) that adds cardiovascular prognostic information beyond traditional risk factors among T2DM patients (Kiran et al., 2017). Although in the past, atherosclerosis was considered a bland lipid storage disease, recent studies have showed that inflammation, underlying cellular, molecular mechanisms and pathophysiologic factors are contributors of atherogenesis (Schillinger et al., 2004).
The study is aimed at evaluating some easily accessible biochemical markers and anthropometric indices implicated in cardiovascular disease amongst T2DM patients.

MATERIALS AND METHODS

Study Area and Population
The study was carried out in Dutse, Jigawa State, North-western Nigeria. A total of two hundred and forty (240) participants, one hundred and sixty (160) type 2 diabetic patients aged 29-60 years; eighty (80) type 2 diabetic patients diagnosed without hypertension (Group 1), eighty (80) type 2 diabetes diagnosed with hypertension (Group 2) and eighty (80) control subjects (Group 3) were recruited into the study through convenience sampling in a cross-sectional pattern. Patients with a history of liver diseases, renal impairment, pregnant women and those who did not consent to participate in the study were excluded. The controls were afebrile, apparently healthy volunteers, matched for gender and age after a complete clinical examination by the physician, with or without a self-reported family history of diabetes or hypertension. Anthropometric indices including weight, height, body mass index, waist circumference, hip circumference, systolic and diastolic blood pressure were measured and documented. Relevant data was obtained using the clinical records and a detailed interviewer-based administered questionnaire. Participants provided informed consent in written form before being enrolled into the study.

Ethical Consideration
Ethical approval was sought and granted by the research ethical committee of Rasheed Shekoni Specialist Hospital Dutse, Jigawa State. Ref: RSSH/GEN/226/V.1/36.

Sample Collection and Laboratory Methods
Five milliliters (5ml) of blood was collected via venipuncture from all participants after a 10-hour overnight fast and transferred into EDTA and plain tubes respectively. Plasma total homocysteine (tHcy) and serum high sensitivity C-reactive protein (hs-CRP) were assayed using Enzyme Linked Immunosorben Assay (ELISA) (Cusabio, China and Monobind Inc, USA), Glycated haemoglobin (HbA1c) was assayed using Immunoturbidimetric assay (Centronic GmbH, Germany). Enzymatic colorimetric methods were used for the assay of lipid profile and fasting plasma glucose using test kits (Agappe diagnostics Switzerland GmbH).

Cut-off for Biochemical Parameters and Anthropometric Indices

Blood pressure Measurement
Normal: Systolic Blood Pressure ≤120 mmHg, Diastolic Blood Pressure ≤80 mmHg.
Prehypertension: Systolic Blood Pressure 120-140 mmHg, Diastolic Blood Pressure 80-90 mmHg.
Hypertension: Systolic Blood Pressure ≥140 mmHg, Diastolic Blood Pressure ≥90 mmHg.

Waist circumference range: Male: 83-98 cm, Female: 78-91 cm.
Hip circumference range: Male: 94-107 cm, Female: 97-108 cm.

Body Mass Index Stratification: Underweight: ≤18.5, Normal: 18.5-24.9, Overweight: 25.0-29.9, Obese: ≥30.0.

Total homocysteine (tHcy): Low risk ≤0.78 nmol/l, Normal: 0.78-50.0 nmol/l, High risk: ≥50 nmol/l.

High sensitivity C-reactive protein (hs-CRP): Low risk ≤1.0 µg/ml, Normal: 1-3 µg/ml, High risk: ≥3.0 µg/ml.

Glycated hemoglobin (HbA1C): Low risk ≤6.0%, Normal: 6-9%, High risk: ≥9.0%.

Fasting Plasma Glucose was assessed using the American Diabetes Association Criteria 2010. The cut-off for total cholesterol, high-density lipoprotein cholesterol, triglycerides and low-density lipoprotein cholesterol were based on local reference ranges.

Statistical Analysis
Statistical Package for Social Sciences version 20.0 (SPSS Inc., Chicago, Illinois, USA) software was used for the statistical analysis of data obtained.
Statistical significance was considered as p≤0.05 and presented as frequency, percentages, mean ± SD, Unpaired Student’s t-test and One-way ANOVA.

RESULTS AND DISCUSSION

Individuals at increased risk of cardiovascular disease (CVD) may exhibit overweight, obesity, hyperglycemia, hyperlipidemia and hypertension (Rahman et al., 2017). Comparable to previous reports (Giorda et al., 2007; Rahman et al., 2011; Petrie et al., 2018; Kenny and Abel, 2019) of increased body mass index (BMI) among type 2 diabetic patients. Our study observed a similar trend among type 2 diabetes (T2D) patients with a marked difference between healthy individuals and T2DM patients diagnosed with hypertension (HTN). Contrary to our report, Gillies et al. (2007) reported increased BMI among type 2 diabetic patients not diagnosed with hypertension. Whether BMI imparts HTN in T2DM or vice versa was not detailed in our study. Our study also verified that increased waist and hip circumference is commoner in type 2 diabetic patients compared to apparently healthy individuals and our finding is similar to (Lima et al., 2007). We suggest that waist circumference may be a more promising anthropometric measure in comparison to hip circumference in predicting cardiovascular disease.

Our findings of elevated systolic blood pressure (SBP) among diabetic patients diagnosed with hypertension compared to healthy individuals may provide insights into the independent consideration of SBP as a more specific measure for diagnosis of hypertension and may serve as an inexpensive screening tool for assessing prehypertension among healthy individuals. The variation of diastolic blood pressure (DBP) across the groups suggests that DBP is a sensitive not specific marker for hypertension. The reported incidences of prehypertension in the control group may be attributable to the increased prevalence of the family history of hypertension in the group. Our findings is in concordance with the studies of

Table 1: Socio-demographic Characteristics of the Study Participants

| Variables                        | Group 1, n = 80(%) | Group 2, n = 80(%) | Group 3, n = 80(%) |
|----------------------------------|-------------------|-------------------|-------------------|
| **Age group (years)**            |                   |                   |                   |
| ≤ 29                             | 6 (7.5)           | 0 (0)             | 40 (50.0)         |
| 30 – 50                          | 36 (45.0)         | 30 (37.5)         | 40 (50.0)         |
| 51 and above                     | 38 (47.5)         | 50 (62.5)         | 0 (0.0)           |
| **Mean ± SD**                    | **Mean ± SD**     | **Mean ± SD**     |                   |
| Mean age                         | 49.3 ± 13.4 years| 55.3 ± 9.4 years  | 30.2 ±6.1 years   |
| **Gender**                       |                   |                   |                   |
| Male                             | 32 (40.0)         | 58 (72.5)         | 36 (45.0)         |
| Female                           | 48 (60.0)         | 22 (27.5)         | 44 (55.0)         |
| **Family history of DM**         |                   |                   |                   |
| Present                          | 23 (28.8)         | 40 (50.0)         | 28 (35.0)         |
| Absent                           | 57 (71.3)         | 40 (50.0)         | 52 (65.0)         |
| **Family history of hypertension**|                   |                   |                   |
| Present                          | 28 (35.0)         | 45 (56.2)         | 44 (55.0)         |
| Absent                           | 52 (65.0)         | 35 (43.8)         | 36 (45.0)         |
| **Family history of obesity**    |                   |                   |                   |
| Present                          | 35 (43.8)         | 54 (67.5)         | 8 (10.0)          |
| Absent                           | 45 (56.2)         | 26 (32.5)         | 72 (90.0)         |
| **Duration of DM (years)**       |                   |                   |                   |
| 1 – 5                            | 46 (57.5)         | 51 (63.8)         | -                 |
| 6 and above                      | 34 (42.5)         | 29 (36.2)         | -                 |
| **Mean ± SD**                    | **Mean ± SD**     |                   |                   |
| Mean duration                    | 5.7 ± 4.7 (mmol/l)*| 4.8 ± 4.1 (mmol/l)*|                   |

*Data presented as frequency (percent); DM = type2 Diabetes Mellitus, SD = Standard Deviation
| Variables                        | Group 1, n = 80(%) | Group 2, n = 80(%) | Group 3, n = 80(%) |
|---------------------------------|-------------------|-------------------|-------------------|
| Waist circumference (cm)        |                   |                   |                   |
| Normal                          | 48 (60.0)         | 53 (66.2)         | 67 (83.8)         |
| Abnormal                        | 32 (40.0)         | 27 (33.8)         | 13 (16.2)         |
| Mean±SD                         | 92.58±11.55       | 93.65±18.91       | 83.15±10.69       |
| Hip circumference (cm)          |                   |                   |                   |
| Normal                          | 51 (63.8)         | 50 (62.5)         | 72 (90.0)         |
| Abnormal                        | 29 (36.2)         | 30 (37.5)         | 8 (10.0)          |
| Mean±SD                         | 96.82±9.01        | 98.96±20.33       | 93.50±22.05       |
| SBP (mmHg)                      |                   |                   |                   |
| Normal                          | 40 (50.0)         | 17 (21.3)         | 44 (55.0)         |
| Pre-hypertension                | 40 (50.0)         | 20 (25.0)         | 36 (45.0)         |
| Hypertension                    | 0 (0.0)           | 43 (53.8)         | 0 (0.0)           |
| Mean±SD                         | 113.50±12.94      | 135.50±22.72      | 113.50±10.20      |
| DBP (mmHg)                      |                   |                   |                   |
| Normal                          | 58 (72.5)         | 45 (56.2)         | 20 (25.0)         |
| Pre-hypertension                | 22 (27.5)         | 15 (18.8)         | 60 (75.0)         |
| Hypertension                    | 0 (0.0)           | 20 (25.0)         | 0 (0.0)           |
| Mean±SD                         | 70.75±8.57        | 75.38±12.62       | 77.00±7.19        |
| Combined (SBP &DBP) status      |                   |                   |                   |
| Absent                          | 80 (100.0)        | 74 (92.5)         | 80 (100.0)        |
| Present                         | 0 (0.0)           | 6 (7.5)           | 0 (0.0)           |
| BMI (kg/m²)                     |                   |                   |                   |
| Under weight                    | 14 (17.5)         | 2 (2.5)           | 8 (10.0)          |
| Normal                          | 21 (26.3)         | 36 (45.0)         | 40 (50.0)         |
| Over weight                     | 30 (37.5)         | 20 (25.0)         | 24 (30.0)         |
| Obese                           | 15 (18.8)         | 22 (27.5)         | 8 (10.0)          |
| Mean ± SD                       | 25.40 ± 4.70      | 26.93 ± 6.50      | 24.84 ± 4.93      |
| Glycated haemoglobin (%)        |                   |                   |                   |
| Low risk                        | 13 (16.3)         | 3 (3.8)           | 44 (55.0)         |
| Normal                          | 37 (46.3)         | 38 (47.5)         | 36 (45.0)         |
| High risk                       | 30 (37.5)         | 39 (48.7)         | 0 (0.0)           |
| Fasting plasma glucose (mmol/l) |                   |                   |                   |
| Normal                          | 42 (52.5)         | 30 (37.5)         | 80 (100.0)        |
| Abnormal                        | 38 (47.5)         | 59 (62.5)         | 0 (0.0)           |
| Total homocysteine (mmol/l)     |                   |                   |                   |
| Low risk                        | 62 (77.5)         | 56 (70.0)         | 72 (90.0)         |
| Normal                          | 10 (12.5)         | 18 (22.5)         | 8 (10.0)          |
| High risk                       | 8 (10.0)          | 6 (7.5)           | 0 (0.0)           |
| hs C-reactive Protein (µg/ml)   |                   |                   |                   |
| Low risk                        | 3 (3.8)           | 7 (8.8)           | 4 (5.0)           |
| Normal                          | 20 (25.0)         | 13 (16.3)         | 36 (45.0)         |
| High risk                       | 57 (71.2)         | 60 (75.0)         | 40 (50.0)         |
| Total cholesterol (mmol/l)      |                   |                   |                   |
| Normal                          | 77 (96.2)         | 64 (80.0)         | 80 (100.0)        |
| Abnormal                        | 3 (3.8)           | 16 (20.0)         | 0 (0.0)           |
| HDL-cholesterol (mmol/l)        |                   |                   |                   |
| Normal                          | 77 (96.2)         | 70 (87.5)         | 72 (90.0)         |
| Abnormal                        | 3 (3.8)           | 10 (12.5)         | 8 (10.0)          |
| Triglycerides (mmol/l)          |                   |                   |                   |
| Normal                          | 54 (67.5)         | 64 (80.0)         | 56 (70.0)         |
| Abnormal                        | 26 (32.5)         | 16 (20.0)         | 24 (30.0)         |
| LDL-cholesterol (mmol/l)        |                   |                   |                   |
| Normal                          | 77 (96.2)         | 68 (85.0)         | 80 (100.0)        |
| Abnormal                        | 3 (3.8)           | 12 (15.0)         | 0 (0.0)           |
Table 3: Mean and Median of Biochemical parameters in the three groups

| Parameters                      | Groups, n = 80 | Mean ± SD    | Median (IQR) |
|--------------------------------|---------------|--------------|--------------|
| Glycated haemoglobin (%)       | 1             | 10.15 ± 4.98*| 8.35 (7.60 – 10.95) |
|                                | 2             | 9.07 ± 1.99  | 8.70 (8.00 – 10.50) |
|                                | 3             | 5.81 ± 0.86  | 5.65 (5.00 – 6.73)  |
| FBG (mmol/L)                   | 1             | 7.83 ± 3.83* | 6.40 (4.80 – 10.80) |
|                                | 2             | 7.74 ± 3.67* | 7.30 (5.10 – 8.10)  |
|                                | 3             | 4.89 ± 0.99  | 5.00 (4.20 – 5.65)  |
| Total homocysteine (nmol/L)    | 1             | 28.35 ± 100.82* | 0.51 (0.23 – 0.70) |
|                                | 2             | 14.85 ± 52.10*| 0.65 (0.45 – 1.06)  |
|                                | 3             | 0.75 ± 1.44* | 0.42 (0.26 – 0.55)  |
| hs C-reactive Protein (µg/mL)  | 1             | 10.00 ± 11.15*| 6.15 (2.88 – 10.82) |
|                                | 2             | 6.72 ± 6.78  | 5.20 (3.04 – 7.68)  |
|                                | 3             | 5.30 ± 6.19  | 2.98 (1.59 – 6.34)  |
| Total cholesterol (mmol/L)     | 1             | 3.30 ± 0.70  | 3.25 (2.80 – 3.70)  |
|                                | 2             | 3.40 ± 0.94  | 3.30 (2.93 – 4.00)  |
|                                | 3             | 3.63 ± 0.35  | 3.60 (3.01 – 4.10)  |
| HDL-cholesterol (mmol/L)       | 1             | 1.12 ± 0.30  | 1.10 (1.90 – 1.40)  |
|                                | 2             | 1.24 ± 0.50* | 1.10 (1.90 – 1.40)  |
|                                | 3             | 1.26 ± 0.35  | 1.30 (1.00 – 1.58)  |
| Triglycerides(mmol/L)          | 1             | 0.79 ± 0.43* | 0.60 (0.40 – 1.10)  |
|                                | 2             | 0.84 ± 0.56* | 0.70 (0.50 – 1.00)  |
|                                | 3             | 0.75 ± 0.48* | 0.60 (0.40 – 0.85)  |
| LDL-cholesterol (mmol/l)       | 1             | 1.88 ± 0.67* | 1.85 (1.40 – 2.40)  |
|                                | 2             | 1.81 ± 0.83* | 1.90 (1.20 – 2.20)  |
|                                | 3             | 2.03 ± 0.55  | 2.00 (1.63 – 2.40)  |

Table 4: Variation in Biochemical Parameters and Anthropometric Indices between groups 1 and 3

| Parameters                      | n = 80 | Mean ± SD  | t-value | p-value | Mean diff | 95% CI  |
|--------------------------------|-------|------------|---------|---------|-----------|---------|
| Glycated haemoglobin (%)       | 1     | 10.15 ± 4.98* | 7.691   | < 0.001 | 4.349     | 3.2319 – 5.466 |
|                                | 3     | 5.81 ± 0.86  |         |         |           |         |
| FBG (mmol/l)                   | 1     | 7.83 ± 3.83* | 6.679   | < 0.001 | 2.948     | 2.0759 – 3.819 |
|                                | 3     | 4.89 ± 0.99  |         |         |           |         |
| Total homocysteine (nmol/l)    | 1     | 28.35 ± 100.82* | 2.448   | 0.015   | 27.598    | 5.3316 – 49.86 |
|                                | 3     | 0.75 ± 1.44* |         |         |           |         |
| hs C-reactive Protein (µg/ml)  | 1     | 10.00 ± 11.15* | 3.296   | 0.001   | 4.7       | 1.8837 – 7.517 |
|                                | 3     | 5.30 ± 6.19  |         |         |           |         |
| Total cholesterol (mmol/l)     | 1     | 3.30 ± 0.70  | -3.331  | 0.001   | -0.33     | -0.5300 – 0.135 |
|                                | 3     | 3.63 ± 0.55  |         |         |           |         |
| HDL-cholesterol (mmol/l)       | 1     | 1.12 ± 0.30  | -2.739  | 0.007   | -0.141    | -0.2431 – 0.039 |
|                                | 3     | 1.26 ± 0.35  |         |         |           |         |
| Triglycerides(mmol/L)          | 1     | 0.79 ± 0.43* | 0.485   | 0.628   | 0.4       | -0.1075 – 0.178 |
|                                | 3     | 0.75 ± 0.48* |         |         |           |         |
| LDL-cholesterol (mmol/l)       | 1     | 1.88 ± 0.67* | -1.469  | 0.144   | -1.469    | -0.0486 – 0.144 |
|                                | 3     | 2.03 ± 0.55  |         |         |           |         |
| Waist circumference (cm)       | 1     | 92.58 ± 11.55| 5.359   | < 0.001 | 9.43      | 5.9560 – 12.907 |
|                                | 3     | 83.15 ± 10.69|         |         |           |         |
| Hip circumference (cm)         | 1     | 96.82 ± 9.01 | 1.247   | 0.214   | 3.32      | -1.9400 – 8.580 |
|                                | 3     | 93.50 ± 22.05|         |         |           |         |
| SBG (mmHg)                     | 1     | 113.50 ± 12.94| 0      | 1       | 0         | -3.6380 – 3.638 |
|                                | 3     | 113.50 ± 10.20|         |         |           |         |
| DBG (mmHg)                     | 1     | 70.75 ± 8.57 | -5.01   | < 0.001 | -6.25     | -8.7140 – 3.786 |
|                                | 3     | 77.00 ± 7.19 |         |         |           |         |
| BMI (kg/m2)                    | 1     | 25.40 ± 5.34 | 0.691   | 0.491   | 0.56      | -1.0429 – 2.1654 |
|                                | 3     | 24.84 ± 4.93 |         |         |           |         |
| Age (years)                    | 1     | 49.30 ± 13.40| 11.621  | < 0.001 | 19.15     | 15.895 – 22.405 |
|                                | 3     | 30.15 ± 6.13 |         |         |           |         |
Table 5: Variation in Biochemical Parameters and Anthropometric Indices across the groups

| Parameters                        | n=80 | Mean ± SD      | f-value | p-value  |
|-----------------------------------|------|----------------|---------|----------|
| Glycated haemoglobin (%)          |      |                |         |          |
| 1                                 |      | 10.15 ± 4.98*  | 41.375  | < 0.001  |
| 2                                 |      | 9.07 ± 1.99    |         |          |
| 3                                 |      | 5.81 ± 0.86    |         |          |
| Fasting plasma glucose (mmol/l)   |      |                |         |          |
| 1                                 |      | 7.85 ± 3.83*   | 23.167  | < 0.001  |
| 2                                 |      | 7.74 ± 3.67*   |         |          |
| 3                                 |      | 4.89 ± 0.99    |         |          |
| Total homocysteine (nmol/l)       |      |                |         |          |
| 1                                 |      | 28.35 ± 100.82*| 3.458   | 0.030    |
| 2                                 |      | 14.85 ± 52.10* |         |          |
| 3                                 |      | 0.75 ± 1.44*   |         |          |
| hs C-reactive Protein (µg/ml)     |      |                |         |          |
| 1                                 |      | 10.00 ± 11.15* | 6.687   | < 0.001  |
| 2                                 |      | 6.72 ± 6.78    |         |          |
| 3                                 |      | 5.30 ± 6.19    |         |          |
| Total cholesterol (mmol/l)        |      |                |         |          |
| 1                                 |      | 3.30 ± 0.70    | 4.187   | 0.016    |
| 2                                 |      | 3.40 ± 0.94    |         |          |
| 3                                 |      | 3.63 ± 0.55    |         |          |
| HDL-cholesterol (mmol/l)          |      |                |         |          |
| 1                                 |      | 1.12 ± 0.30    | 3.020   | 0.051    |
| 2                                 |      | 1.24 ± 0.50*   |         |          |
| 3                                 |      | 1.26 ± 0.35    |         |          |
| Triglycerides (mmol/l)            |      |                |         |          |
| 1                                 |      | 0.79 ± 0.43*   | 0.785   | 0.457    |
| 2                                 |      | 0.84 ± 0.56*   |         |          |
| 3                                 |      | 0.75 ± 0.48*   |         |          |
| LDL-cholesterol (mmol/l)          |      |                |         |          |
| 1                                 |      | 1.88 ± 0.67*   | 1.998   | 0.138    |
| 2                                 |      | 1.81 ± 0.83*   |         |          |
| 3                                 |      | 2.03 ± 0.55    |         |          |
| Waist circumference (cm)          |      |                |         |          |
| 1                                 |      | 92.58 ± 11.55  | 13.238  | < 0.001  |
| 2                                 |      | 93.65 ± 18.91  |         |          |
| 3                                 |      | 83.15 ± 10.69  |         |          |
| Hip circumference (cm)            |      |                |         |          |
| 1                                 |      | 96.82 ± 9.01   | 1.849   | 0.160    |
| 2                                 |      | 98.96 ± 20.33  |         |          |
| 3                                 |      | 93.50 ± 22.05  |         |          |
| Systolic blood pressure (mmHg)    |      |                |         |          |
| 1                                 |      | 113.50 ± 12.94 | 49.162  | < 0.001  |
| 2                                 |      | 135.50 ± 22.72 |         |          |
| 3                                 |      | 113.50 ± 10.20 |         |          |
| Diastolic blood pressure (mmHg)   |      |                |         |          |
| 1                                 |      | 70.75 ± 8.57   | 8.891   | < 0.001  |
| 2                                 |      | 75.38 ± 12.62  |         |          |
| 3                                 |      | 77.00 ± 7.19   |         |          |
| BMI (kg/m2)                       |      |                |         |          |
| 1                                 |      | 25.40 ± 5.34   | 2.959   | 0.054    |
| 2                                 |      | 26.93 ± 6.50   |         |          |
| 3                                 |      | 24.84 ± 4.93   |         |          |
| Age (years)                       |      |                |         |          |
| 1                                 |      | 49.30 ± 13.40  | 135.662 | < 0.001  |
| 2                                 |      | 55.33 ± 9.41   |         |          |
| 3                                 |      | 30.15 ± 6.13   |         |          |

*skewed, SD = Standard Deviation, BMI = Body Mass Index
Table 6: Variation in Biochemical Parameters and Anthropometric Indices between groups 2 and 3

| Parameters                        | n=80 | Mean ± SD | t-value | p-value | Mean diff | 95% CI          |
|-----------------------------------|------|-----------|---------|---------|-----------|-----------------|
| Glycated haemoglobin (%)          | 2    | 9.07 ± 1.99| 13.451  | <0.001  | 3.268     | 2.7881-3.7480   |
|                                  | 3    | 5.81 ± 0.86|         |         |           |                 |
| FBG (mmol/L)                     | 2    | 7.74 ± 3.67*| 6.711   | <0.001  | 2.854     | 2.0142-3.6943   |
|                                  | 3    | 4.89 ± 0.99|         |         |           |                 |
| Total homocysteine (mmol/L)      | 2    | 14.85 ± 52.10*| 2.418   | 0.017   | 14.2      | 2.5793-25.599   |
|                                  | 3    | 0.75 ± 1.44*|         |         |           |                 |
| hs C-reactive Protein (µg/mL)    | 2    | 6.72 ± 6.78| 1.383   | 0.169   | 1.419     | -0.6083-3.4470  |
|                                  | 3    | 5.30 ± 6.19|         |         |           |                 |
| Total cholesterol (mmol/L)       | 2    | 3.40 ± 0.94| -1.935  | 0.055   | -0.230    | -0.4750-0.0050  |
|                                  | 3    | 3.63 ± 0.55|         |         |           |                 |
| HDL-cholesterol (mmol/L)         | 2    | 1.24 ± 0.50*| -0.333  | 0.74    | -0.020    | -0.1561-0.1111  |
|                                  | 3    | 1.26 ± 0.35|         |         |           |                 |
| Triglycerides (mmol/L)           | 2    | 0.84 ± 0.56*| 1.174   | 0.242   | 0.090     | -0.6560-0.2581  |
|                                  | 3    | 0.75 ± 0.48|         |         |           |                 |
| LDL-cholesterol (mmol/L)         | 2    | 1.81 ± 0.83*| -1.935  | 0.055   | -0.220    | -0.4320-0.0045  |
|                                  | 3    | 2.03 ± 0.55|         |         |           |                 |
| Waist circumference (cm)         | 2    | 93.65 ± 18.91| 4.323   | <0.001  | 10.50     | 5.7030-15.2970  |
|                                  | 3    | 83.15 ± 10.69|         |         |           |                 |
| Hip circumference (cm)           | 2    | 98.96 ± 20.33| 1.627   | 0.106   | 5.460     | -1.1680-12.078  |
|                                  | 3    | 93.50 ± 22.05|         |         |           |                 |
| SBP (mmHg)                       | 2    | 135.50 ± 22.72| 7.901   | <0.001  | 22.00     | 16.5000-27.5000 |
|                                  | 3    | 113.50 ± 10.20|         |         |           |                 |
| DBP (mmHg)                       | 2    | 75.38 ± 12.62| -1.001  | 0.319   | -1.620    | -4.8330-1.5830  |
|                                  | 3    | 77.00 ± 7.19|         |         |           |                 |
| BMI (kg/m2)                      | 2    | 26.93 ± 6.50| 2.293   | 0.023   | 2.090     | 0.2899-3.89260  |
|                                  | 3    | 24.84 ± 4.93|         |         |           |                 |
| Age (years)                      | 2    | 55.33 ± 9.41| 20.056  | <0.001  | 25.18     | 22.6960-27.654  |
|                                  | 3    | 30.15 ± 6.13|         |         |           |                 |

*Skewed, SD = Standard Deviation, BMI = Body Mass Index

(Rahman et al., 2009; Petrie et al., 2018) but contrary to the report of (Giorda et al., 2007). Our report brings to fore the possible constellation of anthropometric indices as early predictors of cardiovascular risk in patients with T2DM and the general population.

Our study demonstrated the independent relationship between hyperglycemia, HbA1c levels, diabetes and hypertension. Evidently, glycemic status among healthy non-obese individuals may not serve as an independent early predictor for T2DM and hypertension especially in the presence of a family history of diabetes. Conversely, non-traditional risk factors linked to insulin resistant states may predict CVD outcomes independent of hyperglycemia in healthy individuals. Nonetheless, hyperglycemia may be an independent risk factor for overt cardiovascular disease in the presence of other metabolic, biochemical and physiological changes that may trigger macro or microvascular complications regardless of glycemia. The outcome of our study is in agreement to that of Abdul-Ghani et al. (2017) and Gillies et al. (2007).

Hyperhomocysteinemia is a known risk factor for atherogenesis, CVD and incident T2DM. Majority of our study participants regardless of the group belonged to the tHcy low risk strata. This may be credited to the hypothesis that low homocysteine level serves as an indication of early loss of pancreatic beta cell function independent of glycemia, traditional and non-traditional risk factors for cardiovascular disease. We observed that minority of the participants had abnormal plasma tHcy values particularly type 2 diabetic patients not diagnosed
The discovery may imply that T2DM may be considered a CVD equivalent since hyperhomocysteinemia is influenced by insulin resistance and intact pancreatic beta cell function. Our study found elevations in plasma tHcy levels among patients diagnosed with T2DM as reported by (Gillies et al., 2007; Lima et al., 2007; Rahman et al., 2009; Abdul-Ghani et al., 2017). Conversely, Gillies et al. (2007) reported higher incidences of hyperhomocysteinemia among type 2 diabetic patients diagnosed with hypertension. Screening for tHcy in asymptomatic diabetic patients and healthy individuals may be considered in clinical practice to assess pancreatic function and serve as an early predictor of T2DM or CVD risk in resource constraint settings.

The relationship between increased hs-CRP concentrations and risk of incident type 2 diabetes is well established (Chiha et al., 2012; Dongway et al., 2015) although Kenny and Abel (2019) reported a contrary finding. Patients with elevated hs-CRP often times present with increased risk of coronary heart disease (Petrie et al., 2018) and are likely to benefit from specific lifestyle interventions (Chiha et al., 2012). Our study reported about two-thirds of type 2 diabetic patients and 50% of healthy individuals were within the high-risk strata for hs-CRP which is similar to the reports of (Rahman et al., 2011; Petrie et al., 2018; Wilkinson et al., 2019).

The cofounder in our study may be increased age of the type 2 diabetic patients since hs-CRP has been reported to increase with age (Wilkinson et al., 2019). Whether the family history of diabetes, hypertension and/or obesity among healthy individuals imparts hs-CRP concentrations remains vague in our study. We suggest that larger epidemiological studies consider the family history of participants prior to hs-CRP baseline assay.

The pattern of diabetic dyslipidemia we observed in our study was characterized by hypertriglyceridemia, decreased levels of total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein-cholesterol (HDL-C). Our finding suggests the significant role hypertriglyceridemia plays in diabetic dyslipidemia. Our finding validates the indispensable roles of hypertriglyceridemia, inflammation, obesity and hyperglycemia in the pathogenesis of atherosclerotic CVD among type 2 diabetic patients and healthy individuals. We suggest the measurement of these conventional biochemical parameters in conjunction with the assessment of anthropometric indices as early predictors for future cardiovascular disease in apparently healthy patients with a family history of hypertension, diabetes or obesity in resource limited settings. The finding of our study is in agreement with Petrie et al. (2018) but dissimilar to Gillies et al. (2007), Giorda et al. (2007) and Rahman et al., (2011) although Lima et al., (2007) showed higher TC levels and higher HDL-C levels among controls than diabetic patients.

Our study also noted the absence of abnormal LDL-C levels in the control group suggesting that LDL-C may not be the best gauge for primary dyslipidemia in healthy patients and may not predict future cardiovascular disease risk in apparently healthy patients with family history of hypertension, diabetes and obesity. Our report is similar to Lima et al. (2007) and Wang et al. (2016) but dissimilar to Abdul-Ghani et al., (2017).

The interplay between traditional and non-traditional risk factors for T2DM and hypertension including dyslipidemia, obesity, hyperglycemia, hyperhomocysteinemia and low grade inflammation observed in our study are known contributors of CVD risk. Our study did not capture the presence or absence of macrovascular and microvascular complications, genetic predisposition or insulin resistance among the participants. As a result, we cannot completely rule out the effect of the unmeasured variables and duration of diabetes on the biochemical markers and anthropometric indices of the participants.

Some of the limitations of our study include its cross-sectional design and small sample size due to insufficient resources. As a result, our findings on the association between type 2 diabetes and
The inability of our study participants to undergo electrocardiography and some radiological procedures may also result in bias of some reported findings.

The strengths of our study include its ability to assay dependent and independent variables for cardiovascular risk among the participants and ensuring the sanctity of collected data through the use of trained clinical assistants and interviewers.

CONCLUSION
The assessment of some accessible cardio metabolic markers and anthropometric indices may provide easy tools for prediction and assessment of cardiovascular disease in patients with T2DM especially in resource poor settings

COMPETING INTEREST
Authors declare that they have no competing interests.

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