CHANGES IN SOME COAGULATION PARAMETERS AMONG DIABETIC PATIENTS IN MICHAEL OKPARA UNIVERSITY OF AGRICULTURE, UMUDIKE, ABIA STATE, NIGERIA.

Obeagu Emmanuel Ifeanyi1*, Obarezi Henry Chukwuemeka2, Aloh Godwin Sunday3, Emelike Chinedum Uche1

1. Medical Laboratory Scientist, Diagnostic Laboratory Unit, University Health Services Department, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.
2. Medical Doctor, Department of Obstetrics and Gynaecology, Federal Teaching Hospital Abakaliki, Ebonyi State, Nigeria.
3. Lecturer, Department of Biochemistry, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

ABSTRACT

Diabetes mellitus or diabetes is a metabolic disorder characterised with chronic hyperglycemia which results in polyuria, polydipsia and polyphagia. It has high level of morbidity and mortality in Nigeria. Type 2 diabetes mellitus is common here in Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria. This could be as a result of their lifestyle. The study was carried out using 30 confirmed type 2 diabetics (20 male, 10 female) with average age of 48 years and 30 non-diabetics (20 male, 10 female) with average age of 47 years attending University Health Services Department of the University. The study showed significant prolonged time in mean value of APTT and increased weight of fibrinogen in the diabetics (P<0.05) relative to the non-diabetics and no significant change (P>0.05) in TT and PT. The prolonged time of APTT could be as a result of inhibitors of intrinsic system. The study is aimed at finding out any significant change and how to manage the patient to help in the improvement of health status of the type 2 diabetics.

Keywords: Coagulation study, Intrinsic system, Type 2 diabetes mellitus patients.
INTRODUCTION

Diabetes mellitus is a group of metabolic diseases in which a person has high blood sugar, either because the pancreas does not produce enough insulin, or because cells do not respond to the insulin that is produced (David and Gardner, 2011). This high blood sugar produces the classical symptoms of polyuria, polydipsia, and polyphagia.

There are three main types of diabetes mellitus (DM).

- Type 1 DM results from the body's failure to produce insulin, and currently requires the person to inject insulin or wear an insulin pump. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes".
- Type 2 DM results from insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. This form was previously referred to as non insulin-dependent diabetes mellitus (NIDDM) or "adult-onset diabetes".
- The third main form, gestational diabetes, occurs when pregnant women without a previous diagnosis of diabetes develop a high blood glucose level. It may precede development of type 2 DM.

Other forms of diabetes mellitus include congenital diabetes, which is due to genetic defects of insulin secretion, cystic fibrosis-related diabetes, steroid diabetes induced by high doses of glucocorticoids, and several forms of monogenic diabetes.

Untreated, diabetes can cause many complications. Acute complications include diabetic ketoacidosis and nonketotic hyperosmolar coma. Serious long-term complications include cardiovascular disease, chronic renal failure, and diabetic retinopathy. Adequate treatment of diabetes is thus important, as well as blood pressure control and lifestyle factors such as stopping smoking and maintaining a healthy body weight.

Diabetes mellitus is classified into four broad categories: type 1, type 2, gestational diabetes, and "other specific types". The "other specific types" are a collection of a few dozen individual causes (David and Gardner, 2011).

Type 2 diabetes mellitus is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known.
Diabetes mellitus cases due to a known defect are classified separately. Type 2 diabetes is the most common type.

In the early stage of type 2, the predominant abnormality is reduced insulin sensitivity. At this stage, hyperglycemia can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce glucose production by the liver.

The classic symptoms of untreated diabetes are loss of weight, polyuria, polydipsia, and polyphagia (Cooke and Plotnick, 2008). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.

Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Blurred vision is a common complaint leading to a diabetes diagnosis. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes.

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20), but may be the first symptom in those who have otherwise not received a diagnosis before that time. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease (Emerging Risk Factors Collaboration, 2010). The main "macrovascular" diseases are coronary artery disease, stroke, and peripheral vascular disease. About 75% of deaths in diabetics are due to coronary artery disease (Gara et al., 2013).  

Diabetes also damages the capillaries (Boussageon et al., 2011). Diabetic retinopathy, which affects blood vessel formation in the retina of the eye, can lead to visual symptoms including reduced vision and potentially blindness. Diabetic nephropathy, the impact of diabetes on the kidneys, can lead to scarring changes in the kidney tissue, loss of small or progressively larger amounts of protein in the urine, and eventually chronic kidney disease requiring dialysis.

Another risk is diabetic neuropathy, the impact of diabetes on the nervous system — most commonly causing numbness, tingling, and pain in the feet, and also increasing the risk of skin damage due to altered sensation. Together with vascular disease in the legs, neuropathy contributes to the risk of diabetes-related foot problems diabetic foot ulcers that can be
difficult to treat and occasionally require amputation. Additionally, proximal diabetic neuropathy causes painful muscle wasting and weakness.

Type 2 diabetes is due primarily to lifestyle factors and genetics (Riserus and Willet, 2009). A number of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than thirty), lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60-80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Those who are not obese often have a high waist–hip ratio (David and Gardner, 2011).

Dietary factors also influence the risk of developing type 2 diabetes. Consumption of sugar-sweetened drinks in excess is associated with an increased risk (Malik et al., 2010; Malik et al., 2010). The type of fats in the diet is also important, with saturated fats and trans fatty acids increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk. Eating lots of white rice appears to also play a role in increasing risk (Hu et al., 2012). A lack of exercise is believed to cause 7% of cases (Lee et al., 2012).

Mechanism of insulin release in normal pancreatic beta cells - insulin production is more or less constant within the beta cells. Its release is triggered by food, chiefly food containing absorbable glucose.

Insulin is the principal hormone that regulates uptake of glucose from the blood into most cells. Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all forms of diabetes mellitus.

Humans are capable of digesting some carbohydrates, in particular those most common in food; starch, and some disaccharides such as sucrose, are converted within a few hours to simpler forms, most notably the monosaccharide glucose, the principal carbohydrate energy source used by the body. Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage.
If the amount of insulin available is insufficient, if cells respond poorly to the effects of insulin (insulin insensitivity or resistance), or if the insulin itself is defective, then glucose will not have its usual effect, so it will not be absorbed properly by those body cells that require it, nor will it be stored appropriately in the liver and muscles. The net effect is persistent high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as acidosis.

When the glucose concentration in the blood is raised to about 9-10 mmol/L (except certain conditions, such as pregnancy), beyond its renal threshold, reabsorption of glucose in the proximal renal tubuli is incomplete, and part of the glucose remains in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production and increased fluid loss. Lost blood volume will be replaced osmotically from water held in body cells and other body compartments, causing dehydration and increased thirst.

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following (WHO, 1999):

- Fasting plasma glucose level $\geq 7.0$ mmol/l (126 mg/dl)
- Plasma glucose $\geq 11.1$ mmol/l (200 mg/dL) two hours after a 75 g oral glucose load as in a glucose tolerance test
- Symptoms of hyperglycemia and casual plasma glucose $\geq 11.1$ mmol/l (200 mg/dl)
- Glycated hemoglobin (Hb A1C) $\geq 6.5\%$ (Diabetes Care, 2010).

A positive result, in the absence of unequivocal hyperglycemia, should be confirmed by a repeat of any of the above methods on a different day. It is preferable to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete and offers no prognostic advantage over the fasting test (Saydah et al., 2001). According to the current definition, two fasting glucose measurements above 126 mg/dl (7.0 mmol/l) is considered diagnostic for diabetes mellitus.

Glycated hemoglobin is better than fasting glucose for determining risks of cardiovascular disease and death from any cause (Selvin et al., 2010).

Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases. In 2011 it resulted in 1.4 million deaths worldwide making it the 8th
leading cause of death. This is an increase from 1 million deaths in 2000 (WHO, 2013).

Its rate has increased, and by 2030, this number is estimated to almost double. Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in more developed countries. The greatest increase in rates is, however, expected to occur in Asia and Africa, where most people with diabetes will probably be found by 2030. The increase in rates in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. This has suggested an environmental (i.e., dietary) effect, but there is little understanding of the mechanism(s) at present, though there is much speculation, some of it most compellingly presented (Wild et al., 2004).

Diabetes mellitus is a major health problem that results in significant morbidity and mortality from diverse complications. Thrombo-haemorrhagic complications are well recognised among diabetic populations (Alao et al., 2009).

Over 170 million people worldwide and about 1-7% of the Nigeria population are affected (Wokoma, 2002; Fabiyi et al., 2002). A Nigerian national non-communicable disease survey estimate the prevalence to be 2.2% with over 90% being type 2 diabetes (Akinkugbe, 1997). A prevalence of 3.1 has been reported in Urban Jos (Puepet, 1996). The circulatory disturbances are further compounded by alteration in platelets count and activity, coagulopathy, fibrinolytic aberration, haemorrheological and changes endothelial metabolism (McFarlane, 1997).

MATERIALS AND METHODS

Study Area: The study was done in Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

Subjects: Confirmed Diabetic patients and non-diabetic subjects attending University Health Services Department of Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria were used for the study in the course of Laboratory diagnosis.

Samples: Venous blood samples were collected from the subjects into Sodium citrate anticoagulant containers and the plasma used for the analysis.

Ethics: Oral consents were made to the subjects before the samples were collected.

Statistical Analysis: The results were analysed using t-test and the statistical significance set
RESULTS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>DM(n=30) Mean+/SD</th>
<th>Non-Diabetics(n=30) Mean+/SD</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT(sec)</td>
<td>17.2+-3.2</td>
<td>16.5+-2.8</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>APTT(sec)</td>
<td>29.6+-2.7</td>
<td>27.1+-3.0</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>TT(sec)</td>
<td>19.4+-3.1</td>
<td>18.6+-2.9</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Fibrinogen Weight(g/l)</td>
<td>4.00+-0.8</td>
<td>2.98+-0.50</td>
<td>P&lt;0.05S</td>
</tr>
</tbody>
</table>

PT=Prothrombin Time, APTT=Activated Partial Thromboplastin Test, TT=Thrombin Test

DM=Diabetes Mellitus

DISCUSSION

Diabetes mellitus is a syndrome characterised by presence of chronic hyperglycemia due to defective insulin secretion, insulin action or both(Wokoma,2002).

The study showed that there was significant prolongation (P<0.05) in mean value of Activated Partial Thromboplastin Time(APTT) and significant increase in the mean fibrinogen weight of the type 2 diabetes relative to the controls but there was no significant change(P>0.05) in the mean values of Prothrombin Time(PT) and Thrombin Time(TT) of the diabetics relative to the non-diabetics. The increased levels of fibrinogen weight is in accordance with Mark’s report(2001) of elevated fibrinogen concentration as one of the risk factors for atherosclerosis among diabetics. It also agrees with Tekemotol et al(1996). Bartoli(1994) also reported increased level of fibrinogen. The study agrees with Alao et al(2009) with prolonged time in TT, PT, APTT and significant increase in fibrinogen level(P<0.05) except that in this study there was no significant change(P>0.05) in TT and PT. The significant prolonged time for intrinsic coagulation pathway supposed to be decreased due to hypercoagulable tendency of the diabetes from a shift of thrombo-haemorrhagic balance in favour of thrombosis which was not followed in this study. The prolongation time of APTT may be due to in-vitro intereference of fibrin clot formation by inhibitors as reported by Laffan(1995). This prolonged APTT time may as well be as a result of damages to the liver where most of the coagulation factors are synthesized.

CONCLUSION

The study showed significant prolongation time of APTT and significant increase in
fibrinogen weight of the diabetics. The intrinsic pathway in the diabetics should be monitored closely and should be part of test requested by the clinicians when there is presentation of diabetes mellitus and also the fibrinogen concentration because of its attendant risk to atherosclerosis, stroke, etc. This observation calls for proper management of the type 2 diabetics to avoid uncontrolled bleeding when they sustain injury or during surgery.

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