Flaws in Diagnosis and Outcome of Diabetes

Anil K. Mandal

Abstract

Diabetes mellitus or sugar diabetes or diabetes as most commonly described is very common in medical practice. However, some of them don't have established diabetes. Therefore diabetes is definitely not epidemic. Publicity of epidemic of diabetes comes from wrong diagnosis of diabetes. Elevated fasting blood glucose is very commonly due to antihypertensive drug therapy including beta blocker, calcium channel blocker and most commonly a thiazide diuretic, hydrochlorothiazide or chlorthalidone. Therefore the first step to determine if the patient has established diabetes is to temporarily discontinue the blood pressure lowering drug and repeat basic metabolic panel in the fasting and 2-h post prandial periods in 2 weeks. Thereby the diagnosis of diabetes will be proved or disproved. Hence it is a mistake to prescribe an oral anti diabetic agent without a proven diagnosis of diabetes. It is important to remember that many complications of diabetes emerge in course of time due to wrong diagnosis and wrong treatment in the first place.

Introduction

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia (high glucose level in the blood) and glycosuria (variable amount of glucose in the urine) and is due to deficiency of insulin secretion from pancreas [1]. The chronic hyperglycemia is associated with long term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels [2]. DM remains undetected for a long time in particular in middle aged or elderly subject because hyperglycemia manifests soberly in order age groups. In children or young adults, hyperglycemia produces explosive symptoms such as polyuria, polydipsia and rapid weight loss which force family to seek medical advice resulting in diagnosis of DM. On the other hand, adults seek medical advice for urinary retention (neurogenic bladder), erectile dysfunction, and chest pain or decreased vision and found to have DM for the first time. More often adults are brought into the hospital in poor condition and found to have diabetic ketoacidosis, infected foot ulcer or gangrenous foot or toes and associated renal failure.

Many adults manifest typical symptoms of DM such as polyuria, polydipsia and rapid weight loss like those in adolescents but they refrain from going to the doctor or hospital because they don't have health insurance and have no means to pay to the doctor or to hospital. Some patients who have developed symptoms of DM had gone to family health clinic where they received a diagnosis of Type 2 DM and automatic prescription of metformin and Lisinopril. In course of time, some of them will develop one or more complications and then received a prescription of insulin therapy. The problem is it is too late to start insulin therapy because damage has set in the organs by uncontrolled hyperglycemia.

The delay in diagnosis and delay in initiation of insulin therapy are mainly due to the prevailing gaps of knowledge among the professionals, too much weight put on DM Type 1 and Type 2 classification and total reliance on fasting blood glucose (FBG) or glycosylated hemoglobin (HbA1c) to determine glycemic control. According to World Health organization (WHO), Type 1 DM encompasses the vast majority of cases that are primarily due to pancreatic let beta cell destruction and they are prone to develop diabetic ketoacidosis. This form includes both children and an unspecified number of adults. The class Type 2 DM includes the most prevalent form of DM. Patients with this form of DM are generally overweight or obese and associated with high insulin or insulin resistance.

Analysis of Pitfalls of Diabetes Classification

1. It is very difficult to distinguish clinically between Type 1 and Type 2 DM. Age is not a determining factor.
2. The glycemic pattern of Type 1 and Type 2 DM is very similar. 2-h post prandial glucose (2hPPG) characterized by glucose level of ≥ 200mg/dL (≥11.1 mmol/L) is the hallmark of diagnosis of diabetes mellitus.
3. Elevated glucose level is adults is wrongly diagnosed as Type 2 DM. Elevated glucose level is very commonly due to a variety of medications. The most common medicine is diuretic, hydrochlorothiazide or chlorthalidone. If no medication is found to account for high glucose, patients should undergo 4-h oral glucose
tolerance test 1-h glucose and more importantly 2-h glucose level in excess of 200 mg/dL (11.1 mmol/L) characterizes diabetes mellitus and not Type 1 or Type 2 diabetes mellitus.

4. Obesity is frequently associated with impaired glucose tolerance mimicking diabetes with 2-h postprandial glucose level ≥ 200mg/dL. This hyperglycemia connoted as Type 2 DM undergoes resolution following bariatric surgery. Thus a strong argument can be made that Type 2 DM is not diabetes but a surrogate of metabolic syndrome. 5. The vast majority of patients treated in the office have their FBG and 2hPPG out of range despite insulin therapy because of noncompliance in diet. Hypoglycemic peaks caused by insulin therapy falls short of hyperglycemic peaks produced by big meals.

6. Very few adults who have confirmed diabetes are obese and not insulin resistant. However, it has been noted that with insulin therapy, glucose tolerance improves requiring progressively lower dose of insulin. This was also noted by Frederick Banting [1].

Logistic Approach to Diagnosis and Treatment of Diabetes and Risk Analysis

Like uncontrolled or untreated diabetes, diabetes treated with one or more oral anti diabetic agents is associated with a high risk to develop one or more micro vascular complications. On the other hand, treatment of diabetes with insulin therapy offers protection against micro vascular complications. The most common practice is to order HbA1c to assess glycemic control because it is a convenient test and universally available. Very little information is available with regard to relationship of glycemic control determined by HbA1c or FBG and outcome measures.

Little information is available with regard to outcome measures in diabetes except cardiovascular outcomes. All cardiovascular outcomes namely myocardial information, cerebrovascular disorders are related to 2-h post prandial glucose (2hPPG). To that effect, Decode study group has shown that the risk for cardiovascular death increases 3-fold as 2-h post challenge glucose levels increase from 54 to 199 mg/dL, although these levels are all in the non diabetic range. Data were adjusted for age, gender, weight, systolic blood pressure, cholesterol and smoking during the 11 years of follow up for 29,714 patients in the Diabetes Epidemiology collaborative Analysis of Diagnostic criteria in Europe [2].

Cardiovascular disorders are common in diabetes and most other studies like Decode have shown that 2hPPG above 200 mg/dL is associated with a high risk of mortality [3]. Renally, we have shown that renal function decreases with elevation of glucose at 2 hrpost prandial period. Although the difference was not significant comparing serum creatinine or estimated glomerular filtration rate (eGFR) between fasting and 2-h postprandial peroid, but by innovating delta (d) glucose we found significant elevation of serum creatinine or decrease of eGFR in the post prandial period [4]. Post prandial hyperglycemia has been reported by other authors as a critical factor in diabetic complications [5].

Despite prevailing information about the importance of 2hPPG in diabetes care, providers are educated to order HbA1c every 3 months to assess glycemic control. Here again comes the commercial interest as a guiding principle in diabetes care.

Most oral anti diabetic agents reduce HbA1c, an effect that make providers happy that the patients are doing well and conveys jubilation among the pharmaceutical companies. However, this joy is superficial as no correlation is found between HbA1c and renal function tests. There may be correlation between FBG, 2hPPG and HbA1c but renal function deteriorates as a result of uncontrolled post prandial hyperglycemia [6].

Hindrances to Effective Control of Diabetes Mellitus

It is imperative that we strive for early detection and treatment of DM, so that complication may be averted. Treatment of DM and its complication are costly, the cost analysis of Medicare from 1993 to 2011 shows progressive increase in cost of care for DM. This is due to treatment of its complication for instance, chronic kidney disease (CKD) and limb amputation. The Los Angeles Times as of 2009 shows that the US rate of amputation from complication of DM has seared, approaching 100,000 annually. All these complications are due to inappropriate diagnosis and inadequate therapy. Here is an example of fallacy of diagnosis of diabetes.

Patients Has A Basic Metabolic Panel Drawn In The Fasting State Diagnosis: Diabetes Fallacy

1) Sensitivity 31%
2) Specificity 100%

This test is not sensitive because the elevated glucose could be due to other causes as already discussed. The most common cause of elevated fasting glucose is diuretic therapy. Therefore the diagnosis of DM made in this patient is due to lack of knowledge among the professionals. A group of investigators from Italy studied the outcomes of new onset-diabetes in treated hypertensive subjects compared to those with previously known diabetes. They found that subjects in whom diabetes developed were exposed to diuretics, calcium channel blockers and angiotensin converting enzyme inhibitors more frequently than in those in whom diabetes did not develop [7].

Steps to Be Taken to Avoid Any Error in Diagnosis and Treatment of Diabetes

1. It will be a serious mistake to put a label of diabetes by the finding of elevated blood glucose level at the first instance
2. Take time to check all medicine, Patients may be taking a thiazide diuretic or a beta blocker for control of hypertension. Hypertension is much more prevalent than diabetes
3. For the above, drugs must be discontinued for a period of 2 weeks and repeat fasting glucose and 2hPPG. The dilemma will be settled if both FBG and 2hPPG are normal.
4. You may order HbA1c but it will add nothing to the diagnosis
5. Avoid labeling Type 1 or Type 2 diabetes. This classification adds nothing to diabetes care. It is more appropriate to state diabetes or no diabetes based on 2 hPPG
6. It is important to remember that anyone with established diabetes has a high risk of developing complications if diabetes is not treated with insulin.

References

1. Frederick Banting (1925) Diabetes and Insulin Nobel Prize speech delivered in Stockholm.