ejpmr, 2020,7(5), 18-20

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

UNDERSTANDING PRE-DIABETES? WHAT ARE THE DIAGNOSTIC CRITERIA AND WHAT IS THE CURRENT CONSENSUS OF MANAGING PRE-DIABETES?

Dr. Muhammad Iqbal*

MBBS. CCST-UK. MRCPS-Glasgow. MRCGP-UK. Pg Dip-Diabetes-University of South Wales-UK. MRCP-UK Consultant Family Physician- Ambulatory Health Services- Abu Dhabi-UAE. Consultant GP-UK.

***Corresponding Author: Dr Muhammad Iqbal**

MBBS. CCST-UK. MRCPS-Glasgow. MRCGP-UK. Pg Dip-Diabetes-University of South Wales-UK. MRCP-UK Consultant Family Physician- Ambulatory Health Services- Abu Dhabi-UAE. Consultant GP-UK.

Article Received on 25/02/2020 **Article Revised on 17/03/2020** **Article Accepted on 07/04/2020**

ABSTRACT

The World Health Organization (1999) defined Diabetes Mellitus (DM) as "a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both".[2] Diabetes is commonly associated with obesity, physical inactivity, raised blood pressure, disturbed blood lipid levels and a tendency to develop thrombosis, and therefore is recognised to have an increased cardiovascular risk. It is associated with long-term microvascular and macrovascular complications, together with reduced quality of life and life expectancy. Globally, the prevalence of type 2 diabetes has been high and is rising across all world regions. Some 425 million people worldwide aged 20-79 years, are estimated to have diabetes. By 2045, 693 million people 18-99 years old, or 629 million of people 20-79 years, will have diabetes. (International Diabetes Federation).[4] It is important to understand the condition of pre-diabetes. The aim of this article to increase awareness about pre-diabetes and the need for timely intervention. As most people with prediabetes have no symptoms or not bothered at all.

KEYWORDS: IDF – International Diabetes Federation, WHO – World Health Organisation, IGT - Impaired glucose tolerance, IGF- Impaired fasting glucose, OGTT- Oral glucose tolerance test, FPG- Fasting plasma glucose, ADA- American Diabetes Association, HDL- High Density Lipoprotein, USDPP- United States Diabetes Prevention Programme, FDPS- Finnish Diabetes Prevention Study, ILS- Intensive lifestyle interventions, CDQDPS - the China Da Qing Diabetes Prevention Outcome Study.

INTRODUCTION

Pre-diabetes is a condition in which blood glucose levels are higher than normal but not high enough to be diagnosed as type 2 diabetes. People with pre-diabetes have a higher risk of developing type 2 diabetes and cardiovascular disease.[1] - Diabetes Australia.

It is like a warning sign before diabetes develops. It is also called 'borderline diabetes' and is closely related to obesity. The condition develops gradually and most often has no signs and symptoms.

World Journal of Diabetes[8] mentions that it is an intermediate state of hyperglycaemia with glycaemic parameters above normal but below the diabetes threshold. It remains a state of high risk for developing diabetes with yearly conversion rate of 5%-10% to type 2 diabetes. There is an association between prediabetes and complications of diabetes such as early nephropathy, neuropathy, early retinopathy and risk of macro-vascular disease.

The worldwide prevalence of IGT (impaired glucose tolerance) in 2017 was estimated to be 352 million[4] International Diabetes Federation 2017-IDF).

In the UK, around seven million people are estimated to have prediabetes and thus have a high risk for developing type 2 diabetes (Diabetes UK.[6]

In England, between 2003 and 2011, the prevalence of prediabetes more than tripled, with 35.3% of the adult population, or 1 in every 3 people having prediabetes.[7]

There are two pre-diabetes conditions: (Diabetes Australia[1]

- Impaired glucose tolerance (IGT), when blood glucose levels are higher than normal but not high enough to be diagnosed as diabetes.
- Impaired fasting glucose (IFG), blood glucose levels are escalated in the fasting state but not high enough to be diagnosed as diabetes.

  It is possible to have both Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT).

DIAGNOSTIC CRITERIA
After oral glucose tolerance test OGTT: (Diabetes Australia[1]

Fasting blood glucose level 6.1mmol/L or more but less that 7mmol/L AND blood glucose levels after 2 hours of the sugary drink is less than 7.8mmol/L - This is called Impaired fasting glucose / glycaemia.

Blood Glucose levels after 2 hours of the sugary drink is more than 7.8mmol/L but less than 11mmol/L. This is called impaired glucose tolerance.

The World Health Organization-WHO[2] has defined prediabetes as a state of intermediate hyperglycaemia using two specific parameters, 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 hr 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).

The American Diabetes Association- ADA[3] on the other hand has the same cut-off value for IGT (140-200 mg/dL) but has a lower cut-off value for IFG (100-125 mg/dL) and has additional HbA1c based criteria of a level of 5.7% to 6.4% for the definition of prediabetes

According to Diabetes Canada[5] - Prediabetes refers to blood glucose levels that are higher than normal, but not yet high enough to be diagnosed as type 2 diabetes (i.e. a fasting plasma glucose level of 7.0 mmol/L or higher). Nearly 50 per cent of those with prediabetes will go on to develop type 2 diabetes.

With increasing age the risk of diabetes goes up, therefore Diabetes Canada recommends screening by testing fasting plasma glucose for everyone once they reach age 40 and every three years after that. If someone has risk factors that increase the likelihood of developing type 2 diabetes, they can be tested more frequently or start regular screening earlier.

RISK FACTORS: Diabetes Australia[1]
Risk factors for pre-diabetes are similar to those for type 2 diabetes which are:

- Being overweight – especially those who have central obesity and increased waist circumference (ie: more than 94cm for men and more than 80cm for women).
- Physically inactivity.
- High triglycerides and low HDL-C and/or high total cholesterol.
- High blood pressure.
- Positive family history of type 2 diabetes and/or heart disease.
- Age over 40

Other people at risk include

- Women with Polycystic Ovarian Syndrome.
- Women who have had diabetes in pregnancy (gestational diabetes) or given birth to a big baby (more than 4.5kg)
- Those from certain ethnic backgrounds Afro-Caribbean, South Asian and Native American

TREATMENT: DISCUSSION
Several studies have shown efficacy of lifestyle interventions about diabetes prevention with a relative risk reduction of 40%-70% in adults with prediabetes.

While there is increasing evidence to prove the efficacy of pharmacotherapy in prevention of diabetes in adults with prediabetes, pharmacological treatment options other than metformin are associated with adverse effects that limit their use for prediabetes.

The aim of lifestyle intervention programs is to change the modifiable risk factors of prediabetes and diabetes by targeting obesity with increase in physical activity and dietary changes.

The two largest diabetes prevention studies, the United States DPP- Diabetes Prevention Programme[9] and the Finnish Diabetes Prevention Study- FDPS[10] have both shown beneficial effects of lifestyle interventions.

In the DPP study, after a 3 year follow-up, intensive lifestyle interventions- ILS lead to a 58% risk reduction. The ILS involved changes in diet and physical activity aimed at producing weight. The biggest determinant of risk reduction was noted to be weight loss. This study showed that for every 1 kg decrease in weight, the risk of developing diabetes in future was reduced by 16%.

In the DPS, the benefits were found to be dependent on achievement of the number of pre-defined goals of the intervention by the participant. These goals consisted of weight reduction greater than 5 percent, total fat intake less than 30 percent of energy intake, saturated-fat intake less than 10 percent of energy intake, fibre intake greater than or equal to 15 g per 1000 kcal, and exercise greater than 4 hours/week. While both of these studies were largely among Caucasians, studies in Asian population have also shown similar benefits.

CONSENSUS: CONCLUSION
The aim behind treatment of prediabetes includes prevention of development of diabetes, prevention of consequences of diabetes and prevention of the consequences of prediabetes itself.

The CDQDPS- the China Da Qing Diabetes Prevention Outcome Study[12] - with lifestyle intervention and 20-year follow-up showed nearly 50% relative risk reduction in incidence of severe retinopathy, but there was no difference between the intervention and control groups in the risk of developing other microvascular

complications, such as neuropathy and nephropathy. The evidence regarding effects of interventions on macro vascular complications is inconsistent.

Majority of published literature and guidelines support that lifestyle interventions focusing on dietary modification and increased physical activity should be the main therapy for diabetes prevention in patients with prediabetes.

There is increasing evidence to prove the efficacy of pharmacotherapy and support its use in adults with prediabetes. Due to the long term safety profile and positive outcomes with metformin, ADA has recommended the use of metformin in certain high risk individuals.

According to Diabetes Canada[5], when lifestyle changes are not enough to normalize blood glucose, oral medication like metformin can be considered.

In conclusion, at present there is no solid evidence to generate clinical guidelines for treatment of prediabetes. Lifestyle interventions remain an essential part of management of prediabetes. The use of pharmacotherapy should be on an individual basis. When pharmacotherapy is used to treat prediabetes, such treatment plan should be initiated with predefined goals and end points by the physician.

In my personal experience, I see many patients with pre-diabetes. For some lifestyle measures help to normalize their blood glucose levels but a few did not achieve those goals and a trial of metformin had good results.

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