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Prediabetes: A Review of Current Trends

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ABSTRACT

Different organizations have used different criteria to define prediabetes. In order to define prediabetes, the World Health Organization (WHO) use two specific parameters: Impaired Glucose Tolerance (IGT), Oral Glucose Tolerance Test (OGTT). A person who has impaired glucose tolerance or fasting glucose and at high risk of developing type 2 diabetes is said to have prediabetes. Changes in lifestyle, such as losing weight and exercising or taking metformin is considered as the first line treatments for prediabetes. Nearly 8% of the world's population is expected to have prediabetes by 2040, and 70% of those people will eventually develop type 2 diabetes. Before fully developing diabetes, most people go through a stage of prediabetes. HbA1c or fasting plasma glucose should be used to screen for diabetes in people over 40 and other high-risk individuals. Despite its preventable nature, prediabetes often goes undiagnosed, leading to delayed interventions that can result in long-term health complications. This underscores the importance of widespread awareness, effective screening methods, and access to healthcare resources for early diagnosis and management. Moreover, emerging evidence suggests a link between prediabetes and cognitive decline, indicating that the ramifications of this condition extend beyond physical health. This short overview speaks about risk factors, diagnosis and therapy of prediabetes.

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Introduction

Blood glucose that are higher than normal but not high enough to meet the criteria needed for diabetes diagnosis are referred to as prediabetes, which is a state of disturbed glucose homeostasis. When blood sugar level is high enough to be type 2 diabetes [1]. Between 70 and 99 mmg/dl is the typical range for blood glucose levels. Blood glucose levels in prediabetic patients should be increased, ranging from 110 mmg/dl to 125 mmg/dl. These levels, however fall short of the necessary standards for a diabetes mellitus diagnosis. Because of this, a large number of individuals do not realize they have prediabetes [2-4]. The condition is marked by insulin resistance and metabolic abnormalities, serving as a precursor to more severe metabolic disorders and thus merits significant attention in healthcare research and interventions [5,6].

The prevalence of prediabetes varies by demographics, with higher rates observed in older adults and certain racial and ethnic groups, such as non-Hispanic Black and Hispanic populations. Geographically, incidence rates also fluctuate widely, highlighting the necessity for targeted public health strategies to address this epidemic effectively. Furthermore, systematic reviews indicate that lifestyle interventions, including dietary changes and increased physical activity, can substantially mitigate the risks associated with prediabetes, although the effectiveness of such interventions can vary based on individual circumstances and the quality of the programs implemented [7,8].

The pathophysiology of prediabetes is characterized by a combination of insulin resistance and early beta-cell failure, similar to the mechanisms observed in type 2 diabetes mellitus. This condition serves as a transitional phase where individuals exhibit impaired glucose tolerance and/or impaired fasting glucose, often referred to as the 'prediabetic state' [7,8]. In prediabetes, insulin resistance occurs when cells in muscle, fat, and the liver do not respond effectively to insulin, leading to elevated blood glucose levels. This resistance is typically accompanied by a decrease in the pulsatile secretion of insulin, which is essential for regulating blood sugar levels effectively [7,9]. The early phase of insulin secretion after meals is often reduced, while the subsequent phase may be delayed and prolonged, resulting in higher glycaemic excursions post-meal [7,8].

Individuals with prediabetes also exhibit distinct metabolic abnormalities, including dyslipidemia and hypertension, which contribute to an increased risk of developing type 2 diabetes and cardiovascular diseases. Central to these abnormalities is the accumulation of excess fat, particularly around the abdomen, which is linked to chronic inflammation and insulin resistance [9-11]. Genetic factors, along with lifestyle factors such as physical inactivity and obesity, play significant roles in the development of these metabolic disturbances [12,13].

Based on observational evidence, there may be a link between prediabetes and diabetes complications like fiber nephropathy, early retinopathy & nephropathy. Additionally, prediabetes may increase the risk of lifestyle interventions for the prevention of diabetes, with a 40-70% relative risk reduction. Prediabetes is a disorder that typically presents with no symptoms; it always exists prior to the onset of diabetes. Since blood sugar rise is a progression, prediabetes cannot be ruled out as a completely benign condition [14].

Risk Factors of Prediabetes

Approximately 84 million persons in America have prediabetes at present, according to the centers of the Disease Control and Prevention. This corresponds to one in three American adults. Ninety percent of these adults are unaware that they are at risk of developing prediabetes and all the consequences that come with it. Diabetes is clearly becoming more prevalent worldwide at an accelerating rate. Approximately 1.5 million people are diagnosed with prediabetes each year in America alone. The sharp rise in the prevalence of obesity corresponds with these increases [15-17].

The foremost risk is developing diabetes. In 2007 metanalysis of the transition from prediabetes to diabetes indicated that the annual incidence rate of diabetes was 4%–6% for isolated IGT, 6%–9% for isolated IFG, and 15%–19% for both IGT and IFG [18].

An expert panel has determined that continuous risk scores are more effective than contradictory ones in predicting the likelihood of developing diabetes. It has been demonstrated that diabetes risk scores based on more readily available variables, such as age, sex, ethnicity, fasting glucose, systolic blood pressure, HDL cholesterol, BMI, and history of diabetes in parents or siblings, have a better predictive value than either IFG or IGT [19,20].

Prediabetes is also found to have association with neuropathy as well as nephropathy and kidney disease [21]. Non-invasive assessment of neurological damage in IGT participants has revealed increased heat detecting threshold, increased prevalence of both hyperesthesia and hypoesthesia, and considerably more abnormalities identified by four of five cardiovascular reflex tests [22]. Additionally, there is mounting proof that prediabetic persons with IGT have greater rates of small fiber neuropathy, severe sensory neuropathy, and idiopathic polyneuropathy [23].

In the DPP trial, evidence of diabetic retinopathy was observed in nearly 8% of prediabetic patients. Although some studies have linked prediabetes to an increased risk of diabetic retinopathy, the results differ depending on the detection technique [24]. A total of 129 studies included in a systematic review highlighted the international nature of research on prediabetes, with 50 studies from Europe, 47 from Asia, and others from North America, South America, and Africa [14]. Notably, studies that adequately adjusted for potential confounders showed varying results based on demographics such as sex, ethnicity, and age. For instance, the risk of all-cause mortality associated with prediabetes was found to be higher in Asian patients with atherosclerotic cardiovascular disease compared to their non - Asian counterparts [14].

Cross-sectional studies have revealed a higher prevalence of coronary heart disease in those with prediabetes, however the shared risk factors that both prediabetes and cardiovascular diseases share can influence this correlation [25].

Individuals with prediabetes are at a heightened risk for cardiovascular disease, including heart attack and stroke. The presence of insulin resistance and high blood sugar levels contributes to the buildup of plaque in blood vessels, narrowing them and restricting blood flow. As a result, people with prediabetes may experience cardiovascular problems at a younger age compared to those without glucose metabolism disorders [10]. Individuals with prediabetes are also more susceptible to infections, due to the immune system's reduced effectiveness in the presence of high blood sugar levels. Poor circulation can exacerbate this issue, making it harder for wounds to heal, which can lead to severe infections or gangrene in extreme cases. Thus, monitoring skin integrity and seeking prompt treatment for any wounds is essential [10]. Emerging research suggests that prediabetes may also be linked to cognitive decline. Individuals with prediabetes are at an increased risk for developing dementia and other cognitive impairments, impacting memory and overall cognitive function. These changes can be long-lasting and currently lack effective treatment options [10].

Diagnosis of Prediabetes

The two main parameters used for diagnosis of prediabetes are impaired fasting glucose (IFG) defined as fasting plasma glucose (FPG) of 6.1-6.9 mmol/L (110 to 125 mg/dL) and impaired glucose tolerance (IGT) defined as 2 h plasma glucose of 7.8-11.0 mmol/L (140-200 mg/dL) after ingestion of 75 g of oral glucose load or a combination of the two based on a 2 h oral glucose tolerance test (OGTT) [26].

The American Diabetes Association (ADA), on the other hand, defines prediabetes using additional hemoglobin A1c (HbA1c)-based criteria, with a level of 5.7% to 6.4%. The ADA also uses the same cut-off value for IGT (140-200 mg/dL), but a lower cut-off value for IFG (100-125 mg/dL) [27]. The usefulness of diagnosis of diabetes or prediabetes on basis of IFG and IGT have been challenged due to inability of these blood glucose cut points to capture pathology related to diabetes and probability of developing diabetes in future [28]. Those with one or more anomalies in their glucose excursions make up the overlapping group of people classified as prediabetes according to different alternative criteria. It's probable that individuals with distinct clinical anomalies in their glucose metabolism are identified by the presence of IFG and IGT, and that the occurrence of both of these indicates a more severe impairment in total glucose homeostasis [29,30]. In high-risk patients, screening should start earlier itself and should be followed up. Screening should begin between the ages of 30 and 45, it should be repeated at least every three years [31,32].

Therapy and Surveillance of Prediabetes

A change in lifestyle and demand of rapid weight loss are the most significant aspects of managing prediabetes. The overall objective of management is to reduce weight by 7% using a low-fat diet and engaging in around 30 minutes of exercise each day [33]. Lifestyle interventions have been identified as an effective strategy for managing prediabetes and preventing the progression to type 2 diabetes. Systematic reviews have consistently shown that lifestyle modification, including dietary changes and increased physical activity, is both efficacious and cost-effective for individuals diagnosed with prediabetes [34,35]. A meta-analysis revealed that long-term lifestyle interventions significantly reduce the risk of developing type 2 diabetes [35]. However, the quality of evidence varies, with some studies demonstrating stronger outcomes associated with sustained behaviour change [36].

Patients who have not maintained appropriate lifestyle therapy or who are at high risk of developing type 2 diabetes will require medication. Metformin and acarbose are the most commonly prescribed medications for prediabetes because they help prevent the development of diabetes mellitus and have low side effects in prediabetic patients [37,38].

People with greater FPG and BMI have been reported to benefit more from metformin [38]. Numerous researchers have also looked into the effects of metformin on obese youngsters. The researches indicates that lifestyle modifications can reduce BMI slightly. Although the benefit was statistically significant, it was only temporary, peaking at 6 months and ending at 12 months with no change [39].

Future research should aim to develop and test novel lower-intensity interventions that maintain core Diabetes Prevention Program (DPP) content while addressing the low uptake and retention rates associated with high-intensity programs [40]. Furthermore, it is essential to consider social determinants of health, which can significantly impact the design and delivery of effective diabetes care strategies for vulnerable populations. As noted in recent guidelines, there is a growing emphasis on the importance of holistic care that supports not just physiological but also social and behavioural aspects of health management [41].

The goals of treating prediabetes are to prevent the condition from progressing to diabetes, as well as its aftereffects. Numerous studies have demonstrated the effectiveness of therapies meant to treat prediabetes with a long-term decline in the incidence of diabetes [42,43]. About 70% of individuals with prediabetes will eventually receive a diabetes mellitus diagnosis. That being said, it's not an established fact. Appropriate management of prediabetes can reduce the risk of cardiovascular complications and prevent diabetes mellitus.

A systematic overview was conducted to assess the effects of various interventions on dietary and physical activity behaviours related to prediabetes management. Three reviews reported variable outcomes, with some primary studies indicating significant impacts on behaviour change [36]. One review suggested that longer intervention durations may be essential for achieving sustained behaviour changes and subsequent clinical improvements [36].

Conclusions

Untreated prediabetes can lead to significant long-term health complications, many of which mirror those associated with fully developed type 2 diabetes. These complications can adversely affect multiple organ systems and overall quality of life.

These days, a lot of work is focused on curing prediabetes. An integrative approach is the most effective way to do this. There isn't enough solid data available right now to create clinical recommendations for the management of prediabetes. Interventions related to one's lifestyle are still crucial for managing prediabetes. Pharmacotherapy should be using a case-by-case basis for each patient. Also, the prevalence of prediabetes is high and rising worldwide. Improving prediabetes surveillance is essential for carrying out diabetes preventive programs and policies in an efficient manner.

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