Approach to Diabetes Diagnosis: A Review

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Abstract: Diabetes mellitus, a global epidemic non communicable condition which has affected about 431 million total number of people according to Atlas, 8th edition 2017. Most of the times is diagnosed late, the longer the disease the higher the risks of complications. The patient seek medical assistance at any health care services when either has been alarmed with strange symptoms happening on his body or a result of diabetes disease has occurred on his body and that prompt the investigations which lead to diagnosing the disease. Symptoms like polyuria, polydipsia, and retinopathy are some of the few things a patient presents with in front of health practitioner. There are many types but classified into type 1 and type 2, Insulin dependent and Non-insulin dependent respectively. Other conditions are in transition that is can either develop disease or not but most important thing is to monitor such clients. Blood sample is the specimen that is used to check for glycaemia. The commonly used tests to diagnose diabetes are Oral Glucose Tolerance Test, Fasting blood sugar, Random blood glucose and glycated haemoglobin. Urine can also be used to semi-quantitatively detect sugar in the urine and that will give a good picture of the status of the condition. Most importantly, prevention of complications of the disease will do a great benefit to the health of patient. The results of complications include damage of the nerve, cardiovascular disease, eye problem and kidney problems Therefore, diagnosing and monitoring of condition by employing glycated haemoglobin is crucial. This will help clinicians have a picture of the past 90-120 days of glycaemia and obtain quick results that will help to improve patient care.

Key words: HBA1c = Glycated Haemoglobin, NIDDM = Non-Insulin Dependent Diabetes Mellitus, IDDM = Insulin Dependent Diabetes Mellitus

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Introduction.

Diabetes a non-communicable disease due to metabolic disorder, carbohydrates and lipids are imbalance due to disruption in insulin function resulting to excessive urinary excretion of glucose, hyperlipidaemia and hyperglycaemia. Lifestyle and inactive of people in industrialised world contributes to escalation of the disease. It is major public health concern to the public with social-economic impact, cost of life and health complications. 2.1 Million People die each year of non-communicable disease, diabetes, the ninth leading cause in women entire world (WHO, 2017) and over 199 million are living with diabetes which will upsurge to 313 million by 2040. The young aged 10-19 years reported an annual increase of 7.1% and 1.4% in 2011-2012 in both types 2 and 1 diabetes respectively (Mayer-Davis et al., 2017). 431 million total number of people aged between 18 to 99 years are living with diabetes and those who die of diabetes are under the age of 609 (ATLAS, 8th edition, 2017)

Complication: The persistent rise of blood glucose the blood becomes more viscous and makes flow of blood difficult in small capillaries thereby reducing circulation which will result in progressive vascular complications that will lead to retinopathy, neuropathy and nephropathy the end of it all is death of course. Therefore it is paramount to detect and diagnose the condition at earliest as possible to minimise the complications. There are situations that a patient may not show disease symptoms but present to the clinic with complications of the disease like in type 2 diabetes. On the other hand, the patient seeks health services because of symptoms occurring on his/her body such as polyuria, polydipsia and polyphagia. As such a patient has to go under blood test to confirm the disease; the paper is to present the blood test that should be performed to diagnose diabetes mellitus and an overview of types of diabetes mellitus.

PATHOPHYSIOLOGICAL The pathophysiological mechanisms of diabetes have been explained and these are the key points (a) Pancreatic beta cells secret reduced levels of insulin (b) The alpha cells secret elevated glucacon(c) High glucose production from the liver (d) Increased renal glucose reabsorption (e) The incretin effect on small intestines is reduced (f) The peripheral tissues such as skeletal muscles have impaired or reduced glucose uptake.

It is encouraged and essential for the patients with diabetes to have regular self-monitoring especially those on intense insulin regime for it helps to monitor and prevent hyperglycaemia and possible effects of hypoglycaemia. Besides monitoring for the development of impediments such as retinopathy, neuropathy and renal diseases. It is statistically projected of type more than 70 percent of type 2 diabetic patients shall be in developing countries by 2030. The international Diabetes Federation(IDF) registered the affected 387 million people worldwide and estimated more than 592 million to be affected by 2035(C.Gutierrez-Rodelo, et al.,2017),2.2 million deaths (WHO,Diabetes,2017) and global health care expenditures of 79 percent on diabetes (Atlas,8th edition,2017).Figure 1 and 2 shows the total number of people living with diabetes and undiagnosed cases respectively.

CLASSIFICATION OF DIABETES

The main primary classes of diabetes mellitus are defined by either failure of insulin production by pancreas or failure of peripheral responses to insulin. These are type 1 and type 2 respectively, the former type is known to result to ketoacidosis, if untreated and symptoms such as loss of weight, thirst and bountiful urination force the patient to seek medical attention, the latter is prevalent form of the disease which most of the times show no symptoms and some patients seek health services because of its complications such as heart attack, gangrene and visual loss.(WHO, 2016).In diabetes conditions women have profound difficulty in conceiving and the outcomes may be poor. Lack of proper health services interventions type 1 and type 2 diabetes can yield significant risks of maternal and child morbidity and mortality.
Shaw et al., 2018

Fig. 1 – Total number of people living with diabetes by IDF region, 2017 and 2045 (18–99 years).

Fig. 2 – Number (in millions) and proportion (%) of undiagnosed diabetes cases per IDF region, 2017 (18–99 years).

Shaw et al., 2018
TYPES OF DIABETES MELLITUS

Diabetes Mellitus can be classified as idiopathic and secondary.

**Idiopathic:** It is categorized into two namely insulin dependent usually referred as type 1 diabetes. In absence of Insulin therapy it progresses to a condition known as ketoacidosis. It is also called juvenile onset just because it is often manifested in childhood. The condition results from destruction of the beta-cells of the pancreases by autoimmune antibodies. The other one is type 2 also referred as Non-Insulin-dependent diabetes. It is hardly lead to ketoacidosis but is known to having persistent hyperglycaemia. It is noticeable after age of 40 and hence the name adult onset-type diabetes. Obesity has been associated with this type of diabetes especially in Industrialised countries incidences are escalating in pre and post pubescent children. Genetic defects have also been associated with the problem causing resistance of insulin and insulin deficiency. Type 2 is known to have late onsets and has been divided into two groups that associated with obesity and the other not associated with obesity.

**Secondary:** These are other types of diabetes which are due to different causes such as:

1. **Maturity onset of the young (MODY).** This type of diabetes is caused by mutation in more than 14 different genes. The patients have impaired beta cells function, insulin resistance and late beta-cell failure.

2. **Pancreatic disease:** The conditions like cystic fibrosis and pancreatitis can also lead to damaging the normal function of pancreas. And also removal of pancreas pancreatectomy

3. **Endocrine disease:** When tumours are releasing counter-regulatory hormones that antagonist the action of insulin or inhibit the secretion of insulin. For example glucagon secreted by pancreatic cancer glucagonomas, epinephrine secreted by pheochromacytoma growth hormone in acromegaly and cortisol is excessively secreted in Cushing syndrome.

4. **Drug-induced diabetes:** The use of glucocorticoids and diuretics can interfere with insulin performance.

5. **Anti-Insulin receptor Autoantibodies also termed as Type B insulin resistance**

6. **Mutation in the Insulin receptor gene (INSR):** These have been observed in Donohue syndrome, Rabson Mendenhall, and Type A Insulin resistance syndrome.

7. **Gestational diabetes.** It sets on during pregnancy and after birth it resolves itself. Diabetes in pregnancy is diagnosed in 24th to 28th week which was not evident prior to gestation. (Association, 2017) (Sastre *et al*., 2017)

8. **Many other genetic syndromes.** (Michael W King., 2018)

**Type 1 - IDDM**

This class of diabetes is Insulin dependent. Type 1 has been indicated to be caused by autoantibodies reaction to antigens of the islets cells of the pancreases. There are three types of autoantibodies associated with Insulin Dependent Diabetes Mellitus IDDM namely cytoplasmic antibodies and surface antibodies cellsof Islets and Specific antigenic targets of islet cells.
Pathophysiology of Type 1 Diabetes: Pancreatic beta-cells are attacked and destroyed by autoimmune antibodies the cells responsible for insulin secretion and that lead to metabolic disorders. And because of loss of insulin secretion usually glucagon is also uncontrollably secreted due to abnormal functioning of pancreatic alpha cells in IDDM patients that aggravates metabolic deficiencies. It is therefore linked with complications like aging and osteoporosis (McCabe, 2007). In addition, there is anomaly that the target tissues cannot respond to administration of insulin. Then, will be rise of free fatty acids in plasma due to failure of controlling lipolysis in adipose tissues. The main metabolic disorders resulting from insulin deficiency are protein metabolism, lipid metabolism and glucose metabolism (McCabe, 2007).

Type 2 diabetes

Aetiology: The organ secretes inadequate insulin. The shortage, in this case, to prevent ketoacidosis, it’s not an autoimmune disorder and is a form of idiopathic NIDDM and strongly correlated to heterogeneity of the genes responsible for the susceptibility to NIDDM and the major predisposing factor being obesity. It is also known as non-Insulin dependent diabetes

Pathophysiology: In type 2, there is circulating insulin that is measurable. Others had demonstrated and found that average patients with type 2 had insulin resistance and insulin deficiency. Type 2 has main complications resulted from persistent hyperglycaemia which comes along with pathophysiological consequences. The raise of blood glucose the blood becomes more viscous and makes flow of blood difficult in small capillaries thereby reducing circulation which will result in progressive vascular complications that will lead to retinopathy, neuropathy and nephropathy. Inflammatory markers like tumour necrosis factor receptor 1 were found elevated and linked with advancement of renal ailment and death in type 2 nephropathy (Javieret et al., 2017). Poor wound healing and erectile dysfunction have been mentioned as well. (Michael W King, 2018) compromised bone microarchitecture due to induced abnormal bone cell function and matrix structure, affecting bone homeostasis. (Sanches et al., 2017).Type 2 (DM2) the commonly known endocrine disorder in humans. The risks of the disease are determined by relationship with other factors such as family history of diabetes, ethnicity, metabolic factors, genetics, and history of diabetes in pregnancy with old age, obesity, poordiet, lack of body exercise and smoking (WHO, 2016).In other studies demostrated the relationship with body mass index,circumference of the waist, visceral and body fats,weight of the body and concluded that had a significant association with insulin persistance (Kurniawan et al., 2018).Sometimes there is intermediate conditions in the transition between normality and diabetes the state is termed impaired glucose tolerance (IGT) and Impaired fasting glycaemia (IFG).The state is likely to progress to type 2 diabetes,although is not predictable (WHO 2017).

Hyperuricemia in Diabetes: Studies have found some correlation between joint problems and high serum uric acids in diabetes mellitus (Hessein, 2007), and enhance the effect of insulin resistance on renal urates absorption resulting to glucose intolerance  (Nyenwe EA, 2016) in hypertensive patients it has been associated with cardiovascular risks (Chaudhury et al., 2017).
MANAGEMENT IN TYPE 2

The more effective oral pharmacologic therapy with less adverse effect is metformin. It does not result in gaining of weight besides its economical unless contraindicated. Efficacy can be improved with addition of second agents to it like co-transporter for example -2 (SGLT-2) and class of drugs inhibitors for example dipeptidyl peptidase-4 (DPP-4) (Amir et al., 2017) It’s advisable that elderly taking Metformin should be checking vitamin B12 and folic acid levels for its known to reduce such elements. (Chaudhury et al., 2017). Lifestyle has been one of the contributing factor to development of this non communicable disease, Proper adherence to pharmacological therapy routine glucose monitoring and interventions in lifestyle have been cost-effective on managing and delaying the onset of the condition with 58 percent in risk reduction for 3 years (Chaudhury et al., 2017). During pharmacological management in Type 2 Diabetes mellitus, there have been life threatening moments that leads to hyperglycaemia occurring in Isolation or in combination.

DIAGNOSIS

There are criteria used in diagnosis of diabetes. The fasting serum or plasma glucose must be elevated greater than 126mg/dl, a 2 hour postpragial glucose upon a 75-grams oral glucose administration (Oral glucose Tolerance Test be equal and greater than 200mg/dl; a random serum or plasma glucose be greater than 200gm/dl alongside signs and symptoms of hyperglycaemia, gestational diabetes medical conditions appearing in 24th to or 28th week of pregnancy as well as cystic fibrosis disease of pancreases. Glycated haemoglobin (HBA1c) is another diagnosis indicator if elevated greater than 6.5% (WHO, 2011). Haemoglobin glycation is a wholly glucose that is attached to haemoglobin protein (Michael W King, 2018). A marker reflecting how much blood glucose you have had over a past period of 90 to 120days glycaemia however International Expert committee don’t recommend it in diagnosing Type 1 diabetes Mellitus and gestational diabetes (Standards of medical care in diabetes, 2016) (Chaudhury et al., 2017; Lekva et al., 2018). HBA1c found in blood is directly related to the amount of blood glucose. The lifespan of red cells is estimated around 120 days so the HBA1c giving blood glucose levels for the same past period. In cases of anemia, there are changes in red cells hence affect HBA1c results. HBA1c Interpretation: For diabetic patient it should be aimed at levels between 6.7-7.0%. If the result are higher than 7% indicating hyperglycaemia, the treatment could be revised. In other words chances are higher of developing complications of the eyes and kidneys. The HBA1c value of 6.5% or more can indicate transition diabetes, in such cases other additional sugar test should be performed. However, HBA1c of less than 6,5% is desirable for nondiabetic person. Serum ferritin has been noticed to be accumulating in diabetes cases as the condition progresses. Glucose Intolerance in these cases is accompanied with developing of hemochromatosis and Iron store in the body. It had positive correlation with glycosylated haemoglobin and fasting Blood sugar (Raj S et al., 2013). The experts encourages that each primary care facility should have basic essential to quantify and qualitative glucose such as glucometer, blood glucose test strips, urine protein and ketone test strips, measurement tapes and weighing machine (WHO, 2017).

CONCLUSION: The prevalence of the disease is escalating and the complications are immense that hump social-economic activities, developments, cost of life and many more are affected worst still morbidity and mortality is mounting. Early detection and diagnosis is encouraged as would relieve the burden and improve quality of life. If molecular approach could be further investigated I presume it would bring favourable solutions
and ease the problems. HBA1c is a vital test that does not require someone to fast and can be performed at any time. It requires minimal amount of blood, no need to separate to either extract plasma or serum. Although it is not encouraged to use the test in type 1 and gestational diabetes for diagnosis. It is a good test to monitor glycaemia which always come along with complications of kidneys, eyes and neurons.

REFERENCES


