

Pre-prediabetes, Prediabetes and Type 2 Diabetes Mellitus: Pathophysiological and Management Points

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ABSTRACT

Disorders of glucose metabolism are ubiquitous in general clinical practice, particularly in endocrinological practice. The present article highlights terminological, pathophysiological, and management points of this complex disease.

Keywords: Glucose metabolism; Pre-prediabetes; Prediabetes; Type 2 diabetes mellitus

Commentary

Glucose is the main energy substrate for human beings. During fasting, varied metabolic pathways lead to glucose so that glycemia is constantly maintained within a normal range of 70-99 mg/dL [1]. In addition, in nondiabetics, little (or no) glucose appears in the urine when plasma glucose remains below 180 mg/dL, whereas in poorly controlled diabetics, the renal plasma glucose may largely exceed 240 mg/dL and glycosuria becomes evident [2].

Nevertheless, in the disorders of glucose metabolism, laboratory tests clearly show dividing points that characterize each pathophysiological phase of the disease, thus, conceptually opposing it to a continuum (i.e., with a more gradual character). As the clinical onset of type 2 diabetes mellitus is insidious, it fits this concept.

Prediabetes is initiated by an underlying process that could be called pre-prediabetes, which arises while fasting glucose levels and glucose tolerance are still normal, although insulin levels are increased (hyperinsulinemia), indicating mild insulin resistance, and partially explaining the presence of acanthosis nigricans [3,4]. This compensated hyperinsulinemic phase or pre-prediabetes should be identified among patients at risk to develop type 2 diabetes mellitus and other components of metabolic syndrome (e.g. android obesity, hypertension, dyslipidemia) [5,6]. Although it is worth mentioning a recent study that did not relate the pathophysiology of type 2 diabetes mellitus with that of the metabolic syndrome [7].

According to the American Diabetes Association (ADA), the diagnostic criteria for prediabetes may include impaired fasting glucose from 100 to 125 mg/dL, as well as a 2 hour plasma glucose levels from 140 to 199 mg/dL, and a glycated hemoglobin (A1C) less than, or equal to, 5.7% [8]. According to ADA as well, the diagnostic criteria for type 2 diabetes mellitus are also clear cut and may include a fasting plasma glucose greater than, or equal to, 126 mg/dL, as well as a 2 hour plasma glucose levels greater than, or equal to, 200 mg/dL, and a glycated hemoglobin (A1C) greater than, or equal to, 6.5% [8].

If, on the one hand, type 2 diabetes mellitus is nowadays fully controllable and the well treated patients may lead practically normal lives (in all adult ranges of ages), on the other hand, the disease remains incurable, and therapeutic medical measures should continue to be taken indefinitely. In this case, more than in other chronic diseases, health is achieved on a daily basis with the maintenance of the glycemic balance (and other interdependent metabolisms such as those of lipids and proteins), good dietetic practice, regular physical

activity, and the management of the components of the metabolic syndrome whenever they coexist (e.g., obesity treatment in type 2 diabetes mellitus). For instance, processed foods high in both fats and carbohydrates make up a greater proportion of total energy intake in the United States of America [9]. Each medical appointment should then provide an opportunity to educate patients about the deleterious impact of such foods on their weight and glycemic control, among other important instructions.

Therefore, pre-prediabetes, prediabetes, and type 2 diabetes mellitus are not just a matter of mere scientific neologisms (in fact, the term pre-prediabetes was first introduced in the medical literature as early as 1965) [10]. Prediabetes is an elevated risk state for macrovascular and microvascular outcomes, and the prevention and management of prediabetes should be rigorously considered [11]. Patients should be fully aware of the pathophysiological implications of not only type 2 diabetes mellitus but also of prediabetes in their lives.

However, recent guidelines challenge current thinking and advocate the use of agents other than metformin as first line agents in those with higher cardiovascular risk, potentially unseating metformin from its long held central place [12]. Additionally, in obese people with type 2 diabetes mellitus, the physiological and molecular mechanisms underlying the beneficial glycemic effects of bariatric surgery remain incompletely understood, and a constellation of factors, rather than a single overarching mechanism, likely mediate postoperative glycemic improvement, with the contributing factors varying according to the surgical procedure [13]. Of interest, uncontrolled type 2 diabetes mellitus is associated with a greater likelihood of all cause hospital readmission and reduced weight loss 30 days post metabolic and bariatric surgery [14]. To conclude, patients should know that the quality of their lives significantly depends on the levels of their glycemic control in short, medium, and long term (Figure 1).

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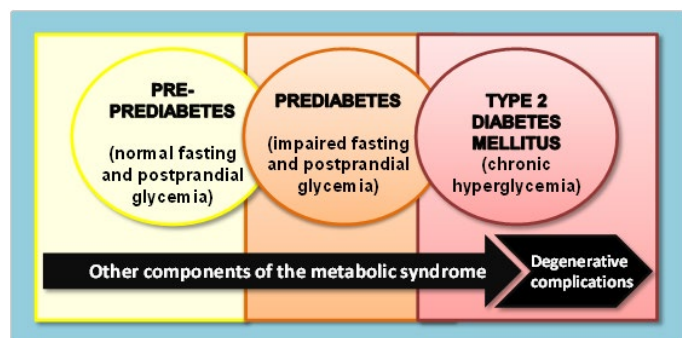


Figure 1: Integrated scheme of different phases of type 2 diabetes mellitus and metabolic syndrome.

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Conflict of Interest

Author declares there is no conflict of interest.

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