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A Comparative Study of Diabetes Mellitus Using Insulin Resistance Indices of Normal, Pre-Diabetic and Diabetic Human Subjects in Predicting and Management of Diabetes Mellitus

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ABSTRACT: This study assessed insulin resistance in normal and diabetic human subjects using homeostatic model (HOMAIR). Bio-data were used to investigate the association between Insulin resistance and diabetes, and to compare the effect of these pathological conditions on human subjects. Assessment of HOMA-IR, TG/HDL-C ratio, and TyG index which is important to normal, Pre-diabetics and diabetic subjects alongside lipid profile were carried out. One hundred and twenty human subjects comprising forty subjects each for control, pre-diabetics, and diabetics (three sets) matched for age, sex, height, weight, and blood pressure were recruited into the study based upon specified criteria. Twenty each for the three sets of human subjects were males and females respectively. Each sample of blood serum and plasma was analyzed using Randox kits to test for various biochemical parameters. Results showed that, there is a correlation between diabetes and the BMI of subjectsThe BMI of the pre-diabetic and diabetic subjects were also significantly higher than that of the non-diabetic subjects. There is also a correlation between diabetes and BP as the BP increased significantly across the normal, pre-diabetic and diabetic subjects in a similar order.In general, diabetic subjects are at increased risk of assay-based disturbance and electrolyte disturbances.Worthy of note, is the creatinine result which showed values of 86.47±3.43 mmol/l, 111.37±4.33 mmol/l, and 120.13±4.39 mmol/l indicating a marked increase in the value of creatinine as we move progressively to the diabetic group. Majority of the lipid profile (CHOL, TG, and LDL) values of the human subjects increased progressively from the non-diabetic, pre-diabetic to the diabetic group.Compared with the human control, the mean values of the parameters were significantly different ($p<0.05$) from each other with few exceptions an increase in HOMAIR was shown with values of 0.94±0.04, 2.28±0.17, and 3.25±0.44 for the three sets respectively. Conclusively, the assessment of insulin resistance studied using the models proved that insulin resistance can be managed when appropriate lifestyle is adopted.

KEYWORDS: Insulin resistance, Diabetes, Homeostatic model, Electrolyte, Lipid profile, Obesity.

1. INTRODUCTION

Insulin is released from the pancreatic ß-cells postprandially, signaling the fed state and directly stimulating glucose disposal into peripheral insulin target tissues as well as suppressing hepatic glucose output (HGO). Interference with any of these actions of insulin (i.e. impairment of insulin sensitivity at a peripheral or hepatic level) will tend to have a blood glucose elevating effect. At an early stage in the pathophysiological process, this may be compensated for by an increase in ß-cell insulin output which maintains normoglycaemia. When the insulin secretion is no longer sufficient to maintain normoglycaemia, then hyperglycaemia and diabetes develop [1].Insulin resistance is a reduced ability of the hormone insulin to exert its biological effects on target tissues - namely adipose tissue, skeletal muscle and liver. In terms of the blood glucose concentration, it can be defined as a situation where the insulin concentration is inappropriately high for the level of glycaemia [2]. It is important to understand at the outset that insulin

sensitivity is a continuous variable. Thus young, lean, physically fit individuals are likely to be highly insulin sensitive whereas obese subjects with type 2 diabetes will have poor insulin sensitivity [1].

The common form of insulin resistance is associated with high levels of triglyceride (TG), increased waist circumference (visceral adiposity), hypertension, hyperglycaemia and dyslipidaemia involving a decreased serum high density lipoprotein (HDL) cholesterol concentration and a preponderence of small dense low density lipoprotein (LDL) particles [1-2]. A hypercoaguable state is often present, as well as increased inflammatory cytokine levels [3].

These are also all features of the metabolic syndrome, a common condition associated with increased cardiovascular risk and increased risk of diabetes [4]. Although the link between obesity and insulin resistance is well established, insulin resistance may be present in non-obese and non-diabetic individuals along with other components of the metabolic syndrome or polycystic ovarian syndrome (PCOS) [5-6].

Insulin resistance is generally accepted to be a major risk factor in the etiology of type 2 diabetes mellitus [7]. Several risk factors (e.g. obesity, physical inactivity, body fat distribution, age and hyperinsulinemia) may be considered markers of insulin resistance. Insulin resistance is a predictor for the development of Type 2 diabetes mellitus even in individuals with normal glucose tolerance. Therefore, it is important to recognize insulin resistance in the pre-disease stage when therapeutic intervention is likely to be more successful than in manifest disease [8].

Insulin resistance is also associated with the development of the metabolic syndrome [9], which represents a cluster of cardiometabolic risk factors which promote the development of cardiovascular disease and type 2 diabetes [10-11]. The individual components of the metabolic syndrome include hyperglycemia, elevated blood pressure, elevated triglyceride levels, low HDL cholesterol levels, and central obesity [12].

Diabetes is a lifestyle non-communicable disease of mankind considered as one of the most significant global health problems that afflict both young and old in all parts of the world irrespective of their gender (International Diabetes Federation [13]). The disease is a metabolic condition caused by the body's inability to produce or make use of insulin, and it drastically decreases the quality of human life. Nigeria has the highest number of people with diabetes in Africa with 3,921,500 cases reported on a prevalence rate of 4.99% [14]. Type 2 diabetes (T2D) accounts for 95% of all cases reported [14-15].

The causes of T2D are multi-factorial which includes both genetic and environmental elements that affect the β-cell function and insulin sensitivity [16-17].

Aim and Objectives of the Study

Aim: The aim of this study is to propose a new system where normal and diabetic subjects coming to assess Fasting Blood glucose will also assess their insulin resistance level and so, be able to assess their TyG, and TG/HDL cholesterol indices so that they would be able to see if any or which of the indices work better at predicting and monitoring or controlling DM best through a comparative study of these indices.

Objectives: The objectives of the study include to:

(a) Determine the level of variation of these indices in both (normal and diabetic) set of subjects. This would give a clear indication of which index produces a better mode of management and control to subjects.

(b) Investigate the association between Insulin resistance and diabetes, and to compare the effect of these pathological conditions on human subjects.

(c) Investigate the association between the TyG Index, insulin resistance and diabetes, and also compare the effect of its variation on the pathological condition in DM.

(d) Investigate the association between TG/HDL cholesterol ratio, insulin resistance and diabetes, and also

compare the effect of its variation on the pathological condition in DM.

(e) Evaluate dyslipidaemia and hyperinsulinaemia in sampled subjects.

(f) Assess the risk of developing cardiovascular disease (CVD) and other complications of DM with Insulinaemia; to monitor and assist treatment.

(g) Monitor subject progress and prognosis in diabetes.

Significance of the Study

In the assessment of insulin resistance, and management of diabetes,this study intends to make available some scientific information on lipid profile, Glucose, TG/HDL cholesterol index or ratio, TyG index, HOMA-IR index, and renal function statuses of normal and diabetic subjects. Subjects with high TyG index have a high risk of diabetes. Insulin resistance (IR) is associated with an increased risk of hyperglycemia, hypertension, and dyslipidemia, which increases the risk of inflammation, altered coagulation, and atherosclerosis.

Many studies have demonstrated that IR is one of the most important contributing factors to CVD [18-19].Furthermore, given that insulin resistance is an important risk factor for development of type 2 diabetes and incident cardiovascular diseases, identification of subjects with insulin resistance is a strategy for identifying high-risk people for targeted preventive interventions [18,20].

Scope of Study/Delimitation

This research work would be delimited to enrolling normal individuals and diabetic human subjects as well for the purpose of:

a. Investigation of Glucose, Lipid Profile, Renal Function (Sodium, Potassium, Chloride, Bicarbonate, Urea and Creatinine).

b. Assessment of TG/HDL-C ratio, and TyG index which is important to normal and diabetic subjects.

Study Area

This study was carried out from Port Harcourt Teaching Hospital (UPTH), in Obio/Akpor Local Government Area of Rivers State, Nigeria. The study area is located in the Niger Delta region, bordering the Atlantic Ocean. The area lies approximately in latitudes 6°54´N and longitudes 4°53´E (Figure 1).

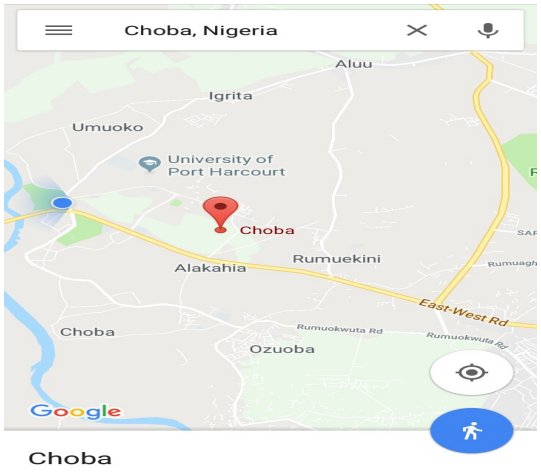

Figure 1: Map of the Study Area (Google)

2. MATERIALS AND METHODS

2.1 Experimental Design

The following approach was employed in grouping the human subjects; the subjects were majorly grouped into two: control GROUP A, and test Groups B and C.

GROUP A: The control group consists of forty (40) normal (non-diabetic) subjects.

GROUP B: The test group consists of 40 pre-diabetic subjects.

GROUP C: The test group consists of 40 diabetic subjects.

Inclusion criteria for human subjects:

a. Subjects aged between thirty six (36) to seventy six (76) years who agreed to participate in the research.

Exclusion criteria for human subjects:

a. Subjects with co-infection with other metabolic disorders.

Study population selection for human subjects:

It consisted of normal and diabetic subjects mainly in the University of Port Harcourt teaching hospital (UPTH).

The entire population size was one hundred and twenty (120) individuals.

Sample size determination for human subjects:

The minimum sample size was calculated employing the formula below [21]:

$N = Z^2 (pq) / e^2$

Where N = minimum sample size,

Z = 1.96 at 95% confidence limits, so that $z^2 = 3.8416$

p = prevalence of increased normal and diabetic subjects' percentage average

q = 1-p

6.80% as the prevalence of increased normal subjects

10.20% as the prevalence of increased diabetic subjects

((6.80 + 10.20)/2)% = (17.00/2)% = 8.50%

8.50% as the prevalence of increased mean of normal and diabetic subjects

p = 8.50% = 0.0850

q = 1-p

= 1-0.0850

= 0.9150

e = error margin tolerated at 5%

= 0.05

$e^2 = 0.0025$

N = ((3.8416(0.0850 x 0.9150))/0.0025 = 119.51 = approximately 120.

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3.2 Blood Sample Collection and Preparation

Preparation before commencement of analysis

1. Subjects were issued or given the informed consent form to fill after listening to a detailed explanation from the researcher.

2. Five (5) ml of blood samples was collected using 5 ml syringe from each subject. Two (2) ml was put into Lithium heparin Bottle, 2 ml into plain bottle and 1ml into Fluoride oxalate bottle.

3. The sample was placed in sample racks and left to stand for at least thirty (30) minutes at room temperature.

4. The sample was centrifuged for 5 minutes using the centrifuge, Hettich Universal 320 at room temperature and a completely cell free non-haemolysed sample was obtained.

5. The samples were then seperated into a one (1) ml sample container which were labelled with the serial number of the subject, and left to refrigerate before use.

Whole Blood Sample Collection

Whole blood samples were collected into plain and heparinized bottles respectively and were allowed to stand for 30 minutes to clot, centrifuged at 3,000 rpm for 10min for proper separation, separated into plain bottles and labeled accordingly. This was stored frozen, until when needed for biochemical and haematological analysis.

Information sources and search strategy

Published studies that assess insulin resistance between normal and diabetic subjects (especially T2DM) were searched in MEDLINE, EMBASE and PubMed databases covering the period from 2000 to 2018. Literature search was then carried out using the combination of terms "insulin", "insulin resistance", "TG/HDL ratio", "HOMA-IR", "HbA1c", "TyG", "Blood sugar", "diabetes", "diabetes mellitus", "type II diabetes", "T2D", "T2DM", "type 2 DM", "IGT", "risk factor", "epidemiology", "review". The reference lists of the retrieved articles and reviews of this field [22-25] were also searched. The search was limited to human studies and English publications.

3.3 Measurement of normal and diabetic subjects

Collecting information about normal subjects and persons suffering from diabetes was difficult. Two issues were addressed at the outset: the kind of data collection instrument that would be used, and the unit of measurement that would be employed.

i. Collection instruments

The main types of instruments for collecting information about normal and diabetic subjects were:

Sample surveys (general social surveys/specific health surveys) and;

Administrative collections and registries.

Each of these tools was used to measure aspects of diabetes in the study population.

Sample surveys are shorter surveys designed to be administered to the study sub-population selected by some other instrument (often a census) that focus on specific issues; normal and diabetic subjects in this case. They were put into the field to answer specific questions about the study population. As such, they were provided the opportunity to ask more detailed questions about being normal and being diabetic. More detailed information was useful in itself, of course, and it helped to reduce the number of false positive and negative responses, therefore offering a more accurate prevalence measure of being normal and being diabetic. The sample survey was an independent survey focusing entirely on normal and diabetic subjects.

Administrative collections and registries are composed of information that is collected as part of the normal operation of some service or programme. In this case, it is the information found on the participant informed consent form. These collections provided useful information on the characteristics of people accessing normal routine and diabetes services as well as details about the services provided. They do not guarantee an accurate measure of non-diabetes and diabetes prevalence since there would be no coverage of events. The quality of this type of administrative register information is closely related to the quality of administrative system, in particular, how well it has been maintained and how closely the concepts align with the normal and diabetic subjects' concept of interest. In this work, most of the diabetic subjects were drawn from members of the Diabetic Society of Nigeria (DAN), who already have established meeting days and documented records.

ii. Choice of selection and measurement unit

The second preliminary issue that was addressed was the unit for which the diagnostic parameters were measured. The selection unit was a collection of normal and diabetic subjects. The measurement unit was mmol/l for the lipid profile, blood sugar and renal profile parameters, percent (%) for HbA1c, and IU/L for Insulin test determination.

Administrative collections

What is an administrative information collection?

Besides surveys, administrative information collection (specific administrative systems) intended to serve normal and diabetic subjects was an important method of gathering information about these subjects and their characteristics. In this method, any information collected was organized and became part of normal service administration procedure such as the information gathered using standard participant informed consent forms for health services. Administrative information collections can take several forms, depending on the nature of the service, the format used, the type of information collected, and the method and frequency of collection.

3.4 ANALYSIS

Biochemical Analysis

The Bio-data comprising the Blood pressure (Systolic and Diastolic) and BMI was analysed. Also, Lipid Profile, Renal profile, and Blood Glucose were analysed using Randox Kits (RANDOX, USA). HbA1c test was analysed using WondfoFinecare System (WONDFO, CHINA). Insulin was analysed using Calbiotech Inc., enzyme-linked immunosorbent assay (ELISA) Kit while Thyroid Function was analysed using Accubind Elisa Kits (ACCUBIND, USA). The homeostatic model and other indices were also analysed.

Determination of Blood Pressure (BP)

Blood pressure (BP) was measured on the right arm in the sitting position using a standard mercury sphygmomanometer after at least 5 minutes of rest. The first and fifth Korotkoff sounds were recorded [26].

Determination of Body Mass Index (BMI)

Body weight, height and circumference of waist and hip were measured with standard methods [26]. Body weight was measured with electronic scales to the nearest 0.1 kg. Body height was measured to the nearest 0.1 cm by using a stadiometer[26]. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

Lipid profile

Determination of Total Cholesterol (CHOL)

The quantitative *in vitro* determination of CHOL in serum and plasma was done on the Rx Monza analyser.

3.5 Statistical analysis

All data were subjected to statistical analyses. Statistical analysis was performed using SPSS version 21 (IBM, U.S.A). The data was analyzed using one-way analysis of variance (ANOVA) and significant differences were determined using post Hoc Duncan multiple comparison test ($p<0.05$). The results were considered significant at 95% confidence level. The values were represented as mean ± standard error mean (SEM) and data obtained was analyzed using the SPSS. Data was shown as mean ± SD and displayed in figures. Qualitative variables of gender categories were summarized as proportions. Quantitative variables such as age were summarized as mean. Difference in mean of parameters was compared using ANOVA.

4.RESULTS

4.1 Bio data of human subjects

The height, weight, and other bio-information such as the age were used to determine the BMI of the individual subjects involved in the study. The same table showed the blood pressure of the 3 groups of subjects. The height of the non-diabetic and diabetic groups was not significantly different (176.20±1.25cmand 173.47±0.93cm), but the height of the pre-diabetics (170.82±1.09cm) was significantly different ($p \leq 0.05$) from the other 2 groups. 120 subjects made up of 40 non-diabetics, pre-diabetics, and diabetics (3 groups of subjects) respectively were recruited for the study. The sub groups comprised 20 non-diabetic males and females respectively, 19 pre-diabetic males and 21 pre-diabetic females, and 20 diabetic males and females respectively. The weight of the pre-diabetics was higher but not statistically different from that of the non-diabetics, the weight of the diabetics (76.27±2.13kg) was statistically different ($p \leq 0.05$) from that of the non-diabetics (70.77±0.89kg) and pre-diabetics (72.32±1.24kg). Analysis of the BMI showed that the BMI was not statistically different ($p \leq 0.05$) in the pre-diabetics (25.10±0.43) and diabetics (25.34±0.10), however, both groups were significantly higher than that for the non-diabetics (22.88±0.43). Both the systolic and diastolic pressure of the diabetics (119/75 mmHg) differed significantly ($p \leq 0.05$) from that of the non-diabetics (110/72 mmHg). Systolic pressure of the diabetics was also statistically different ($p \leq 0.05$) from that of the pre-diabetics but the diastolic pressure was not statistically different ($p > 0.05$), 119/75 mmHg and 112/74 mmHg respectively.

Table 4.1 Bio-data of human subjects for the non-diabetic control, pre-diabetic, and diabetic groups.

GROUP	SEX		AGE (years)	HEIGHT (cm)	WEIGHT (kg)	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)	BMI
	F	M						
NON-DIABETIC	20 ±0.03	20 ±0.04	50.70 ±1.16 bc	176.20±1.25 b	70.76± 0.89 c	110.12±1.59	71.77 ±0.89	22.88± 0.43 bc
PRE-DIABETIC	21 ±0.13	19 ±0.11	54.87 ±1.67 a	170.82±1.09 ac	72.32± 1.24 c	111.52±1.96	74.07 ±0.94	25.10± 0.43 a
DIABETIC	20 ±0.00	20 ±0.00	56.12 ±1.62 a	173.47±0.93 b	76.27± 2.13 ab	119.77±1.96	75.70 ±0.88	25.34± 0.10 a

Data are expressed as Mean ± Standard error mean (SEM), n=120 where n represents the number of human subjects. Values found in a column with common superscript letter a, are significantly different (p≤0.05) when compared to the non-diabetic. Values with the superscript b, are significantly different (p≤0.05) relative to the pre-diabetic. Values with the superscript c, are significantly different (p≤0.05) compared to the diabetic group.

Where:F – Female; M – Male; BMI – Body Mass Index

4.2 Lipid profile of human subjects

Majority of the lipid profile (CHOL, TG, and LDL) values of the human subjects increased progressively from the non-diabetic, pre-diabetic to the diabetic group having values of 4.41±0.13 mmol/l, 5.05±0.12 mmol/l, 5.22±0.15 mmol/l for CHOL; 1.46±0.08 mmol/l, 1.83±0.11 mmol/l, 2.45±0.11 mmol/l for TG; and 2.60±0.10 mmol/l, 3.21±0.10 mmol/l, 3.37±0.12 mmol/l for HDL; respectively for the non-diabetic, pre-diabetic and diabetics. There was a statistical difference (p≤0.05) between all groups for the CHOL. There was no statistical difference (p≤0.05) between the pre-diabetic and the diabetic groups for the LDL though both groups were statistically different (p≤0.05) from the normal group. The TG and HDL of the pre-diabetic and diabetic group were also statistically different (p≤0.05) from the non-diabetics but showed no statistical difference (p>0.05) from each other as shown in table 4.2 below.

Table 4.2 Lipid profile of human subjects for the non-diabetic control, pre-diabetic, and diabetic groups

GROUP	CHOL (mmol/l)	TG (mmol/l)	HDL (mmol/l)	LDL (mmol/l)
NON-DIABETIC	4.41±0.13^{bc}	1.46±0.08^{bc}	1.10±0±0.03^{bc}	2.60±0.10^{bc}
PRE-DIABETIC	5.05±0.12^{ac}	1.83±0.11^{a}	1.01±0.03^{a}	3.21±0.10^{a}
DIABETIC	5.22±0.15^{ab}	2.45±0.11^{a}	0.94±0.02^{a}	3.37±0.12^{a}

Data are expressed as Mean ± Standard error mean (SEM), n=120 where n represents the number of human subjects. Values found in a column with common superscript letter a, are significantly different (p≤0.05) when compared to the non-diabetic. Values with the superscript b, are significantly different (p≤0.05) relative to the pre-diabetic. Values with the superscript c, are significantly different (p≤0.05) compared to the diabetic group.

Where:CHOL – Cholesterol (Total Cholesterol); TG – Triglyceride; HDL – High Density Lipoprotein; LDL – Low Density Lipoprotein.

4.3: Renal profile of human subjects

The table 4.3 below reveals the renal profile of the non-diabetic, pre-diabetic and diabetic subjects. Though there was a progressive increase in the value of Na^+ from the non-diabetic to thediabetic group,there was no significant difference (p>0.05) in the Na^+ levels across the groups as the table reveals. The values for K^+ on the other hand differed significantly ($p \leq 0.05$) from each other having values of 3.78±0.06 mmol/l for the non-diabetics, 4.03±0.07 mmol/l for the pre-diabetics, and 4.50±0.09 mmol/l for the diabetics. The urea and creatinine values both showed statistical differences ($p \leq 0.05$) with progressive increase in values from the non-diabetic group to the diabetic group. Worthy of note, is the creatinine result which showed values of 86.47±3.43 mmol/l, 111.37±4.33 mmol/l, and 120.13±4.39 mmol/l indicating a marked increase in the value of creatinine as we move progressively to the diabetic group, as shown below. Cl^- showed a trend of linearity where the non-diabetic subjects had a value of 97.05±0.35 mmol/l followed by a decrease in value to 94.65±5.82 mmol/l for the pre-diabetic group and 93.88±0.63 for the diabetic group. While the Cl^- level of the diabetic and pre-diabetic groups was not statistically different ($p > 0.05$) from each other, they were both significantly different ($p \leq 0.05$) from that of the non-diabetic group. H_2CO_3 level was highest in the non-diabetic group (26.57±5.76 mmol/l) followed by the pre-diabetic (23.57±5.76 mmol/l) and the diabetic group (22.85±0.51 mmol/l), and followed the same pattern as Cl^- , with the level of H_2CO_3 in the diabetic group not differing statistically ($p > 0.05$) from that of the pre-diabetic group but with the level in both groups differing significantly ($p \leq 0.05$) from that of the non-diabetics as shown in table 4.3 below.

Table 4.3 Renal function in the non-diabetic control, pre-diabetic, and diabetic groups of human subjects

GROUP	Na^+ (mmol/l)	K^+ (mmol/l)	Cl^- (mmol/l)	$H_2CO_3^-$ (mmol/l)	Urea (mmol/l)	Creatinine (mmol/l)
NON-DIABETIC	141.75 ±2.48	3.78 ± 0.06 bc	97.05± 0.53 bc	26.15± 0.43 bc	3.93 ± 0.18 bc	86.47±3 .43 bc
PRE-DIABETIC	138.80 ±0.78	4.03 ± 0.07 ac	94.65± 5.82 a	23.57± 5.76 a	4.52 ± 0.21 ac	111.37± 4.33 ac
DIABETIC	138.55 ±0.97	4.50 ± 0.09 ab	93.88± 0.63 a	22.85± 0.51 a	4.89 ± 0.19 ab	120.13± 4.39 ab

Data are expressed as Mean ± Standard error mean (SEM), n=120 where n represents the number of human subjects. Values found in a column with common superscript letter a, are significantly different ($p \leq 0.05$) when compared to the non-diabetic. Values with the superscript b, are significantly different ($p \leq 0.05$) relative to the pre-diabetic. Values with the superscript c, are significantly different ($p \leq 0.05$) compared to the diabetic group.

Where:Na^+ - Sodium ion; K^+ - Potassium ion; Cl^- - Chloride ion; $H_2CO_3^-$ - Bicarbonate ion

4.4: HOMA-IR, TYG and TG-HDL Indices of the Human Subjects

The HOMA-IR, TYG and TG-HDL indices of the non-diabetic, pre-diabetic and diabetic human subjects are shown in table 4.5.

The table reveals an increasing trend in the HOMA-IR and TYG index across the groups. HOMA-IR values were 0.94±0.04 for the non-diabetics, 2.28±0.17 for the pre-diabetics, and 3.25±0.44 for the diabetics. The TYG index were also linear showing 3.69±0.02 for the non-diabetics, 3.90±0.02 for the pre-diabetics, and 4.04±0.02 for the diabetics. Both HOMA-IR and TYG index were significantly different across the groups. The TG-HDL index was also statistically different across the groups but did not follow a linear pattern, being highest in the pre-diabetic group. TG-HDL index was 1.34±0.07, 1.93±0.15 and 1.69±0.11 respectively for the non-diabetic, pre-diabetic, and diabetics as shown in table 4.5 below.

Table 4.5 Homeostatic model and other indices of human subjects for the non-diabetic control, pre-diabetic, and diabetic groups

GROUP	HOMA-IR	TYG INDEX	TG-HDL INDEX
NON-DIABETIC	0.94±0.04 bc	3.69±0.02 bc	1.34±0.07 bc
PRE-DIABETIC	2.28±0.17 ac	3.90±0.02 ac	1.93±0.15 ac
DIABETIC	3.25±0.44 ab	4.04±0.06 ab	1.69±0.11 ab

Data are expressed as Mean ± Standard error mean (SEM), n=120 where n represents the number of human subjects. Values found in a column with common superscript letter a, are significantly different ($p<0.05$) when compared to the non-diabetic. Values with the superscript b, are significantly different ($p<0.05$) relative to the pre-diabetic. Values with the superscript c, are significantly different ($p<0.05$) compared to the diabetic group.

Where:HOMA-IR – Homeostatic Model Assessment of Insulin Resistance; TYG - Triglyceride-Glucose; TG-HDL - Triglyceride/High density lipoprotein

4.2 Discussion

Due to the complexity in determining an individual prone to insulin resistance, it becomes also difficult to interpret the animal model of insulin resistance as an inference to what is obtainable in humans. According to Aleixandre & Miguel [27], the usefulness of rat model of non-insulin dependent diabetes mellitus (NIDDM) is nevertheless questionable, and they never can consider a clear experimental model of hypertension. In view of this, this research tends to join both the human and the animal models to intensively assessthe insulin resistance in normal and diabetic subjects using homeostatic model and other indices. There is a correlation between diabetes and the BMI of subjects. In fact, obesity is believed to account for 80 to 85% of the risk of developing type 2 diabetes while recent research suggests that obese people

are up to 80 times more likely to develop type 2 diabetes than those with a BMI of <22 [28]. Insulin sensitivity is a continuous variable. Thus young, lean, physically fit individuals are likely to be highly insulin sensitive whereas obese subjects with type 2 diabetes will have poor insulin sensitivity [1].This is supported by the bio-data obtained from the subjects used in this research. The average body weight of the human subjects showed a trend of increase from the non-diabetic, pre-diabetic to the diabetic subjects. The BMI of the pre-diabetic and diabetic subjects were also significantly higher than that of the non-diabetic subjects. There is also a correlation between diabetes and BP as the BP increased significantly across the normal, pre-diabetic and diabetic subjects in a similar order. Other risk factors such as genetics, ethnicity and age are also correlated to type 2 diabetes but were not considered in this work. Type 2 diabetes has a direct correlation with an increased risk of visceral fat deposition [29]. Low insulin as well as unresponsive insulin will promote gluconeogenesis (breakdown of various substrates to release glucose), glycogenolysis (the breakdown of glycogen to release glucose), glycolysis, lipolysis (breakdown of lipids to release glucose), and proteolysis (breakdown of proteins to release glucose). With increased glucose production, reverse feedback mechanism occurs leading to increase in the lipid profile parameters. HDL levels were lower in the diabetic than the normal.The HDL concentration levels increased as the diabetic case increased. The same trend was observed as there was a similar significant increase in the LDL, CHOL and TG of the pre-diabetic and the diabetic subjects relative to the non-diabetic groups.

There are a number of factors which can contribute to becoming obese such as eating a high calorie diet (high fat diet), not getting enough physical exercise, genetics, medical conditions and being on medications. Loss of body weight has been shown to improve blood glucose levels [28], and has allowed people with type 2 diabetes to come off or avoid going onto insulin resistance. Obesity is also thought to trigger changes to the metabolism of the body. These changes cause adipose tissue to release fat molecules into the blood which can affect insulin responsiveness in cells and lead to reduced insulin sensitivity. Obesity causes pre-diabetes, a metabolic condition that usually results in type 2 diabetes [7]. Type 2 diabetes affects the homeostasis acid-base regulation. High glucose concentration results in an osmotic force that draws water to the extracellular space. This dilutes extracellular sodium and results in lower blood sodium level [30]. In our result, a decrease in blood sodium level was observed as we moved from normal, to pre-diabetic and diabetic subjects, though the decrease were not statistically significant at $p<0.05$. Potassium levels are also altered in diabetes. High plasma glucose concentrations result in potassium efflux to the extracellular space, causing hyperkalemia [30]. This was observed in this study. Diabetic ketoacidosis is a clinically significant assay-based disturbance in diabetes. It occurs due to an increase in the rate of hepatic ketoacid generation. Bicarbonate (H_2CO_3) degrades to carbon (IV) oxide and water, and anion gap acidosis results. This is observed in the significantly lower Bicarbonate levels in the pre-diabetic and diabetic groups. The chloride values also follow the same trend. In general, diabetic subjects are at increased risk of assay-based disturbance and electrolyte disturbances. The increased risk is due to the diseased state of diabetes itself and the associated disruptions in glucose homeostasis, drugs used to treat diabetes, and the organ damage associated with diabetes [30]. The urea and creatinine levels of the pre-diabetic and diabetic groups were higher than that of the non-diabetics. This is in agreement with other studies which reported that hyperglycaemia is one of the major causes of progressive renal diseases [31]. Approximately 20% to 30% of diabetics will develop abnormal kidney function, represented by a reduced glomerular filtration rate and a rise in serum urea and creatinine. In this study, we found that insulin resistance was increased significantly in the pre-diabetic and diabetic groups as depicted by the

HOMA-IR index, in the human subjects. This is expected and in line with other studies as it is known that insulin resistance is a major risk factor and predicts Type 2 diabetes [7]. The hall-mark of Type 2 diabetes is an abnormally high glucose that is unresponsive or only slightly responsive to insulin regulation. It is known that, TyG index shows a positive correlation with HOMA-IR [32]. In this work, TYG index also followed the same pattern, being significantly increased in the pre-diabetic and diabetic human subjects. TG-HDL was also increased in the pre-diabetic and diabetic human subjects. However, it did not follow a linear pattern as HOMA-IR and TYG index as the TG-HDL index was higher in the pre-diabetic than the diabetic group. This may reflect life style changes as subjects that were already known diabetics may already be taking intervention measures to ameliorate the diabetic condition.

5. CONCLUSION

The assessment of insulin resistance studied using the homeostatic model proved that insulin resistance can be managed when appropriate lifestyle is adopted. Obesity causes pre-diabetes, a metabolic condition that usually results in type 2 diabetes.The average body weight of the human subjects showed a trend of increase from the non-diabetic, pre-diabetic to the diabetic subjects. The BMI of the pre-diabetic and diabetic subjects were also significantly higher than that of the non-diabetic subjects. There is also a correlation between diabetes and BP as the BP increased significantly across the normal, pre-diabetic and diabetic subjects. It is known that, TyG index shows a positive correlation with HOMA-IR. The urea and creatinine levels of the pre-diabetic and diabetic groups were higher than that of the non-diabetics. Recognition and monitoring of insulin resistance in the normal and diabetic patient will likely lead to a more successful preventive approach and a better therapeutic intervention measure and management of the diabetic patient.

6RECOMMENDATIONS

It is recommended that this research should be further carried out on other homeostatic indices other than those studied in this research work so as to ascertain the nexus between these intermediaries. A large sample size should also be adopted to enhance precision. The research also should be carried out, not only on one ethnic group or location as variation in geographical location affects the genetic factor and limit the generalization of the research findings.

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