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Hormonal and Hematologic Profile of Pre-Diabetic and Diabetic Patients in the University of Port Harcourt Teaching Hospital

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Abstract **Original Research Article**

This examination investigated haematologic and hormonal profile in human diabetic subjects. The assessment solidified the human diabetic subjects and took the blood analytes to screen for diabetes. 120 male and female human subjects containing forty subjects each for control, pre-diabetics, and diabetics (three sets) facilitated for age, sex, height, weight and BMI were enrolled into the assessment reliant upon decided measures. Twenty each of the three sets of human subjects were males and females independently. Every illustration of blood serum and plasma was explored using Randox and Accubind packs and an autoanalyser to test for various biochemical and hematological limits. The overall results revealed a colossal differentiation ($p \leq 0.05$) in the limits of the analytes, except for that of Na^+. ***Contributions to Knowledge*:** Based on the findings, analytes are good for predicting and managing DM, by comparing the blood analytes of non-diabetics, pre-diabetics, and diabetics in order to monitor the onset of diabetes and proffer possible solutions to enhance early detection and manage diabetes.

Keywords: Analytes, non-diabetics, pre-diabetics, diabetics, biochemical, hormonal, haematological.

INTRODUCTION

Diabetes mellitus (DM) is a lifestyle non-communicable disease of mankind that represents one of the most significant global health problems that afflict both young and old in all parts of the world, irrespective of gender (International Diabetes Federation [IDF], 2015). This metabolic disease arises from the inability of the body to produce or utilize insulin, and this drastically decreases the quality of human life.

Nigeria has the highest number of people with DM in Africa with approximately 4 million cases reported at a prevalence rate of 4.99% (IDF, 2015). The disease is broadly classified into types 1and 2, based on their dependence on insulin. Diabetes mellitus type 2 (DM-2), is dependent on insulin and accounts for 95% of all cases reported (IDF, 2013; ADA, 2014), while type 1 is known as non-insulin dependent diabetes mellitus (NIDDM), a selective autoimmune destruction of pancreatic beta cells, leading to insulin deficiency. Globally, approximately 150 million people suffer from DM, with the figure likely to double by the year 2025 (WHO, 2013).

The etiology of DM are multi-factorial, including both genetic and environmental elements that affect the β-cell function and insulin sensitivity (Schaalan *et al*., 2009; Willett, 2002). Metabolic health lies in the space between insulin and its sensitivity to glucose (Vogeser, 2007; Maurer, 2014). Diabetes, on its own, is associated with certain endocrine conditions, such as insulin resistance and insulin sensitivity, and insulin is produced and secreted by the β cells of the liver. Insulin resistance is usually associated with pre-diabetes, DM and a host of other serious health challenges and complications, including, severe hyperglycemia and hypoglycemia, heart attacks, strokes, kidney disease, eye problem and cancer. Symptoms observable in insulin resistance includes, extreme thirst or hunger, feeling hungry even after meal and increased or frequent urination.

The diagnosis of DM and other blood sugar-related disorders is mainly by routine fasting blood sugar test, which is an indication of glycaemic state, which is subject to diurnal fluctuations. Another test, usually done to monitor the glucose level is the glycated haemoglobin (HbA1c) test, which reveals the fasting

blood sugar (FBS) level in the recent 3 months. High HbA1c is indicative of consistently high blood sugar level in the past 3 months, with the likelihood of predisposing the individual to long-term complications (WHO, 2013). However, current research trends favour markers predictive of DM, and they possess the benefit of detecting DM at the pre-diabetic state. It thus implies that once any of such markers begin to rise, the individual may be at risk of developing DM or any cardiovascular disorder (CVD) (Wild *et al.*, 2004), and this compounds the fact that elevated blood pressure (BP) has been associated with a form of DM, diabetes mellitus- type 2, which is thought as partly due to the underlying impact of insulin resistance on the vascular system and kidney (Ferrannini & Cushman, 2012), while other metabolic abnormalities associated with DM, such as elevated body mass index, also transiently leads to consistent increase in blood pressure (LeePark *et al.*, 2006). Plasma lipids are also usually associated with DM, due to the concomitant adverse effects of these lipids on the vasculature. Commonly, fasting lipid profile of triglycerides, total cholesterol, low density and high density lipoprotein cholesterols are conducted and are helpful in determining likely morbidity. Typically, elevated plasma lipid, hyperlipidemia, will lead to complications and disorders in the vasculature and other organs (Brunzell *et al.*, 2008). The collective disorders associated with DM is collectively termed metabolic syndrome (Bernstein, 2007). Some lifestyles, such as active and heavy smoking is also reported as a risk factor for developing DM (Willi *et al.*, 2007), as well as, sedentary lifestyle and fatty meals.

Diabetes mellitus poses some burden on the kidney. It is thus, important that renal function for some electrolytes be conducted. Typically, these plasma electrolytes will be observed to have deviated from their normal range (Inkler *et al.*, 2016), which also varies between adult and younger diabetic patients (Inkler *et al.*, 2016; Rodwell *et al.*, 2015).

It is, therefore, important that both hormone and haematologic parameters, such as, insulin, HbA1c (glycosylated haemoglobin), glucose, lipid profile, thyroid stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4), renal function (sodium, potassium, chloride, bicarbonate, urea and creatinine) and full blood count (FBC) are investigated in normal and diabetic subjects. Glycosylated hemoglobin test remains the main assay when studying antihyperglycemic agents in both types of DM (Fuchtenbusch *et al.*, 2000). These variables can provide baseline that will be useful for physicians in assessing insulin resistance, as well as, management of diabetes.

METHODOLOGY

The study was conducted at Choba and Aluu communities, as well as, University of Port Harcourt and University of Port Harcourt Teaching Hospital (UPTH), in Obio/Akpor and Local Government Areas of Rivers State, Nigeria. The materials used were cotton wool, methylated spirit, micropipettes, micropipette tips, pipettes, plain bottles, sample containers, syringes and needles, test-tubes, test-tube racks and tourniquet. The chemicals used were of analytical grade, while the reagents were used in accordance to the manufacturers' recommendations. The minimum sample size was calculated using the formula (Anderson *et al.*, 1991);
$N= Z^2 (pq)/e^2$

Where,
N = minimum sample size,
Z = 1.96 at 95% confidence limits,
p = prevalence (normal and diabetic subjects; 6.80+10.20/2) and q = 1-p.
N = ((3.8416(0.0850 x 0.9150))/0.0025 = 119.51 = approximately 120.

The respondents were drawn from individuals coming to UPTH for monitoring their glucose level, hematologic profile and insulin resistance over a 2-month period, with each individual presented an informed consent form and those willing to donate an aliquot of their blood samples for the purpose of the research were recruited and grouped into 3; A (control group consisting of 40 non-diabetic subjects), B (test group consisting of 40 pre-diabetic subjects) and C (test group consisting of 40 diabetic subjects). The inclusion criterion was 36-76 years, while the exclusion criteria were co-infection and other metabolic disorders. Also 5ml of venous blood was taken and distributed into lithium heparin (2ml), plain (2ml) and fluoride oxalate (1ml) bottles. The data was analyzed using statistical package for social sciences (SPSS) version 21, while the results are presented in tables and charts, as frequencies and percent.

RESULTS

Table 1: Bio-data of respondents (n= 120)

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^{c}	176.20±1.25^{b}	70.76±0.89^{c}	110.12±1.59	71.77±0.89	22.88±0.43^{c}
PRE-DIABETIC	21±0.13	19±0.11	54.87±1.67^{a}	170.82±1.09^{c}	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}

The height of the non-diabetic and diabetic groups was not significantly different (176.20±1.25cm and 173.47±0.93cm), but that of the pre-diabetics (170.82±1.09cm) was significantly different ($p<0.05$) from the other 2 groups. 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 higher ($p<0.05$) than that of the non-diabetics (70.77±0.89kg) and pre-diabetics (72.32±1.24kg). The BMI was not statistically different ($p<0.05$) in the pre-diabetics (25.10±0.43) and diabetics (25.34±0.10), but, both groups were significantly higher than that for non-diabetics (22.88±0.43). Both the systolic and diastolic blood pressure of the diabetics (119/75 mmHg) were significantly ($p<0.05$) higher than that of the non-diabetics (110/72 mmHg). Systolic blood pressure of the diabetics was also statistically higher ($p<0.05$) than that of the pre-diabetics but the diastolic blood pressure was not statistically different ($p>0.05$), 119/75 mmHg and 112/74 mmHg respectively.

Table 2: Lipid profile

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}	$1.10\pm0\pm0.03^{bc}$	2.60 ± 0.10^{bc}
PRE-DIABETIC	5.05 ± 0.12^{c}	1.83 ± 0.11^{a}	1.01 ± 0.03^{a}	3.21 ± 0.10^{a}
DIABETIC	5.22 ± 0.15^{b}	2.45 ± 0.11^{a}	0.94 ± 0.02^{a}	3.37 ± 0.12^{a}

Majority of the lipid profile (CHOL, TG, and LDL) values increased progressively from the non-diabetic, pre-diabetic to 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. There was a statistical difference ($p<0.05$) between all groups for the CHOL, while there was no significant difference ($p<0.05$) between the pre-diabetic and diabetic groups for LDL, though both groups were significantly higher ($p<0.05$) than that of the normal group. The TG and HDL of the pre-diabetic and diabetic group were also significantly higher ($p<0.05$) and lower respectively than that of the non-diabetics but showed no significant difference ($p>0.05$) from each other as shown in table 2 above.

Table 3: Renal profile

GROUP	Na^+ (mmol/l)	K^+ (mmol/l)	Cl^- (mmol/l)	HCO_3^- (mmol/l)	Urea (mmol/l)	Creatinine (mmol/l)
NON- DIABETIC	141.75±2.48	3.78 ± 0.06^{bc}	97.05 ± 0.53^{b}	26.15 ± 0.43^{b}	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}

Table 4: Glycemic Indices and Hormonal profiles

GROUP	GLU mmol/l	HbA1c mmol/l	INS mIU/L	TSH mU/ml	fT3 pmol/L	fT4 ng/dL
NON-DIABETIC	4.49 ± 0.08^{bc}	4.75 ± 0.05^{bc}	4.77 ± 0.19^{bc}	1.55 ± 0.15^{bc}	3.22 ± 0.11^{bc}	1.11 ± 0.05^{c}
PRE-DIABETIC	6.00 ± 0.11^{ac}	5.73 ± 0.08^{ac}	8.48 ± 0.59^{a}	3.97 ± 0.09^{a}	3.05±0.12	1.07±0.06
DIABETIC	10.84 ± 0.96^{a}	9.74 ± 0.47^{a}	7.13 ± 0.73^{ab}	3.72 ± 0.08^{ab}	2.61 ± 0.09^{ab}	0.97 ± 0.05^{ab}

Glucose (GLU) and HbA1c (Glycemic indices), Insulin (INS) and Thyroid Function profile ((free triiodothyronine (fT3) and free thyroxine (fT4)) of the human subjects are shown in Table 4.4. The Glucose and HbA1c showed a significantly increasing trend with values of 4.49±0.08 mmol/l, 6.00±0.11 mmol/l, and 10.84±0.96 mmol/l for Glucose; and 4.75±0.05 mmol/l, 5.73±0.08 mmol/l, and 9.74±0.47 mmol/l for HbA1c, for the non-diabetics, pre-diabetics, and diabetics respectively. All values were significantly higher ($p<0.05$) across the groups for both Glucose and HbA1c. Insulin levels were also significantly higher ($p<0.05$) across the groups but did not show the same linearity having the highest value with the pre-diabetic group. The levels were 4.77±0.19 mIU/L, 8.48±0.59 mIU/L, and 7.13±0.73 mIU/L for the non-diabetics, pre-diabetics and diabetics respectively. The fT3 and fT4 showed progressive decrease in values having values of 3.22±0.11 pmol/L, 3.0±0.12 pmol/L, and 2.61±0.09 pmol/L for fT3; and 1.11±0.05 ng/dL, 1.07±0.06 ng/dL, and 0.97±0.05 ng/dL for fT4; respectively for the non-diabetics, pre-diabetics, and the diabetics while the TSH values increased significantly when compared to the normal. TSH for the pre-diabetic group was however slightly higher than that for the diabetics as shown in Table 4.4 above.

Table 5: Haematological Profile

GROUP	RBC($\times10^6$ cells/cmm)	Hb (g/dL)	PCV (%)	PLT ($\times10^9$/L)	WBC ($\times10^9$/L)	NEU ($\times10^9$/L)	LYMP ($\times10^9$/L)	MONO ($\times10^9$/L)	EOS ($\times10^9$/L)	BAS ($\times10^9$/L)
NON-DIABETIC	4.29 ± 0.07^{c}	13.98±0.51	42.30±0.75	186.95 ± 6.04^{c}	5.52±0.13	25.20 ± 0.59^{c}	64.55 ± 0.66^{c}	6.10 ± 0.20^{c}	3.25 ± 0.11^{c}	0.15±0.07
PRE-DIABETIC	4.38 ± 1.05^{c}	14.03±0.17	43.70±0.53	206.70 ± 8.72^{ac}	5.60±0.20	26.37 ± 1.48^{c}	65.42 ± 1.70^{c}	6.32 ± 0.28^{ac}	3.62 ± 0.16^{a}	0.15±0.05
DIABETIC	4.90 ± 0.11^{ab}	14.12±0.29	43.92±0.84	229.97 ± 11.21^{ab}	5.68±0.37	29.47 ± 8.63^{ab}	68.52 ± 2.35^{ab}	6.82 ± 0.46^{b}	3.80 ± 0.15^{a}	0.10±0.04

Table 5 above, the haematology result, shows that RBC was significantly higher ($p<0.05$) in the diabetic subjects. The values were 4.29±0.07 mL, 4.38±1.05 mL, and 4.90±0.11 mL for the non-diabetic, pre-diabetic and diabetics respectively. Hb and PCV were not statistically different ($p>0.05$) across the groups though the non-diabetic patients had a slightly lower Hb and PCV than the other groups. Platelet (PLT) count, on the other hand, were significantly increased ($p<0.05$) in the pre-diabetic and diabetic groups with values of 186.95±6.04 mL, 206.70±8.72 mL, and 229.97±11.21 mL respectively for the non-diabetics, pre-diabetics and diabetics. WBC count was slightly increased in the pre-diabetic and diabetic groups although the increase was not statistically significant. Neutrophil count of the diabetics was statistically higher ($p<0.05$) than that of the non-diabetics and pre-diabetics with values of 25.20±0.59 cells/µL, 26.37±1.48 cells/µL, and 29.47±8.63 cells/µL for the non-diabetics, pre-diabetics and diabetics respectively. Lymphocytes counts also increased progressively from non-diabetic to pre-diabetics and diabetics but the increase was only significant ($p<0.05$) in the diabetic group. Eosinophil count increased progressively across the groups with the increase being significant ($p<0.05$) in the diabetic group relative to the non-diabetic and pre diabetic groups as shown in the Table 5 above. Monocyte count was also significantly different across the groups with values of 6.10±0.20 cells/µL, 6.32±0.28 cells/µL, and 6.82±0.46 cells/µL for non-diabetic, pre-diabetics and diabetics respectively. Basophil count on the other hand, was basically the same across all groups as represented in the table 4.6 above.

DISCUSSION

There is a correlation between diabetes and the body mass index (BMI) of individuals. 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 80 times more likely to develop type 2 diabetes than those with a BMI of <22 (McGill, 2005). 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 (Greeve, 2005), as supported by this study. The average body weight of the respondents showed trend of increase from non-diabetic, pre-diabetic to diabetic. The BMI of the pre-diabetic and diabetic subjects were also significantly higher than that of non-diabetic subjects. With a correlation between diabetes and high blood pressure (BP), as BP increases significantly across normal, pre-diabetic and diabetic subjects in a similar order, in addition to other risk factors. Type 2 diabetes has a direct correlation with an increased risk of visceral fat deposition (Simmons, 2019). This agreed with this research. There was significant increase in the LDL, CHOL and TG of the pre-diabetic and diabetic subjects relative to the non-diabetic groups. Loss of body weight has been shown to improve blood glucose levels (McGill, 2005), 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 (Bray, 2004). 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 (Palmer and Clegg, 2015). 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 (Palmer *et al.*, 2015). This was observed in this study. 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. 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 (Palmer and Clegg, 2015). 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 (Bamanikar *et al.*, 2016). Approximately 20% to 30% of diabetics will develop abnormal kidney function, represented as reduced glomerular filtration rate and rise in serum urea and creatinine. Analysis of thyroid function (TSH, fT3 and fT4) showed that the thyroid function of pre-diabetics and diabetics differed significantly from that of normal non-diabetic subjects. There was a significant increase in the TSH of the pre-diabetic and diabetic subjects and this increase was highest in the pre-diabetic subjects, which suggests that the diabetic subjects may have already taken intervention measures. The complications of diabetes reduce mostly as intervention measures are taken and prevention of long term complications is one of the major reasons of drug and lifestyle interventions in diabetes patients (Greenapple, 2011). On the other hand, fT3 and fT4 were decreased in the pre-diabetic and diabetic state. The decrease in fT3 and fT4 followed the glycaemic state as indicated by the Glucose and HbA1c levels and was lowest in the diabetic subjects. Thyroid dysfunction is widely reported in diabetes (Ogbonna *et al.*, 2019). Diabetes mellitus and thyroid dysfunctions are two commonly encountered endocrine disorders encountered in the hospital clinic. Both insulin and thyroid hormones are antagonistic in their actions. Insulin resistance was significantly higher in the hypothyroid patients and TSH was positively correlated with insulin resistance (Chutia *et al.*, 2018; Ogbonna *et al.*, 2019). This study agreed with this, as TSH was higher in pre-diabetic and diabetic groups with increased glycaemia as represented by the Glucose and HbA1c concentrations.

Analysis of the haematological parameters revealed alterations in haematological indices in the diabetic state. Diabetes is a metabolic disease that is characterized by hyperglycaemia, dyslipidemia, hypertension, and impaired hematological indices. Several hematological changes affecting red blood cells (RBCs), white blood cells (WBCs) and coagulation factors are shown to be directly associated with DM (Biadgo *et al.*, 2016) and they dysfunction in DM (Gkrania-Klotsas *et al.*, 2010). In this study, PCV, Hb and RBC were all higher in the pre-diabetic and diabetic subjects relative to the controls, though the difference was not significant for PCV and Hb. RBC was, however, significantly higher in the diabetic subjects. This might be partly explained by the increased HbA1c in the diabetic state (Marar, 2011). In this study, HbA1c of the diabetic patients were also higher than that of the controls. Platelet count and WBC count and its components were also elevated in the pre-diabetic and diabetic subjects. This is in agreement with findings reported by several previous studies and might be the indirect features of insulin resistance syndrome (Biadgo *et al.*, 2016). Increase in WBC indices in the diabetic group compared with the control group might also be the result of the increased oxidative stress triggered by the high levels of hyperglycemia in the diabetic patients. In contrast to this study, another study reported decrease in RBC count, Hb and PCV levels (Ezenwaka *et al.*, 2008). This might be expected in diabetes of long duration as chronic hyperglycaemia and glycation of red blood cell membrane proteins will lead to accelerated aging of RBCs. Diabetics with long term complications such as Diabetic Nephropathy will also have reduced kidney function and reduced production of erythropoietin and ultimately decreased RBC count.

SUMMARY/CONCLUSION

Insulin resistance is generally accepted to be a major risk factor in the etiology of type 2 diabetes mellitus (Bray, 2004). Several risk factors (obesity, physical inactivity, body fat distribution, age and hyperinsulinemia) may be considered markers of insulin resistance. Insulin resistance predicts the development of Type 2 diabetes mellitus even in individuals with normal glucose tolerance. It is thus, vital to recognize insulin resistance in the pre-disease stage when therapeutic intervention may be more successful than in overt disease (Boden, 2001). In conclusion, it is important to recognize that haematologic and biochemical deviations of diabetes in the pre-disease stage, as this may aid therapeutic intervention, dyslipidaemia and hyperinsulinaemia was seen in sampled subjects and risk factors such as obesity, physical inactivity, body fat distribution, age and hyperinsulinemia, may be considered markers of diabetes.

It is therefore, recommended that this research be further undertaken using larger population of subjects, while similar study should also be conducted in the various geographical locations as variations in

different locations affect the genetic factor and limit the generalization of the research findings.

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