



Printed in Nigeria

TITLE: COMPARATIVE ANALYSIS OF HANDGRIP STRENGTH AND URINE C-PEPTIDE CREATININE RATIO AS BIOMARKERS FOR GLUCOSE REGULATION IN YOUNG ADULT FEMALES IN THE UNIVERSITY OF ILORIN: A CROSS-SECTIONAL STUDY.

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MS/No BKM/2022/012© 2022 Society for Experimental Biology of Nigeria

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ABSTRACT

Handgrip strength (HGS) is a robust biomarker predicting future disability, metabolic syndrome, and diabetes. Urinary C-peptide creatinine ratio (UCPCR) emerges as a novel, non-invasive tool under exploration for assessing beta cell function and glucose regulation. Despite their significance in gauging muscle strength, mass, and overall metabolic function, gaps remain in understanding the full extent of handgrip strength and UCPCR's efficiency. This study aimed to identify a better biomarker for glucose regulation by studying the relationship between handgrip strength, urine c-peptide creatinine ratio, and blood glucose levels in adult females. Using ELISA, the study measured handgrip strength, blood glucose levels, and urine samples. Social demographic data was obtained through standard questionnaires, and statistical analysis was done using IBM 25 SPSS software with Pearson's correlation, linear regression at $P < 0.05$, and T-test. The study found that handgrip strength (HGS) had a slight non-significant positive correlation with fasting blood sugar (FBS) ($P=0.386$). However, there was a significant correlation between HGS and 2 hours postprandial glucose (2HPG) in both dominant and non-dominant hands ($P=0.045$ vs $P=0.017$). Additionally, the study found that handgrip strength in the dominant hand was significantly stronger than that in the non-dominant hand ($P=0.001$). On the other hand, the urinary C-peptide creatinine ratio (UCPCR) had no significant correlations with FBS and 2HPG. Handgrip strength measurements provide an indicative approach for glucose regulation and are a better biomarker for blood glucose regulation than UCPCR.

Keywords: Handgrip strength; UCPCR; fasting blood sugar; 2 hours postprandial; glucose regulation.

INTRODUCTION

Glucose is a critical component of our daily existence as it is the body's primary sugar and energy source. The body's digestive system breaks down carbohydrates or sugar into glucose carried to the bloodstream (Salomon *et al.*, 2019). Insulin helps in glucose uptake into cells for either storage or energy utilisation. A fasting blood glucose level within the range of 80 and 90 mg/dl is considered normal after eight to fifteen hours of the last meal (Hulman *et al.*, 2013). After eating, postprandial

blood glucose levels typically increase to 120-140 mg/dl, but the body's feedback system brings the glucose levels back to normal within two hours (Nakrani *et al.*, 2020). When there are dysregulations in the homeostatic mechanisms, hyperglycemia may occur, causing persistently elevated blood sugar levels and leading to life-threatening complications (Higuera *et al.*, 2018; Eberle, 2020). Therefore, it is essential to maintain blood glucose levels in a specific range for the optimal functioning of the system.

Blood glucose measurements are essential to determine blood glucose levels. The most popular and widely accepted tests include fasting blood sugar, oral glucose tolerance, 2-hour postprandial, random blood glucose, and glycated haemoglobin (HbA1c). Many young adults avoid invasive diagnostic tests, contributing to the prevalence of metabolic disorders in this age group, such as diabetes mellitus (Sebastian *et al.*, 2023). High glucose levels in young adults can cause cognitive impairment and other diseases later in life (Nakrani *et al.*, 2020). Early detection and treatment of hyperglycemia can help manage and prevent metabolic disorders, including hypertension and cardiovascular risks (Eberle, 2020). The number of people affected by metabolic diseases like diabetes mellitus is expected to rise to 1.3 billion by 2050 from 529 million in 2021 (Ong *et al.*, 2023).

The skeletal muscles play an essential role in regulating glucose levels in the body, and researchers have recently discovered that measuring handgrip strength is an accurate way to assess the muscles' quality, mass, and strength (Lee *et al.*, 2022). Handgrip strength is a reliable indicator of future disability, metabolic syndrome, and diabetes mellitus, and a decrease in handgrip strength has been linked to health risks such as hypertension and cardiovascular disease (Li *et al.*, 2018). Previous studies have established that handgrip strength is associated with glycemic control and may also be a risk factor for type 2 diabetes mellitus, according to a recent meta-analysis of observational cohort studies (Cenitus *et al.*, 2005; Van der Kooi *et al.*, 2015).

On the other hand, UCPCR is a newly explored non-invasive outpatient marker for beta cell function and glucose regulation. Endocrinologists face difficulties categorising diabetes, especially in young patients, and UCPCR has proven to be very useful in distinguishing different variants of diabetes mellitus. Unlike the traditional clinical symptoms and laboratory testing methods, UCPCR offers a simple, rapid, efficient, and convenient way of testing. It outshines the 24-hour urine and blood C-peptide tests, making it a promising diagnostic tool (Wang *et al.*, 2019; Reintar *et al.*, 2023).

Urinary C-peptide and insulin are secreted in equal amounts. However, unlike insulin, the kidney filters urinary C-peptide, resulting in 5%

of it being excreted intact in the urine. This allows for a better assessment of the body's beta cell function than insulin (Oram *et al.*, 2013). A recent study found that UCPCR is a good predictor of prediabetes, with a biannual follow-up (Reintar *et al.*, 2023).

Handgrip strength and UCPCR are valuable markers for assessing muscle strength, mass, and overall metabolic function (Lee *et al.*, 2022; Wang *et al.*, 2019; Thomas *et al.*, 2012). However, there is still limited knowledge about the efficiency of these markers, and a direct comparison between HGS and UCPCR as biomarkers for glucose regulation is currently unavailable.

MATERIALS AND METHODS

This study was conducted at the University of Ilorin in the ancient city of Ilorin, about 500 kilometres from Abuja, the Federal capital of Nigeria. Ethical approval was collected from the University of Ilorin Teaching Hospital Research Ethics Committee, Ilorin Kwara state, with the reference number UITH/CAT/189/VOL.21^B/486. Informed consent was also obtained from the research subjects.

Study Design and Population

Human subjects were used and comprised female undergraduate students. The issues filled out questionnaires to determine their medical and sociodemographic history. The investigation was conducted in the human physiology lab at the College of Health Sciences at the University of Ilorin. The subjects were under no stressful or extreme conditions during the experiment. The research was a cross-sectional study design where sociodemographic information, urine and blood samples of female undergraduate students were taken. Urine samples for UCPCR were collected in boric acid bottles before and 120 minutes after a large meal. Fasting and postprandial blood sugar measurements were made using Accucheck and on-call glucometers. Participants who had eaten within 8-12 hours prior to the experiment were excluded as they needed to fast before providing urine and blood samples. Participants who had chronic conditions such as cardiovascular disease, kidney disease, and sarcopenia that could have influenced their handgrip strength or glucose metabolism were excluded from the study.

Individuals with renal and hepatic impairment were also excluded, which may have affected the UCPCR results. Participants who had missing or incomplete data on handgrip strength or fasting blood glucose measurement were excluded from the study.

Measurements

Handgrip Strength

Grip strength was measured three times on both hands with a Camry model EH101 electronic digital hand dynamometer in kilogram (kg). The subjects were seated upright with their elbow bent at a 90° angle. The subjects were asked to squeeze the dynamometer handle with a maximum voluntary contraction for 5 seconds only; this was repeated with a 30-second interval between readings (Huang *et al.*, 2022). Body mass index (BMI)-normalised grip strength, known as relative handgrip strength (RGS), an indicator of muscle quality that accounts for body weight and height, was calculated as the sum of the maximum grip strength for both hands of each subject (absolute grip strength) divided by the BMI (Lee *et al.*, 2016). BMI was calculated by dividing the body weight in kilograms by the square height (kg/m^2).

Weight and Height

The body weight of each subject was measured using a weighing scale calibrated in kilograms (kg). Subjects were obliged to remove heavy clothing and shoes before taking weight measurements (Ross and Wing, 2016). The subjects maintained an upright position with hands by their sides while on the weighing scale. The size and height of each subject were measured in centimetres (cm) using a stadiometer. While standing in an upright position with their heads facing forward, the subjects' peak heights were measured and recorded. (Standard Operating Procedure, Use of Height and Weight Scales (SOP-UHWS-02; 2019)

Blood Glucose Levels

Before the testing day, the subjects fasted for about 8-12hrs. Fasting blood glucose levels were measured using sterile lancets and glucometers and recorded in mg/dl. Preparation of the site on the thumb was done using sterile alcohol swabs, which were followed by the sterile lancet needle

and the use of glucometer strips. Postprandial blood glucose levels were measured two hours after a large meal using sterile lancets and glucometers. Preparation of the site on the thumb was done using sterile alcohol swabs, which were followed by the sterile lancet needle and the use of glucometer strips. The glucometer reading of postprandial blood glucose was recorded in mg/dl (Pickering and Marsden, 2014).

Biochemical procedures

All biochemical assays were done at Bridge Bio-Tech Laboratory GRA in Ilorin, Nigeria.

Urinary c-peptide Assay

The Calbiotech C-peptide ELISA kit was used for the biochemical assay of C-peptides in urine. Calbiotech Kit with catalogue No: CP441S was sourced from 1935 Cordell CT, EI Cajon, CA 92020 USA. Urinary C-peptide was assayed as described by the manufacturer.

Reagents were prepared and mixed at room temp. Streptavidin-coated microwells were arranged, and standard/testing sample wells were prepared with urine sample dilution added. C-peptide conjugate reagent was added to the wells, then the microwells were closed and incubated. After removing excess liquid and drying the wells, washing buffer was added and removed multiple times. TMB (3, 3', 5, 5'-Tetramethylbenzidine) was added and incubated, leading to a colour change. A stop solution was added, changing the colour from blue to yellow. The intensity of the colour was measured using an ELISA micro-plate reader.

Calculations for Urinary C-Peptide

A standard curve was used to determine the amount of the unknown sample. The standard curve was generated by plotting the average O.D (450nm) for each C-peptide common point (vertical x-axis) versus the C-peptide average concentrations (horizontal y-axis) on a linear graph paper.

The mean O.D. value for each standard and sample was calculated. All the O.D. values were subtracted by the mean value of the blank well before the result was interpreted. The standard curve was then constructed.

The amount of C-peptide in each sample was determined by locating the O.D value on the Y-axis and extending a horizontal line to the

standard curve. At the point of intersection, a vertical line was drawn to the axis, and the corresponding concentration was read in ng/ml.

Urinary Creatinine Assay

A Fortress ELISA kit, with product code No: BXC0111, was used for the biochemical assay of creatinine in urine. The kit was sourced from Unit 2C, Antrim Technology Park, Antrim, BT41 1QS, United Kingdom. The assay for urinary creatinine was carried out as described by the manufacturer. Urine samples were diluted 1+49 with distilled water. Before the assay, all the reagents were at room temperature. Equal quantities of NaOH and Picric acid solution were mixed. Following this mixture, 50 microliters of the urine sample were added to the micro-plate wells and the standard. 100 microliters of the working reagent were added to the wells which contained the standard as well as the sample. The solutions were mixed in the wells, and a stop solution was added. The mixture was then inserted into the automated analyzer and read at an absorbance wavelength of 492nm.

Calculations for Urinary Creatinine

Urinary creatinine was calculated by: change in the sample divided by change in standard multiplied by standard concentration in ($\mu\text{mol/l}$) multiplied by 0.05 in mmol/l.

$\text{Creatinine} = \text{change sample/change standard} \times 0.05$

Creatinine clearance is measured by dividing mg creatinine/dl urine multiplied by ml urine 24 hours by mg creatinine/dl serum multiplied by 1440 in ml/min.

UCPCR Calculation

After a large meal, two urine sample bottles were labelled A (for 0 hours before the meal) and B (for 120 minutes after the meal) for each subject. Before a large meal, UCPCR calculations were made using C-peptide and creatinine concentrations in urine 120 minutes before and after the large meal as the ratio of urinary c-peptide (nmol/l)/creatinine (mmol/l) (Oram *et al.*, 2013).

Statistical Analysis

IBM SPSS (version 25.0) was used for data analysis, and six times the average grip strength value was chosen for additional examination. The baseline parameters of the study population are

expressed as the mean $\pm$ standard deviation (SD). The CAMRY dynamometer's measurement bias and dependability were evaluated to ascertain accuracy and agreement with the Jamar device. P less than 0.05* (95% confidence interval) was considered significant. In a bivariate study, the data were displayed as tables and box plots demonstrating the regression and correlation between the variables. The mean differences in HGS between the dominant and non-dominant hands were calculated using a student t-test, while to examine the correlations between HGS and fasting blood glucose levels (FBS) and 2 hours postprandial glucose levels (2HPG), correlation analysis was performed using Pearson's correlation coefficient. Bivariate linear regression models were developed to quantify the extent to which changes in HGS impact variations in blood glucose levels.

Furthermore, the relationship between UCPCR and blood glucose levels was investigated. In both the fasting and 2-hour postprandial settings, low Pearson correlation coefficients suggest that the correlation studies showed little to no correlations. Using bivariate linear regression models, which additionally assessed the contribution of changes in UCPCR to variations in blood glucose levels, the non-significant nature of these correlations was brought to light. These meticulous statistical methods provided a strong foundation for drawing essential inferences from our findings and illuminating the intricate connections between muscle strength and glucose metabolism.

RESULTS

Table 1 demonstrates the difference between the dominant (right) and non-dominant (left) hands based on handgrip strength analysis of 21 female undergraduate students. There was a significant difference in the mean strength of both hands ($P = 0.001$). The distribution of the strength values was also represented with the help of a box plot (Fig 1), which further highlighted the observed disparity.

The statistical study conducted on HGS in 21 female undergraduate students shows that the dominant (right) and non-dominant (left) hands have significantly different mean handgrip strengths ($P = 0.001$). This highlights the right hand's dominance. The interquartile ranges (IQR)

of the dominant hand showed different values of 18.70 (the 25th percentile), 20.50 (the 50th percentile), and 23.90 (the 75th percentile). In contrast, the non-dominant hand had IQR values of 15.60, 18.60, and 21.20 at the corresponding percentiles. Descriptive statistics further revealed that the median values were 18.60 and 20.50, the maximum values were 29.80 (dominant) and 25.80 (non-dominant), and the minimum values were 11.50 (dominant) and 13.80 (non-dominant). To gain insight into deviations from the mean, the dominant hand's mean HGS was 21.07 ± 4.98 , while the non-dominant hand's was 18.70 ± 3.77 .

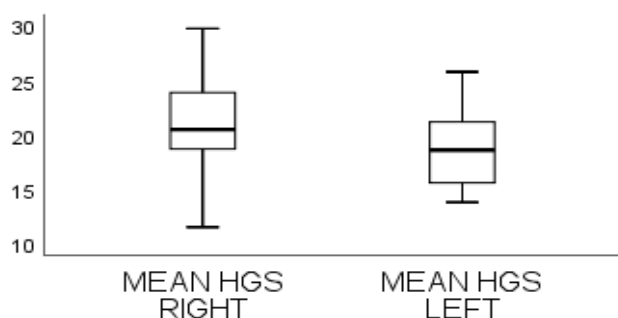


Figure 1: Box Plot compares Mean HGS of dominant (Right) and non-dominant hand (Left) in females.

The dominant hand was significantly stronger ($P=0.001$) than the non-dominant hand. The box plot shows the median, mean, minimum, maximum and interquartile range, highlighted in table 1.

Figures 2 and 3 provide the correlations between urine C-peptide creatinine ratios (UCPCR), mean handgrip strength (HGS) in the dominant and non-dominant hands, 2-hour postprandial glucose, and fasting blood sugar (FBS). A slight positive correlation ($r=0.315$) was observed for the dominant hand between mean HGS and FBS.

However, this association lacked statistical significance ($P=0.386$), and only 9% of HGS changes were attributed to FBS.

Figure 2 shows the correlations between mean handgrip strength in dominant and non-dominant hands and fasting blood sugar (FBS) and 2-hour postprandial glucose levels. A slight positive correlation exists between FBS and mean handgrip strength for the dominant hand, and a moderately positive association exists between dominant hand handgrip strength and 2-hour postprandial glucose.

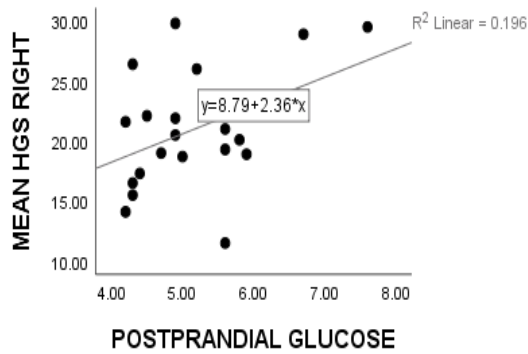
On the other hand, a statistically significant ($P=0.045$) moderately positive association ($r=0.442$) was found between dominant hand HGS and 2-hour postprandial glucose. In this case, 19.6% of HGS changes were linked to postprandial glucose. Similar patterns were observed for the non-dominant hand, with a more significant association ($r=0.515$, $P=0.017$) between 2 hours of postprandial glucose and HGS and less positive correlations ($r=0.199$, $P=0.164$) between FBS and HGS.

DISCUSSION

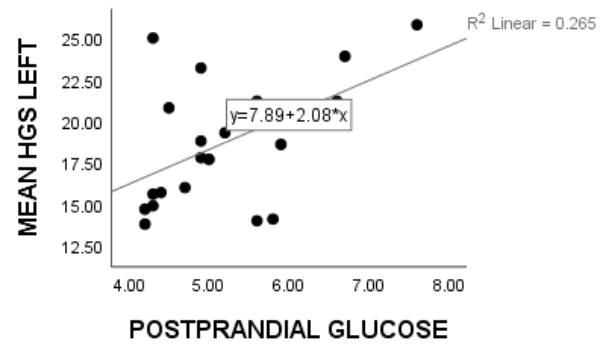
This study investigated the correlation between HGS and UCPCR in healthy young adult female students (aged 18-30) from the University of Ilorin College School campus. The levels of handgrip strength in both the dominant and non-dominant hands were found to be significantly and positively correlated with 2HPG. This could be a basis for determining glucose regulation rather than relying solely on the popular blood glucose diagnostic tests. This study found that UCPCR was not correlated with fasting and postprandial blood glucose levels, which could provide further insight for future research.

Table 1: Descriptive Statistics of Dominant and Non-dominant Handgrip Strength.

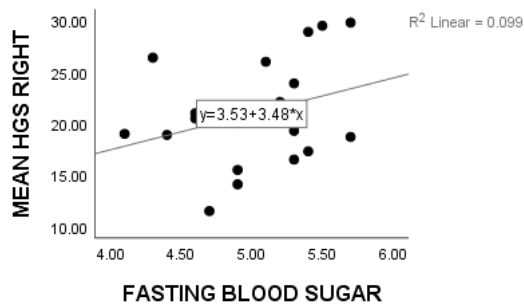
Variable	Mean $\pm$ sd	Median	Minimum	Maximum	Interquartile ranges			P-value
Hgs					25	50	75	
Right (dominant)	21.07 ± 4.98	20.50	11.50	29.80	18.70	20.50	23.90	.001
Left (non-dominant)	18.70 ± 3.77	18.60	13.80	25.80	15.60	18.60	21.20	



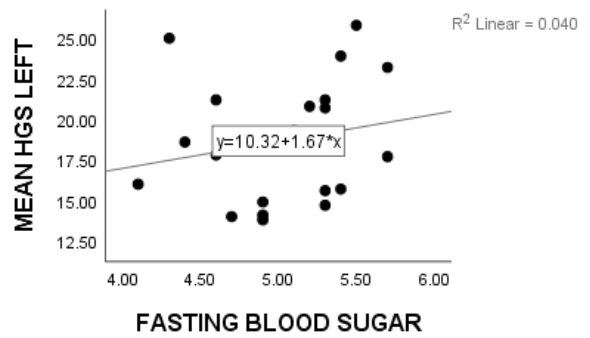
a.



b.

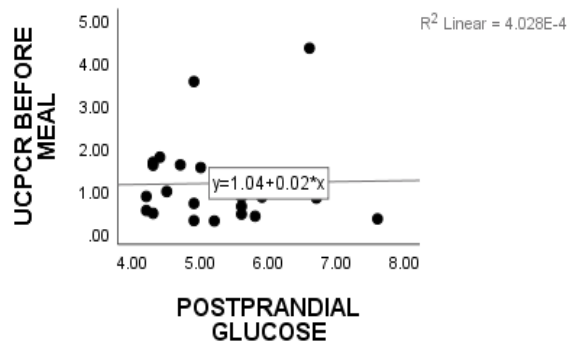


c.

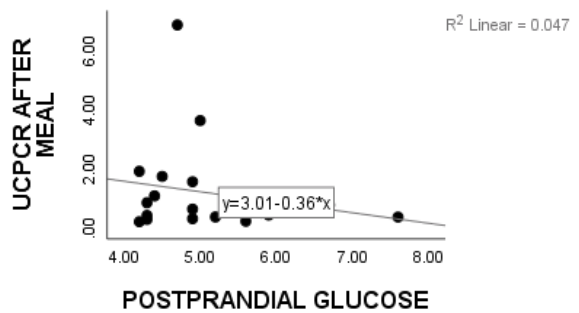


d.

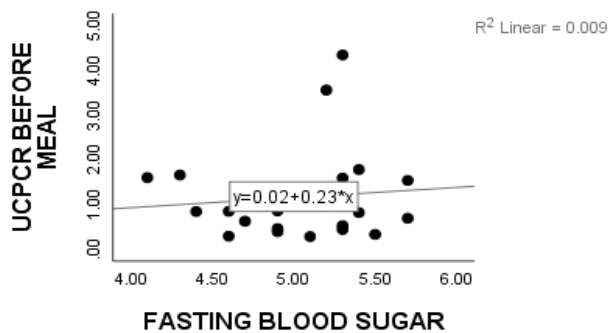
Figure 2: Scatter plot displaying the relationship between handgrip strength and blood glucose levels



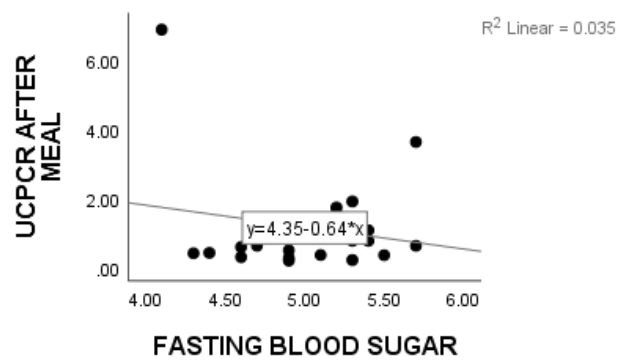
a.



b.



c.



d.

Figure 3: Scatter plot depicting the relationship between urine c-peptide creatinine ratios (UCPCR) and blood glucose levels. The correlations between UCPCR with fasting blood sugar (FBS) and 2-hour postprandial glucose levels are shown. There are weak correlations at various time intervals, with each correlation below 5% and lacking statistical significance ($P > 0.05$).

Comparison between Dominant and Non-Dominant Handgrip Strength

The study found that healthy females had significantly stronger dominant HGS than non-dominant HGS. The difference in HGS between the dominant and non-dominant hand is likely due to the frequent use of a particular limb, which can lead to greater muscular strength and endurance (Awotidebe *et al.*, 2021). This is because activating more muscle groups and motor units in the dominant limb results in greater force during contraction, leading to greater muscle strength. Also, the synergistic action between extensor and flexor muscles and the interactions of muscle groups is essential in grip power (Fuglevand, 2011).

Previous research, Incel *et al.*, (2002) has confirmed that right-handed individuals' dominant hand is significantly stronger. However, in contrast, this study compared right-handed individuals' grip strength with that of left-handed individuals. It found that left-handed individuals had no significant increase in power compared to their non-dominant hand. Another study found that handedness and laterality significantly influenced handgrip strength, with right handgrip strength being more significant than left handgrip strength in healthy males and females (Adedoyin *et al.*, 2009). It is essential to appropriately define handedness in studies involving handgrip strength, as it has been shown to influence normative values (Clerke and Clerke, 2001). In a recent study exploring the relationship between handgrip strength and upper limb anthropometric characteristics, dominant HGS was stronger than non-dominant HGS in males and female (Awotidebe *et al.*, 2021).

A significant correlation was observed between HGS and 2HPG. Still, no substantial correlation was found between HGS and FBS in both dominant and non-dominant hands. The study categorised HGS < 18kg as low and >18kg as usual. Normal FBS levels were defined as 3.9-5.9mmol/l, and 2HPG levels < 7.8 mmol/l. Measured HGS values were in the normal range, averaging 21.07kg and 18.70kg for dominant and non-dominant hands, respectively. FBS and 2HPG recorded mean values of 5.0 mmol/l and 5.2 mmol/l, respectively.

Prior research, such as Stenholm *et al.*, 2010, highlighted that catabolic biomarkers like CRP,

IL-6, IL-1RA, and TNF- α elevate oxidative stress, diminishing muscle mass and strength in older people. However, our study's young adult participants, free from diabetes mellitus, did not exhibit significant correlations between FBS and HGS.

Conversely, other studies (Howard *et al.*, 2007; Manini *et al.*, 2012; Leite *et al.*, 2012) have indicated a negative correlation between FBS and HGS, suggesting that higher FBS levels correspond to decreased handgrip strength. Liang *et al.* (2020) also reported an inverse correlation between FBS and HGS in normoglycemic women, reflecting a dose-response relationship. The differing age groups in these studies compared to ours likely account for the variance in findings.

Our study observed significant correlations between 2HPG and HGS in both hands, with higher significance in the non-dominant hand ($P=0.045$ and 0.017 for dominant and non-dominant hands, respectively). A simple linear regression model indicated that changes in HGS could be attributed to approximately 19% and 26% of the changes in postprandial glucose for the dominant and non-dominant hands, respectively ($R^2 = 0.196$ vs 0.265). This correlation could be attributed to glucose uptake stimulated by skeletal muscle contractions, enhancing GLUT4 vesicle translocation to the plasma membrane. Furthermore, exercise improves blood flow, augmenting skeletal muscle's glucose absorption capacity (Merz *et al.*, 2010).

Increased metabolic activity in skeletal muscle cells generates energy for muscular contractions through glycolytic, citric acid cycle, and oxidative phosphorylation pathways (Baker *et al.*, 2010). Briet and Jeejeebhov (2001) showed that malnutrition can impede mitochondrial complex activity in the oxidative phosphorylation pathway, thereby diminishing muscle energy generation and strength levels. Based on findings from our study, proper nutritional intake could significantly enhance HGS in young women. Conversely, persistent blood glucose levels, typical in hyperglycemic, prediabetic, and diabetic individuals, are associated with reduced HGS in older adults (Bentes *et al.*, 2017; Karvonen-Gutierrez *et al.*, 2018; Ma *et al.*, 2023). Diabetes exacerbates muscle strength loss and insulin resistance, marked by accelerated skeletal muscle

mass loss and increased intramuscular fat infiltration. Advanced Glycation End Products (AGEs) also contribute to muscle damage, reducing flexibility and affecting handgrip strength and agility in older individuals. The lower physical performance often linked with diabetes is further compounded by reduced exercise frequency in diabetic individuals compared to non-diabetics.

There were no significant correlations between FBS and 2HPG with UCPCR. In line with the findings of McDonald *et al.* (2009), this study utilised second-void fasting urine samples, which are less variable than first-void urine samples for UCPCR measurements in non-diabetic adults. Overnight urine samples, accumulating C-peptide in response to the previous evening's meal (Oram *et al.*, 2013), offer a valuable metric for assessing C-peptide secretion.

The Mixed-Meal Tolerance Test (MMTT) is considered the gold standard for measuring endogenous insulin secretion and has demonstrated a strong correlation with the UCPCR test, a sensitive and specific indicator for absolute insulin deficiency (Palmer *et al.*, 2004). UCPCR, with its ease of access, stability at room temperature for up to three days, and potential for universal non-invasive testing, holds promise for older, more vulnerable populations. However, its application and efficacy in younger, healthier demographics still need to be understood.

In individuals without diabetes and free of chronic renal disease, fasting the second morning, UCPCR has been proposed to assess insulin resistance (Oram *et al.*, 2013), significantly impacting glucose regulatory mechanisms due to insulin's crucial role in glucose uptake (Merz and Thurmond, 2010). The lack of significant correlations between UCPCR and FBS in this study might be attributed to the participants' normoglycemic status, encompassing both fasting and postprandial blood glucose within the standard range. This group consisted predominantly of young adult students without a history of diabetes, potentially explaining the absence of notable correlations between FBS levels and UCPCR.

While UCPCR has effectively distinguished various forms of diabetes mellitus (Besser *et al.*, 2011), its utility in conducting diagnostic tests for glucose regulation in healthy individuals appears

limited. This study suggests that UCPCR, although invaluable in specific clinical contexts, may not be as effective in gauging glucose regulation in a young, healthy population without diabetes.

CONCLUSION

The present research sheds new light on the intricate relationship between blood glucose levels, handgrip strength, and UCPCR among young adult female students. Findings revealed a positive correlation between handgrip strength and 2-hour postprandial glucose levels. However, no correlation was found between fasting blood sugar and handgrip strength. Additionally, there was no correlation between UCPCR and blood glucose levels in healthy females.

RECOMMENDATION

We suggest that, compared to UCPCR, handgrip strength may be a better indicator of glucose control. However, more diverse and extensive cohorts need to be studied to confirm and expand on these initial findings. If future research confirms these findings, handgrip strength assessment techniques could be a valuable and accessible tool for glucose monitoring and assessment in various groups, particularly in Nigeria. The clinical implications of such applications could be significant in transforming the field of glucose monitoring and assessment.

ACKNOWLEDGEMENTS

We thank the Department of Physiology College of Health Sciences, University of Ilorin, for the immense support and grounds provided for completing the study.

Conflicts of Interest

None declared.

Abbreviations

FBS: Fasting Blood Sugar

HGS: Handgrip strength

2HPG: 2-hour postprandial glucose

UCPCR: Urine C-Peptide Creatinine Ratio

MMTT: Mixed Meal Tolerance Test

TNF- α : Tumor Necrosis Factor Alpha

IL-6: Interleukin 6

CRP: C - reactive protein

IL-1RA: Interleukin 1 receptor antagonist

REFERENCES

- Adedoyin, R.A., Ogundapo, F.A., Mbada, C.E., Adekanla, B.A., Johnson, O.E., Onigbinde, T.A., Emechete, A.A. (2009) Reference values for handgrip strength among healthy adults in Nigeria. *Hong Kong Physiother J* 27(1):21-29.
- Awotidebe, T.O., Odetunde, M.O., Okonji, M.A., Odunlade, A.J., Fasakin, O.M., Olawoye, A.A., Ayesoro, B.P., Adedoyin, R.A., Kolawole, B.A. (2021) Relationships between Hand Grip Strength, Upper Limb Anthropometric Characteristics and Hand Disability in Middle-Aged and Older Adults with Type-2 Diabetes Mellitus. *Int J Diabetes Clin Res*. 8:135.
- Baker, J.S., McCormick, M.C. and Robergs, R.A. (2010) Interaction among skeletal muscle metabolic energy systems during intense exercise. *J Nutr Metab*. 2010.
- Banday, M.Z., Sameer, A.S., Nissar, S. (2020) Pathophysiology of diabetes. An overview. *Avicenna J Med* 10(04):174-188.
- Bentes, C.M., Costa, P.B., Resende, M., Miranda, H.L., Silva, C.M., Netto, C.C., Marinheiro, L.P. (2017) Association between muscle function and body composition, vitamin D status, and blood glucose in postmenopausal women with type 2 diabetes. *Diabetes Metab Syndr* 11:S679-S684.
- Besser, R.E., Ludvigsson, J., Jones, A.G., McDonald, T.J., Shields, B.M., Knight, B.A., Hattersley, A.T. (2011) The urine C-peptide creatinine ratio is a noninvasive alternative to the mixed-meal tolerance test in children and adults with type 1 diabetes. *Diabetes Care* 34(3):607-609.
- Briet, F. and Jeejeebhoy, K.N. (2001) Effect of hypoenergetic feeding and refeeding on muscle and mononuclear cell activities of mitochondrial complexes I–IV in enterally fed rats. *Am J Clin Nutr* 73(5):975-983.
- Cetinus, E., Buyukbese, M.A., Uzel, M., Ekerbicer, H., Karaoguz, A. (2005) Hand grip strength in patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract*. 70(3):278-286.
- Clerke, A. and Clerke, J. A (2001) literature review of the effect of handedness on isometric grip strength differences of the left and right hands. *Am J Occup Ther* 55(2):206-211.
- Eberle, R. (2020) The relationship between glucose levels and physical activity. Available at : scholarworks.uark.edu
- Fuglevand, A.J. (2011) Mechanical properties and neural control of human hand motor units. *J Physiol*. 589(23):5595-5602.
- Higuera, V. (2018) Insulin Resistance. Causes, Symptoms, Diagnosis, and Consequences | Everyday Health. [online] EverydayHealth.com. Available at: <https://www.everydayhealth.com/type-2-diabetes/insulin-resistance-causes-symptomsdiagnosis-consequences/>
- Howard, C., Ferrucci, L., Sun, K., Fried, L.P., Walston, J., Varadhan, R., Guralnik, J.M., Semba, R.D. (2007) Oxidative protein damage is associated with poor grip strength among older women living in the community. *J Appl Physiol* 103(1):17-20.
- Huang, L., Liu, Y., Lin, T., Hou, L., Song, Q., Ge, N., Yue, J. (2022) Reliability and validity of two hand dynamometers when used by community-dwelling adults aged over 50 years. *BMC Geriatr* 22(1):1-8.
- Hulmán, A., Færch, K., Vistisen, D., Karsai, J., Nyári, T.A., Tabák, A.G., Brunner, E.J., Kivimäki, M., Witte, D.R., (2013). Effect of time of day and fasting duration on measures of glycaemia: analysis from the Whitehall II Study. *Diabetologia* 56, 294–297.. <https://doi.org/10.1007/s00125-012-2770-3>
- Incel, N.A., Ceceli, E., Durukan, P.B., Erdem, H.R., Yorgancioglu, Z.R. (2002) Grip strength: effect of hand dominance. *Singapore Med J* 43(5):234-237.
- Karvonen-Gutierrez, C.A., Peng, Q., Peterson, M., Duchowny, K., Nan, B., Harlow, S. (2018) Low grip strength predicts incident diabetes among mid-life women. The Michigan Study of Women's Health Across the Nation. *Age Ageing*. 47(5):685-691.
- Lee, S.B., Moon, J.E. and Kim, J.K. (2022) Association of Handgrip Strength with Diabetes Mellitus in Korean Adults According to Sex. *Diagnostics* 12(8):1874.
- Lee, W.J., Peng, L.N., Chiou, S.T., Chen, L.K. (2016) Relative handgrip strength is a simple indicator of cardiometabolic risk among middle-aged and older people: a nationwide

- population-based study in Taiwan. *PLoS One* 11(8):e0160876.
- Leite, L.E.D.A., Resende, T.D.L., Nogueira, G.M., Cruz, I.B.M., Schneider, R.H., Gottlieb, M.G.V. (2012) Envelhecimento, estresse oxidativo e sarcopenia. uma abordagem sistêmica. *Rev Bras Geriatr Gerontol* 15:365-380.
- Li, S., Zhang, R., Pan, G., Zheng, L., Li, C. (2018) Handgrip strength is associated with insulin resistance and glucose metabolism in adolescents: evidence from National Health and Nutrition Examination Survey 2011 to 2014. *Pediatr Diabetes* 19(3):375-380.
- Liang, X., Jiang, C.Q., Zhang, W.S., Zhu, F., Jin, Y.L., Cheng, K.K., Lam, T.H., Xu, L. (2020) Glycaemia and hand grip strength in ageing people. Guangzhou biobank cohort study. *BMC Geriatr* 20:1-10.
- Ma, G.C., Zou, L.L., Dai, W., Wang, Z.Z., Cao, Y.H. (2023) The association between glucose fluctuations with sarcopenia in elderly patients with type 2 diabetes mellitus. *Eur Rev Med Pharmacol Sci* 27(5):2
- Manini, T.M. and Clark, B.C. (2012) Dynapenia and aging: an update. *J Gerontol A Biol Sci Med Sci* 67(1):28-40.
- McDonald, T.J., Knight, B.A., Shields, B.M., Bowman, P., Salzmann, M.B., Hattersley, A.T. (2009) Stability and reproducibility of a single-sample urinary C-peptide/creatinine ratio and its correlation with 24-h urinary C-peptide. *Clin Chem* 55(11):2035-2039.
- Merz, K.E. and Thurmond, D.C. (2010) Role of skeletal muscle in insulin resistance and glucose uptake. *Compr Physiol* 10(3):785-809.
- Nakrani, M.N., Wineland, R.H. and Anjum, F. (2020) Journal of Physiology, glucose metabolism.
- Ong, K.L., Stafford, L.K., Mclaughlin, S.A., Boyko, E.J., Vollset, S.E., Smith, A.E. *et al.*, (2023) Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet* 402, 203–234.. [https://doi.org/10.1016/s0140-6736\(23\)01301-6](https://doi.org/10.1016/s0140-6736(23)01301-6)
- Oram, R.A., Rawlingson, A., Shields, B.M., Bingham, C., Besser, R.E.J., McDonald, T.J., Knight, B., Hattersley, A.T. (2013) Urine C-peptide creatinine ratio can be used to assess insulin resistance and insulin production in people without diabetes: an observational study. *BMJ Open* 3(12):e003193.
- Palmer, J.P., Fleming, G.A., Greenbaum, C.J., Herold, K.C., Jansa, L.D., Kolb, H., Lachin, J.M., Polonsky, K.S., Pozzilli, P., Skyler, J.S., Steffes, M.W. (2004) C-peptide is the appropriate outcome measure for type 1 diabetes clinical trials to preserve β -cell function: report of an ADA workshop, 21–22 October 2001. *Diabetes* 53(1): 250-264.
- Pickering, D. and Marsden, J. (2014) How to measure blood glucose. *Community Eye Health*.
- Reintar, S., Pöchlacker, M., Obermayer, A., Eberhard, K., Zirlik, A., Verheyen, N., von Lewinski, D., Scherr, D., Hutz, B., Haudum, C.W., Pieber, T.R. (2023) Urinary C-Peptide to Creatinine Ratio (UCPCR) as Indicator for Metabolic Risk in Apparently Healthy Adults—A BioPersMed Cohort Study. *Nutrients* 15(9):2073.
- Ross, K. M., & Wing, R. R. (2016). Concordance of in-home ‘smart’ scale measurement with body weight measured in-person. *Obesity Science & Practice*, 2(2), 224-228. <https://doi.org/10.1002/osp4.41>
- Salomon, S. (2019) Speaking Diabetes. A Glossary of Formal and Informal Terms Used to Describe Tests, Treatment, Patients, and More.
- Sebastian, M.J., Khan, S.K., Pappachan, J.M., Jeeyavudeen, M.S. (2023) Diabetes and cognitive function. An evidence-based current perspective. *World J Diabetes* 14(2):92.
- Stenholm, S., Maggio, M., Lauretani, F., Bandinelli, S., Ceda, G.P., Di Iorio, A., Giallauria, F., Guralnik, J.M, Ferrucci, L. (2010) Anabolic and catabolic biomarkers as predictors of muscle strength decline. the InCHIANTI study. *Rejuvenation Res* 13(1):3-11.
- Thomas, N.J., Shields, B.M., Besser, R.E.J., Jones, A.G., Rawlingson, A., Goodchild, E., Leighton, C., Bowman, P., Shepherd, M., Knight, B., McDonald, T.J. (2012) The impact of gender on urine C-peptide creatinine ratio interpretation. *Ann Clin Biochem* 49(4):363-368.

Van der Kooi, A.L.L., Snijder, M.B., Peters, R.J.G., Van Valkengoed, I.G. (2015) The association of handgrip strength and type 2 diabetes mellitus in six ethnic groups. *An analysis of the HELIUS study*. 10(9).

Wang, Y., Gao, Y., Cai, X., Chen, L., Zhou, L., Ma, Y., Gong, S., Han, X., Ji, L. (2019) Clinical implications of urinary C-peptide creatinine ratio in patients with different types of diabetes. *J Diabetes Res*.