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ROLE OF A DIAGNOSTIC LABORATORY IN THE MANAGEMENT OF DIABETES MELLITUS

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ABSTRACT
Objective: To elucidate the role of a modern diagnostic laboratory in the management of diabetes mellitus

Sources of Data: Available literature on local and international studies on the role of the laboratory in the management of diabetes mellitus

Results: Preclinical diagnosis of diabetes mellitus, good monitoring of short, medium and long-term glycaemic control necessary to avoid diabetic complications in poor resource settings are now possible with modern diagnostic laboratories.

Conclusion: Creating the required awareness on the roles of a diagnostic laboratory in the management of diabetes mellitus is needed now more than ever before in resource poor nations otherwise the success achieved by the developed world where diabetic patients become insulin independent after islet cell transplant with glucocorticoid free immunosuppression cannot be attained in the near future.

Keywords: Diabetes mellitus, test utilizations (*Accepted 31 January 2007)*

INTRODUCTION

Diabetes mellitus is a major health problem both in the developed[1] and the developing countries[2-4] with its prevalence being on the increase[5]. The disease has been known to mankind for over 2000 years[6] but until recently, this global epidemic,[7,8] recognized increasingly as a major health problem in the developing countries was made to look like a disease of Europe and the Americas[6]. Poverty has made laboratories in this environment incapable of keeping pace with modern laboratory management of diabetes mellitus leading to underutilization of laboratory facilities where available, and making diagnosis of diabetes at the preclinical stage hardly possible [9-11]. The debt forgiveness of poor countries, including Nigeria, the sustained high price of crude oil and the global fight against corruption and bad governance are expected to raise the socioeconomic status in the poor resource countries leading to sedentary lifestyle and obesity known to increase the rising prevalence of type 2 diabetes mellitus. This will mean that the current services provided to people with diabetes will need to be revised in the now poor resource countries. Therefore, the review aims at highlighting the roles of clinical laboratory in the modern management of diabetes mellitus at preclinical and clinical levels of the disease, a necessary requirement at stemming the challenges of this global epidemic.

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ROLES OF CLINICAL LABORATORY IN THE MANAGEMENT OF DIABETES MELLITUS

Laboratory medicine, which is the scientific base for the practice of 21st century medicine, differentiates modern medicine from traditional medicine. While the roles of clinical laboratories in the management of diabetes mellitus are fully achievable in the developed countries, the same cannot be said for the developing economies. Amongst the roles of clinical laboratories in the management of diabetes mellitus are:

1. Preclinical diagnosis of diabetes mellitus

Preclinical diagnosis detects potential diabetics before the subject presents with clinical symptoms of diabetes mellitus. Waiting for the clinical features like polyuria, polydipsia, polyphagia, weight loss or the laboratory diagnosis of clinical diabetes mellitus like consecutive fasting hyperglycaemia above 7.0 mmol/l or unequivocal hyperglycaemia with the above symptoms delay the detection of potential diabetics. Delayed detection of diabetes generally promotes diabetic complication (s) known to raise the cost of management even in poor resource settings[9] where diabetic patients can hardly afford the cost of

of diabetic management. Markers of immune destruction of tissues or hormone responsible for the metabolism of glucose like islet cell auto antibodies, antibodies to insulin or its receptors, and antibodies to glutamic acid decarboxylase are present in about 90% of individuals with type 1 diabetes mellitus when fasting hyperglycaemia is initially detected[12]. Fasting hyperglycaemia diagnosing diabetes mellitus also occurs long time before the clinical features of diabetes mellitus, as only hyperglycaemia that has exceeded the renal threshold presents with poyuria which leads to the polydipsia, the early clinical presentations of diabetes mellitus. Conscious of the delay and the need to avoid the attendant complications arising there from, the American Diabetes Association has called for the screening of immune related markers in first-degree relatives of individuals with type 1 diabetes[13] for about a decade now. To move in pace with the global trend, it is time to create the required awareness for the early diagnosis of diabetes mellitus and monitor the introduction of appropriate management to avoid complications.

A. **Timely detection of immunological markers in potential diabetics**

Immunological markers can be detected early in the laboratories of developed countries, sometimes about a decade before the manifestation of clinical diabetes mellitus. Immunological markers of interest for the preclinical diagnosis of diabetes mellitus include:

Islet cell antibody. An antibody that slowly destroys the ß cells of the islet of Langerhans,which produces and secretes insulin. Depending on the severity and duration, the body insulin may be too low to maintain metabolic functions, leading to diabetes mellitus with the potential of developing complications if not properly controlled on time.

Insulin Auto antibody destroys already formed insulin, which leads to insulin inactivity.

Insulin receptor Auto antibody destroys the insulin receptor, which prevents the receptor-insulin binding required for insulin activity.

Anti glutamic acid decarboxylase is also an immunological marker for preclinical diagnosis of diabetes mellitus.

2. Screening patients at risk of diabetes mellitus

A population or an individual at risk of diabetes mellitus is screened for the disease. Subjects not at the risk of the disease could be screened periodically during medical check up. Screening has increased the rate of self reported diabetes mellitus in the developed countries,[10] which has made diagnosis of asymptomatic patients possible, unlike in developing countries where diagnosis is delayed to the extent of patients presenting for the first time not only with symptom [14] but also with lethal diabetic complication [10]. Women with poor obstetric historyor first-degree relative of diabetics need to be screened for gestational diabetes mellitus using 50g glucose dose irrespective of the time of last meal during the 18^{th} to 24^{th} week of gestation. Screening for gestational diabetes mellitus is important as early detection and strict glycaemic control protect both the foetus and the mother from complications. Therefore, obstetricians and chemical pathologists in developing countries need to develop the teamwork approach for the early detection and management of good glycaemic control to avoid diabetic complication during pregnancy. Access to point of care diabetic control facilities; search for diabetes mellitus during pregnancy and enlightenment of potential mothers for the need for screening are also recommended.

2. Clinical diagnosis of diabetes mellitus

Diabetes mellitus, being a chronic disease, demands for timely and precise diagnosis as mislabeling a patient has grave consequences. Diagnosis of clinical diabetes should not be based on a single hyperglycaemic glucose result in an

asymptomatic individual, but two consecutive results in the diagnostic ranges or an unequivocal hyperglycaemia in a symptomatic subject. Hyperglycaemia detected under acute infective condition, traumatic or stressful conditions like circulatory disorders are not conclusively diagnostic of diabetes mellitus.

The following diagnostic criteria are required for diagnosing the disease:

i. Classical symptoms of diabetes mellitus with casual plasma glucose level of $\geq$11.1 mmol/l. Casual glucose refers to the blood glucose estimated irrespective of the time of the last meal.

ii. Fasting plasma glucose equal to or greater than 7.0 mmol/l on more than one occasion or

iii. Two hour non-gestational oral glucose tolerance test that is equal or greater than 11.1 mmol/l on more than one occasion.

Values greater than the normal fasting blood glucose but lower than the diagnostic levels for diabetes are considered impaired fasting glucose, which is defined as fasting plasma glucose greater than the upper reference limit of fasting plasma glucose but less than 7.0 mmol/l, or and 2 hour OGTT between 7.8 and 11.0 mmol/l. Such individuals need to be monitored periodically for early diagnosis

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4. Monitoring diabetes mellitus

Monitoring the success of transplant of pancreas or of the transplant of islet cells of Langerhans involves the estimation of insulin and or C peptide. Fasting plasma glucose monitors short-term glycaemic control while intermediate and long term control are monitored by fructosamine and glycated haemoglobulin respectively. Complications of diabetes mellitus and those of therapy are also monitored by the clinical laboratory.

5. Classification of diabetes mellitus

Clinical laboratory is very essential in the classification of diabetes mellitus, as the disease is no longer classified based on the therapeutic needs but on its aetiopathologenesis.

- Type 1 diabetes mellitus. This encompasses the majority of cases, which are primarily due to pancreatic islet beta- cell destruction and are prone to ketosis. Laboratory also has a role in differentiating between autoimmune and idiopathic origin of this class of disease.
- Type 2 diabetes mellitus. This class results from relative deficiency in insulin secretion early in the disease, usually with insulin resistance. Later in the disease, absolute insulin deficiency results. It has been reported that insulin resistance is the primary defect, preceding the derangement in insulin secretion and clinical diabetes by as much as 20 years[15]
- Impaired fasting glycaemia, which classify individuals with fasting blood glucose values above normal values but below those diagnostic of diabetes
- Gestational diabetes mellitus, which also includes gestational impaired glucose tolerance. Close monitoring of both maternal and fetal clinical conditions need to be maintained by teamwork approach consisting of laboratory physicians with the other team members. Monitoring of maternal urinary glucose is not useful in the management of gestational diabetes mellitus, therefore; clinicians should desist from such practices.[16]
- Other specific types
  - Diseases of the exocrine pancreas
  - Genetic defects in insulin action
  - Genetic defects of the beta-cell function
  - Infections
  - Drug or Chemical induced
  - Genetic syndromes associated with diabetes
  - Uncommon forms of immune mediated diabetes
  - Other endocrine disorders associated with hyperglycaemia

Malnutrition related diabetes mellitus and impaired glucose tolerance tesclassification as impaired glucose tolerance is ts are now deleted from the observed in any hyperglycemic disorder. Classification is needed for the proper choice of therapy, anticipation of disease complications, its transmission and prognosis. Chemical pathology laboratory is needed to achieve these goals.

6. Acute management of diabetes mellitus

i. Acute management of diabetes requires the estimation of blood glucose concentration for short-term glycaemic control. Urine glucose is also estimated, a procedure that can be done by the patient even in a village setting. Negative urine glucose has the disadvantages of not differentiating between hypoglycaemia and normoglycaemia or even hyperglycaemia below the renal threshold. More so, by the time glycosuria is detected, the glycaemic control is already poor, a possibility for the development of diabetic complication.

ii. Measurement of ketone bodies in plasma and urine detects disease complication early enough for prompt management

iii. Estimation of the acid base status is useful in type 1 diabetes mellitus where diabetic ketoacidosis is a common and dangerous complication.

iv. Analysis of serum electrolytes to elucidate fluid and electrolyte derangement and guide its management.

Determination of plasma osmolarity detects type 2 diabetics at risk of developing hyperosmolar non-ketotic coma and guides management early enough for better outcome

7. Chronic management of diabetes mellitus

i. Determination of plasma glucose remains popular and gives the understanding of current level of blood glucose at the time of blood sampling.

ii. Determination of glycated proteins for the determination of short and long term glycaemic control.

iii. Determination of urinary proteins detects renal complications of the disease on time

iv. Tests for renal function to establish or otherwise renal complication of the disease that are common in poor resource settings

v. Tests for lipid profile to detect the metabolic syndrome X and other lipid derangements known to be associated with this disease.

vi. Tests for the success of islets or pancreatic transplants as indicated earlier.

vii. Checking for complications of diabetes mellitus

COMPLICATIONS OF DIABETES MELLIUS

Diabetic complication cuts across medical specializations including Chemical pathology, Nephrology, Neurology, Medical microbiology, Opthalmology, general and vascular surgery among

others. Following the demonstration of a correlationbetween blood glucose concentrations and the development of long term complications of diabetes,[17,18] more emphasis is mounted on monitoring glycaemic control to avoid diabetic complications.

- **Diabetic ketoacidosis**. Severe ketoacidosis is responsible for most deaths among patients with insulin requiring diabetes[10]. A common complication of diabetes mellitus occurring in insulin dependent diabetes mellitus when insulin is insufficient leading to metabolism of fat through ß-oxidation for alternative source of energy producing excess ketone bodies. Maintenance of good short and long term glycaemic control prevents diabetic ketoacidosis complicating diabetes mellitus. Severe cases of diabetic ketoacidosis are associated with coma.
- **Hyperosmolar Non Ketotic Coma**. It is a complication of diabetes mellitus that occurs when the insulin activity is enough only for fat metabolism but not to maintain glycaemic control thereby leading to hyperglycaemia and hyperosmolarlity without ketosis.
- **Hypoglycaemia.** This is a diabetic complication that occurs when there is overzealous theraphy for diabetes mellitus or appropriate drug ingestion without feeding. Tight glycaemic control in insulin dependent diabetics may be associated with a hypoglycaemic feature once a week.
- **Hyperlipidaemia**. Glycosylation of low density lipoprotein prevents its uptake and clearance from blood by receptors and catabolizing enzymes[19].
- **Infection.** Glycosulation of proteins include immunoglobulins, which causes dysfunction of humoral immunity leading to infection among other causes
- **Retinopathy**. This complication is encountered by about one third of diabetic patients. The retina and the lens are damaged through the polyol pathways dysfunction which leads to excess accumulation of sorbitol that damages optic tissues[20].

- **Neuropathy** is more likely to affect long-standing diabetics and those with sustained poor glycaemic control. Neuropathy causes: numbness, urinary bladder dysfunction, paralysis, prickling, tingling, burning aching or sharp jabs of needle like pain is a complication of diabetes occurring in two[21] to thirty[22] percent of diabetics depending on the prevalence of complications in the study location. Painful sensory symptoms and anaesthetic foot contribute significantly to morbid foot problems,[23,24] which simple screening has been shown to reduce amputation rates significantly. Diabetes is preventable even in high risk individuals[25] when the clinical laboratory takes up its appropriate roles in the management of diabetes mellitus.

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