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Dilemma in Diabetes Care Relates to Its Complications: Strategies for Prevention

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Abstract

The dilemma concerning the prevailing classification of Type 1 and Type 2 diabetes is a serious hindrance to effective diabetes care. Many patients who are classified with Type 2 diabetes have symptoms and require treatment similar to those classified with Type 1 diabetes. In addition, patients are often diagnosed with diabetes as a result of elevated fasting blood glucose instead of 2-hour postprandial glucose levels or oral glucose tolerance tests. The misdiagnosis of diabetes accompanied by prescription of oral hypoglycemic agents or antihypertensive therapy, have caused unwarranted health problems in people who may not have diabetes.

In this article, patients are presented who illustrate the misdiagnosis of diabetes and the need of proper testing to uncover diabetes. Additional case histories indicate the effect that oral hypoglycemic agents and antihypertensive medications may have on patient health. Suggestions are made regarding proper diagnosis and care. In patients with established diabetes, adequate control of glycemia with insulin, diet restriction and weight reduction, fundamental to prevention of microvascular and macrovascular complications, is stressed. Hospitalizations are preventable if professionals spend time explaining details of diabetic care to patients thereby enabling them to take full responsibility of their illness. Glucose control with insulin therapy, concomitantly with means for weight reduction in obese individuals, must be discussed in a repetitive fashion with the patient. Uncontrolled diabetes, resulting in frequent hospitalizations for a variety of complications, has markedly escalated the cost of diabetic care. Patient education and cooperation are the cornerstone of successful diabetes therapy and the mainstay of prevention of diabetes complications. Thereby, the cost of diabetes care will be reduced.

The classification of Type 1 and Type 2 diabetes conveys little to the patients about diabetes which is a potentially devastating disease, nevertheless, with full attention to glucose control, healthy living is attainable. Utmost care should be taken to identify if the person does or does not have diabetes by appropriate testing and attention to proper therapy.

Keywords: Diabetes, insulin therapy, 2-hour postprandial glucose, glycosylated hemoglobin, oral glucose tolerance test

Introduction

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycemia or raised blood sugar is a common effect of uncontrolled diabetes and over time, leads to serious damage to many of the body's systems, especially the nerves and blood vessels (WHO) [1]. The World Health Organization (WHO) classifies diabetes as follows:

Type 1 diabetes, previously known as insulin-dependent, juvenile or childhood-onset, is characterized by deficient insulin production and requires daily administration of insulin.

Type 2 diabetes , formerly called non-insulin dependent or adult-onset, results from the body's ineffective use of insulin. Type 2 diabetes comprises 90% of diabetic patients around the world, and is largely the result of excess body weight and physical inactivity. Symptoms may be similar to Type 1 diabetes, but often less marked. As a result, the disease may be diagnosed several years later, once complications have already arisen.

Gestational diabetes is hyperglycemia with onset or first recognition during pregnancy

The prevailing classification of diabetes, into Type 1 and Type 2 diabetes, limits a complete understanding of diabetes and creates a serious dilemma in treatment. According to the WHO diabetes fact sheet (2012), until recently, Type 2 diabetes was seen only in adults but it

is now also occurring in children. Because this does not follow the current classification of diabetes, it may be more appropriate to connote the diagnosis of diabetes rather than Type 1 or Type 2 diabetes. This connotation of diagnosis is quite appropriate as an undefined number of adults appear in the emergency rooms of local hospitals with a history of polyuria and polydipsia mimicking Type 1 diabetes and consequently are found to have severe hyperglycemia. Furthermore, these patients require daily insulin injections to keep hyperglycemia under control and to remain symptom free, identical to those with Type 1 diabetes (WHO).

Typically adults with elevated fasting blood glucose (FBG) levels > 126 mg/dL (> 7mmol/L) irrespectively are diagnosed with Type 2 diabetes and automatically prescribed one or more oral hypoglycemic agents (OHA) by doctors or more often by the physician-assistants or nurse practitioners. These OHA are biguanides (metformin), sulfonylurea, (glyburide, glipizide or glimepiride), thiazolidinedone (rosiglitazone or pioglitazone) or more recently dipeptidyl-peptidase-4 inhibitor (sitagliptin or saxagliptin).

Diabetes is defined by a 2-hour postprandial glucose (2-hPPG) level of > 200 mg/dL (>11.1 mmol/L), determined by an oral glucose tolerance test, according to WHO [1] and others [2]. In most patients, since a diagnosis of Type 2 diabetes is made on the basis of FBG of > 126 mg/dL (7 mmol/L) or glycosylated hemoglobin (HbA_1c) > 6.5%, and not by 2-hPPG, it is difficult to ascertain how many patients with the diagnosis of Type 2 diabetes actually have well-defined diabetes.

The purpose of this communication is to develop a critique of the prevailing classification of diabetes, into Type 1 and Type 2 diabetes, in order to improve the outcomes associated with uncontrolled diabetes. In addition, diabetes will be compared to merely elevated, fasting blood glucose levels (hyperglycemia). Common causes of fasting hyperglycemia are those induced by drugs, such as thiazide diuretics, steroids, or tacrolimus, mimicking diabetes. In this communication, the profile of several patients will be presented to exemplify misdiagnosis of diabetes and overenthusiastic prescription of OHA for the sake of prevention of diabetes. In addition, relevant testing to establish or exclude diabetes and individualization of therapy based on 2hPPG will be described. The author's (AKM) practice is limited to adults with diabetes.

Patient presentations

Patient #1: This patient reveals ambiguities in the diagnosis of diabetes. A 70 y white male, weighing 261 pounds, was referred to the author in April of 2007 for diabetic neuropathy and pain and swelling of the lower extremities. His medication at the first visit consisted of dutasteride 0.5 mg PO daily, gabapentin 300 mg PO daily, furosemide 20 mg PO daily, pioglitazone 15 mg PO daily, lansoprazole 40 mg PO daily, amitriptyline 25 mg at bedtime daily, and simvastatin 20 mg PO daily. He showed prominent varicose veins in both lower extremities, and decreased deep tendon reflexes suggesting neuropathy. His sitting blood pressure (BP) was 120/80 mmHg. Initial laboratory could not be obtained except for HbA_1c of 5.8%. He was treated for Type 2 diabetes with pioglitazone. The first action was to discontinue furosemide for 5 days and obtain FBG, 2-hPPG, HbA_1c, and renal function parameters. They were 107 mg/dL (5.94 mmol/L), 145 mg/dL (8.05 mmol/L), 6.0% and eGFR > 60 ml/min, respectively. Thereafter, pioglitazone was put on hold for 8 days. After 8 days, FBG, 2-hPPG, HbA_1c and 24 h urinary studies were done. Results were 108 mg/dL (6 mmol/L), 121 mg/dL (6.72 mmol/L), and 6.1%, respectively. Thus, 2-hPPG was lower without pioglitazone than with pioglitazone. FBG and HbA_1c were the same with and without pioglitazone. His 24-hour urine protein was 150 mg and creatinine clearance 158.4 ml/min.

Thus, based on laboratory findings, it was safe to state that the patient did not have diabetes. The question remains, why did he develop neuropathy? Could he have pre-diabetes with a high insulin response? A 4-hour oral glucose tolerance test (OGTT) was done and results are shown in **Table 1**.

Surely OGTT was abnormal. The 1-hour glucose level was consistent with diabetes but this increase was not sustained. He showed a high insulin response with a decrease in glucose levels after 1 hour. He was recommended a 1600 calorie diabetes diet. He is doing well. It is important to note that the patient was needlessly taking pioglitazone, which causes swelling of the lower extremities.

Patient #2: This patient exemplifies that complete testing for glycemic parameters in an obese individual may uncover diabetes.

A 78 y African American male, weighing 228 pounds, had an office visit with the author during the first week of May, 2008. The patient had a history of uncontrolled hypertension, but no history of diabetes. Sitting and standing BPs were 140/90 mmHg and 150/90 mmHg, respectively. Medication

Table 1. Results from a 4-hour Glucose Tolerance Test (Patient 1)

Time after Glucose Ingestion (hours)	Glucose (mg/dL)	Glucose (mmol/L)
FBG	116	6.4
1	214	11.8
2	113	6.27
3	105	6.0
4	104	5.7

FBG = Fasting Blood Glucose

included clonidine 0.1 mg PO BID and diltiazem 240 mg PO daily. Actions included increasing clonidine to three times daily and ordering a blood count and serum chemistry.

A laboratory study done at the end of July, 2008 showed FBG 162 mg/dL (9 mmol/L), 2-hPPG 214 mg/dL (11.8 mmol/L), HbA_1c 7.5%, C-peptide 1.2 ng/ml (n=0.8-3.1 ng/ml), BUN 12 mg/dL, serum creatinine 1.30 mg/dL, and eGFR > 60 ml/min. Hemoglobin was 17 g/dL. At this time he was considered to have developed diabetes based on 2-hPPG, but he had no discernible complications. Because a robust association exists between an elevated 2-hPPG and cardiovascular disorders (CVD) [3], it was felt that keeping his 2-hPPG under control with antidiabetic therapy was important. Thus he was prescribed glyburide 5 mg PO after lunch and dinner. He was also prescribed enalapril, 5mg PO, daily to reduce hemoglobin which may further reduce BP [4,5].

He was seen in the office in the first week of May, 2009. Sitting and standing BPs were much reduced. They were 120/70 mmHg and 130/70 mmHg, respectively. His 2-hPPG was 92 mg/dL (5.1 mmol/L), eGFR > 60 ml/min, and hemoglobin 14 g/dL [4,5]. The therapy was working perfect for him. Diabetes was not considered by previous physicians and blood pressures were not under control however, glycemia and hypertension were brought under control which will reduce his risk of CVD.

Patient #3: This patient represents a typical case of drug-induced hyperglycemia but not diabetes. A 65 y African American female was referred to the author for obesity, hypertension and renal insufficiency in October 2010. Her medication consisted of hydrochlorothiazide (HCTZ) 25 mg PO BID, slow K 10 mEq PO BID, amlodipine 5 mg PO BID, amiloride 2.5 mg PO daily and magnesium oxide 400 mg PO TID. She was taking all these medications since December of 2004. Her laboratory and change of therapy are shown in **Table 2**.

Normoglycemia observed in September and November, 2011 after discontinuation of Triam/HCTZ documents that the patient does not have diabetes. As of September 2011, 2-hPPG of 207 mg/dL was clearly due to HCTZ, and will probably be interpreted by many professionals as Type 2 diabetes. Glucose levels did not increase with use of bumetanide suggesting that thiazide diuretics most commonly produce hyperglycemia mimicking diabetes.

The next two patient examples will reinforce the problems with the diagnosis of Type 2 diabetes and hence-forth initiation of therapy with oral antidiabetic agents which eventually results in severe diabetes.

Patient #4: Presented is a 33 y African American female weighing 240 lbs, diagnosed to have Type 2 diabetes and treated with OHA. She was first seen by the author (AKM) at the end of May, 2011 for diabetes. She gave a history of gestational diabetes and hypertension during each of two pregnancies. Both babies were big. She also gave history of seizures. Her medication at the time of her first visit were metformin 500 mg PO BID, Lisinopril 20 mg PO daily, Escitalopram 20 mg PO daily, and Levetiracetum 1000 mg PO BID (for seizures). Her laboratory from mid-April 2011 showed FBG 134 mg/dL, HbA_1c 6.1%, eGFR 87.3 ml/min. Her BUN and serum creatinine were 13 and 0.90 mg/dL, respectively. It was doubtful if she had diabetes, however she was advised to continue metformin until the next visit. Lisinopril was discontinued and atenolol 25 mg PO daily was prescribed for blood pressure control. One month later, her FBG, 2-hPPG, and HbA_1c were 126 mg/dL, 179 mg/dL and 6.6% respectively. Renal function improved, BUN, serum creatinine and eGFR were 9 mg/dL, 0.70 mg/dL and > 110 ml/min, respectively. It is evident that Lisinopril decreased renal function. Blood pressure was elevated

Table 2. Drug therapy, blood glucose, serum creatinine and potassium in a patient with drug-induced hyperglycemia (Patient 3)

Date	Therapy	Glucose (mg/dL)		Scr (mg/dL)		Serum K (mmol/L)	
		F	2-hPP	F	2-hPP	F	2-hPP
Dec 2004	HCTZ, SlowK, Amiloride, Amlodipine, MgOxide	104	ND	1.2	ND	3.6	ND
Feb 2005	Same as before	117	ND	1.2	ND	3.9	ND
Oct 2010	Triam+HCTZ (37.5/25) Mon,Wed,Fri	123	ND	1.3	ND	4.1	ND
Sept 8, 2011	Triam/HCTZ-NO Mon, Fri, Amlodipine 10 mg BID, Slow K	123	207	1.3	1.47	4.2	3.4
She was told by her primary physician that she was developing diabetes. Action: Hold Triam/HCTZ, add Aldomet 250 mg TID to control blood pressure, reduce KCl to 20 mEq once daily.							
Sept 23, 2011	Hold Triam/HCTZ	114	144	1.2	1.3	4.0	4.0
Actions: 1) Triam + HCTZ discontinued, 2) Bemetamide 0.5 mg PO Mon, Wed, Fri, 3) ↑KCl 20 mEq BID							
Nov 2011	Bumetanide	108	118	1.3	1.4	4.1	4.0

ND = Not Done Scr= Serum Creatinine F = Fasting 2-hPP = 2 hour Postprandial

but it was similar in both visits. Atenolol was increased to 50 mg/dL. At her next office visit in mid-August, 2011, her FBG and 2-hPPG had increased to 343 mg/dL and 302 mg/dL, respectively. Her BPs were further elevated. She was then-confirmed to have severe diabetes. The possibility remains that the beta blocker, atenolol, may have aggravated diabetes because of baseline elevated glucose levels [6] and probably because of impairment of pancreatic insulin release by a beta adrenergic receptor blocker [7]. In addition, she developed hypokalemia which further aggravates hyperglycemia [8]. Actions at this visit included discontinuation of metformin and initiation of Glargine insulin, 25 units after breakfast and 25 units after dinner [9]. She was advised to perform glucose monitoring at home upon wakening, 2 hours after each meal, and at bedtime. She was prescribed potassium chloride 20 mEq PO BID and amiloride 2.5 mg PO twice daily to minimize hypokalemia.

At a visit in early October 2011, her FBG and 2-hPPG were decreased to 177 mg/dL, and 199 mg/dL, respectively. Plasma renin and aldosterone were 0.1 ng/ml/hour and 4.7 ng/dL respectively. Her BP's were further elevated. Action included increase of atenolol to 50 mg twice daily, discontinuation of amiloride, prescription of triamterene/hydrochlorothiazide (Triam/HCTZ) 37.5/25 X1 PO daily, and increase of Lantus to 50 units after both breakfast and dinner. At a visit in late December 2011, her BP was still elevated at 140/100 mmHg. FBG and 2-hPPG were reduced to 142 mg/dL and 206 mg/dL, respectively. Clonidine 0.2 mg PO BID was added to her regimen. She returned at the end of February, 2012. Her diastolic BP remained elevated at 100 mmHg. Systolic BP ranged between 120 and 130 mmHg. FBG and 2-hPPG further decreased to 146 mg/dL, and 189 mg/dL, respectively. Her HbA_1c was 6.8% and average glucose 148 mg/dL. The 2-hPP serum potassium was 3.5mEq/L. At this visit, action included discontinuation of Triam/HCTZ, prescription of chlorthalidone 12.5 mg PO daily and spironolactone 12.5 mg PO twice daily. She had to be hospitalized for markedly elevated glucose levels of FBG 366 mg/dL and 2-hPPG 529 mg/dL which resulted from intake of a large dose of steroid. She had developed dermatitis of the hands and went to a local hospital emergency room where she was prescribed high dose of prednisone. Her latest office visit in early June, 2012 showed marked improvement of glucose control. FBG, 2-hPPG and HbA_1c were 130 mg/dL, 165 mg/dL, and 7.7% respectively. Her insulin regimen consisted of Lantus 50 units after breakfast and 55 units after dinner (12 hours apart) and regular insulin on a sliding scale determined by finger-stick glucose levels 2-hPP and at bedtime. Her BP is normal and she takes atenolol 50 mg BID, clonidine 0.2 mg twice daily, chlorthalidone 12.5 mg daily, and potassium chloride 20 mEq BID. Her renal function was normal with eGFR > 110 ml/min.

This patient illustrates that development of overt diabetes with insulin resistance may be an outcome in patients who had mildly elevated glucose levels initially but were treated with high doses of metformin which may cause exhaustion of beta cells over time and lead to overt diabetes [10].

Patient #5: There is much to learn from this patient history. This 59 y African American male had his first visit with the author (AKM) in mid-February, 2012. He is a good historian and exhibits much responsibility in his care. In 2008, he was found to have coronary artery disease and treated with stent placement. During this hospital admission he was told that he had diabetes. He recalled that prior to hospitalization, he used to urinate frequently and drink a lot of fluids. He further gave an interesting family history of diabetes. His sister had diabetes and was treated with metformin and Lisinopril. She developed acute renal failure (ARF) and died. His mother had diabetes, was treated similarly to his sister and she also developed ARF and died. These family events made him cognizant of mistreatment of diabetes giving rise to renal failure and death.

At this visit his BP was mildly elevated, 160/80 mmHg. FBG was elevated at 162 mg/dL but renal function was normal. Medication consisted of amlodipine 5 mg PO daily, metoprolol 25 mg PO daily, and clopidogrel 75 mg PO daily. He was taking, as prescribed, metformin 2000 mg PO daily, but discontinued six months prior to this visit because he felt that it was not helping to reduce his glucose level. He took Lisinopril 10 mg PO daily until he ran out of it. He did not renew the prescription because he had read that Lisinopril causes kidney problems. At the first office visit, he was advised to stay off metformin and Lisinopril but take amlodipine and metoprolol for BP control and return to the office with required laboratory studies. Laboratory findings, BP recordings and therapy of his office visits from February to June, 2012 are presented in **Table 3**. He was seen in the office, with laboratory data, frequently with the goal of achieving BP and glucose control.

In this patient BP control was a real issue and required chlorthalidone to reduce BP. BP control was achieved, but at the expense of increased glucose level and reduction of renal function. Finally with a prescription of insulin, Glargine 25 units subcutaneously twice daily [9], his glucose levels decreased to normal and was accompanied by normal BP and improvement in renal function within a month (**Table 3**). He continued to take the thiazide diuretic, chlorthalidone, to keep BP under control.

Patient #6: This patient was diagnosed to have diabetes and treated with OHA. Subsequently she was found not to have diabetes.

A 72 y white female was referred to author (AKM) with the question of whether she had diabetes. She was followed by a nephrologist, in the state of Kentucky, for kidney problems and was told that she had diabetes and placed on pioglitazone. Thirty-five years ago, she had an automobile

Table 3. Blood pressure therapy, blood glucose levels and data from kidney function tests in a patient with hypertension and diabetes (Patient 5)

Date 2012	Blood Pressure (Sitting and Standing) Systolic/Diastolic (mmHg)	FBG (mg/dL)	2-hPPG (mg/dL)	HbA_1c (%)	Scr/eGFR (mg/dL - ml/min)	
					F	2hPP
Feb 24	180/100 160/100	168	124	6.5	1.64 46	1.65 46
↑ metoprolol to 50 mg daily	Added chlorthalidone 25 mg daily					
Apr 10	160/90 150/100	140	148	6.8	1.74 43	1.88 39
Therapy: chlorthalidone 25 mg daily	Patient did not take metoprolol					
May 15	130/80 110/80	307	357		1.94 38	1.96 37
Therapy: Metoprolol 50 mg/d, chlorthalidone 25 mg/d, KCl 20 mEq/d Action: Reduced chlorthalidone to 12.5 mg/d, increased KCl to 20 mEq BID						
May 22	130-140/90 140/100	286	289		2.06 35	1.89 39
Therapy: As above	Prescribed Lantus insulin 25 units after breakfast and 25 units after dinner					
June 22	120/82 110/80	88	133		1.62 47	1.67 45
Action: Continue current therapy	Return with Lab in in 6 weeks					

Scr= Serum creatinine eGFR=estimated glomerular filtration rate

accident which destroyed her left kidney. An ultrasound done in November of 2011 showed the absence of a left kidney. The right kidney was decreased in size with a moderately diffuse echogenic cortex. She told author (AKM) that she took pioglitazone for some time, then stopped. Her BP in the office were; sitting 150/90 mmHg and standing 140/90 mmHg. Medications included levothyroxine 50 to 75 µg PO daily, omeprazole 20 mg PO daily, allopurinol 100 mg PO daily. Results from her laboratory studies are shown in **Table 4**.

Author (AKM) informed the patient that she currently did not have diabetes. However, low 2-hPPG (lower than FBG) with a high 2-hPP insulin response suggests that she may develop diabetes in the future. Thus she is advised to adopt a carbohydrate restricted 1800 calorie diabetes diet. The patient was pleased to know that she did not have diabetes.

Table 4. Blood glucose levels and data from kidney function tests in a patient incorrectly diagnosed with diabetes (Patient 6)

Dates	Glucose (mg/dL)		Scr (mg/dL)		eGFR (ml/min)		HbA_1c (%)	Therapy Change
2011	F	2-hPP	F	2-hPP	F	2-hPP		
Nov 17	110	112	1.39	1.41	38	37	6.3	None
Dec 28	106	158	1.48	1.58	35	32		
Insulin: F 19.9 UIU/ml, 2-hPP 125.1 UIU/ml Renal function decreased. Reason: took Lisinopril from roommate for blood pressure control. Action: discontinue Lisinopril. Prescription: amlodipine 5 mg PO daily								
2012								
Feb 7	113	120	1.36	1.30	39	41	6.5	Small, frequent meals
July 11	114	94	1.21	1.23	44	44	ND	
Insulin: F 17.6 UIU/ml 2hPP 55.3 UIU/ml								

Scr= serum creatinine eGFR=estimated glomerular filtration rate ND= Not Done

Discussion

The diagnosis of Type 2 diabetes continues to be ambivalent in distinguishing fasting hyperglycemia from overt diabetes. Clearly, Type 2 diabetes means diabetes but many individuals with so-called Type 2 diabetes may not have diabetes as in patient #6. Elevated fasting glucose levels are often due to antihypertensive therapy [11]. Type 2 diabetes was not defined in a statement by an American Association of Clinical Endocrinologists / American College of Endocrinology Consensus Panel on Type 2 diabetes mellitus [12]. This panel asserted that in order to minimize the risk of diabetes-related complications, the goal of therapy was to achieve an HbA_1c of 6.5% or less. This panel considered monotherapy, dual therapy, and triple therapy including eight major classes of medications (biguanides, dipeptidyl-peptidase-4 inhibitors, incretin mimetics, thiozolidinediones, a-glucosidase inhibitors, sulfonylureas, meglitinides, and bile acid sequestrants) and insulin therapy (basal, premixed and multiple daily injections) with or without orally administered medications. This panel did not define either Type 1 or Type 2 diabetes or relate glycemic levels associated with reduction of HbA_1c with multiple oral medications or even with insulin.

Even the WHO report does not clarify Type 2 diabetes except stating that Type 2 diabetes is due to ineffective use of insulin [1]. The WHO report also states that Type 2 diabetes represents 90% of diabetes cases worldwide and treatment may involve lifestyle changes and weight loss alone, or oral medications or even insulin injection. The report does not specify the basis of different treatment categories (Type 1 or Type 2 diabetes) leaving the treating physicians in an indecisive state in the delivery of patient care.

The diagnosis of Type 2 diabetes is very commonly used in the media which makes most everyone think that diabetes is epidemic, but it is not. Why? Most individuals with the diagnosis of Type 2 diabetes have either elevated FBG as stated earlier, or mildly increased HbA_1c, for instance 6.5 to 7%. The 2-hPPG or OGTT is rarely done to document or exclude diabetes (**Table 5**). A most important aspect in this article is that the patients presented, who have uncontrolled Type 2 diabetes, also have severe hypertension. They were most commonly prescribed a thiazide diuretic such as HCTZ, Triam/HCTZ, or chlorthalidone to control their hypertension [11]. Thiazide diuretics commonly increase FBG and HbA_1c, but rarely increase 2-hPPG [8]. Thiazide diuretics increase glucose levels because of volume depletion, hypokalemia, or by other mechanisms not yet elucidated [8].

Thus the complications including worsening of diabetes noted in patients #4 and #5, as a result of previous therapy with OHA, illustrates serious gaps in the understanding of the pathophysiology of diabetes. As a result, relevant testing, such as 2-hPPG or OGTT, to document diabetes and intention to initiate treatment with insulin to achieve adequate glycemic control, is lacking. Thus diagnosis of overt diabetes may be missed and omitting treatment with insulin could result in complications, namely end stage renal disease, heart attack and death or foot ulcer, gangrene and amputation. This again exhibits the inadequacy of the WHO report which does not specify which diabetes patients should be treated with which paradigm of therapy. Therefore authors feel compelled to make the following suggestions to adequately define diabetes and treat this metabolic disorder appropriately with a defined goal to prevent diabetic complications.

I. Type 2 diabetes is a misnomer. It does not convey any message to the patients including that diabetes is a serious disorder but with proper therapy, which is insulin, will permit healthy living with few or no complications.

II. When an elevated blood glucose level is found, professionals must ascertain that the patient is not receiving thiazide diuretics, steroid, calcineurin inhibitor or psychotropic drugs before labeling the patient with Type 2 diabetes, thereby spuriously inflating the perceived epidemic of diabetes. Once again, it is important to know that diuretics markedly increase blood glucose or exacerbate elevated baseline blood glucose [6].

III. An essential step to document or exclude diabetes is to order a basic metabolic panel at fasting and two hours after breakfast or lunch (2-hPP), and HbA_1c which will allow the observation of glucose levels, renal function and electrolyte changes. Glucose levels at 2-hPP of $>$ 200 mg/dL (11.1 mmol/L) is diagnostic of diabetes (**Table 5**); 2-hPPG $<$ 200mg/dL requires retesting to confirm or deny diabetes.

IV. The oral glucose tolerance test (OGTT) is the gold standard for the diagnosis of diabetes. Since OGTT is inconvenient for the patient as well as laboratory personnel, 2-h PPG after a major meal is the most sensitive alternative test for the diagnosis of diabetes and is more convenient for the patients and laboratory personnel [2](**Table 5**).

V. In a 4-hour oral glucose challenge test if the glucose level does not decrease to less than 200 mg/dL by the 4th hour, the cornerstone of therapy is insulin. On the other hand, if the glucose level in the 2nd to 4th hour decreases to

Table 5. Sensitivity and specificity of fasting plasma glucose to diagnose Type 2 diabetes (US population aged 40 – 69 years)

	Sensitivity (%)	Specificity (%)	Positive Predictive Value
2h post glucose challenge Plasma Glucose			
>200 mg/dL (>11.1 mmol/L)*	97	100	100
Fasting Plasma Glucose			
≥100 mg/dL (>5.5 mmol/L)	83	76	21
≥120 mg/dL (6.6 mmol/L)	54	98	76
≥140 mg/dL (7.7 mmol/L)	31	100	100

*1mM = 18 mg/dL Adapted from Harris MI. Diabetes Care 1993; 16: 642-652

the FBG level as in patient #1, the recommended therapy is a 1600 to 1800 calorie diabetes diet. Oral hypoglycemic agents may be prescribed to reduce 1-hPPG for protection against cardiovascular risk [3,13]. It has been stated that isolated postprandial hyperglycemia (2hPPG>140mg/dL) along with normal FBG (<110mg/dL) and normal HbA_1c (<6.1%), is associated with a two-fold increased risk of death from cardiovascular disease [13].

Evidence is meager with regard to the relationship between 2-hPPG and other disorders such as nephropathy. To obviate the dilemma between FBG and 2-hPPG, we innovated the factor of dglucose (2-hPPG – FBG) and found excellent correlation between dglucose and serum creatinine and eGFR with 2-hPPG > 200 mg/dL (11.1 mmol/L). In patients whose 2hPPG is greater than 200 mg/dL, for every 100 mg/dL increase in dglucose, serum creatinine increases by 0.11 mg/dL and deGFR (2hPPG – FBG) decreases by 3.73 ml/min; while in patients whose 2hPPG is < 200 mg/dL for every 100 mg/dL increase in dglucose little change was seen in dScr (-0.04mg/dL). HbA_1c was poorly correlated with fasting renal function parameters and showed low *r* and insignificant *p* values [14]. In another study, FBG and HbA_1c were found to be less sensitive than 2hPPG in predicting retinopathy and nephropathy [15].

Finally, like these authors, other authors have felt disarray in the diagnosis and treatment of diabetes [16]. Saudek and colleagues have concluded in their article "There are serious deficiencies in the current criteria for diagnosing diabetes, including the requirement that the patient be fasting and the lack of agreed upon screening criteria. These deficiencies make it unnecessarily inconvenient for clinicians to diagnose diabetes, thereby delaying the diagnosis and contributing to avoidable morbidity and mortality" [16].

Competing interests
The authors declare that they have no competing interests.

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