

PRE-DIABETES: A REVIEW

Sushma N*, A.B.Raju

St.Peter's Institute of Pharmaceutical Sciences, Vidyanagar, Hanamkonda, Warangal, A.P-506001

Corresponding author*: sushma.n3@gmail.com

This article is available online at www.ssjournals.com

SUMMARY

Recent reports suggested increased prevalence of diabetes in India (40.9 million) and other countries like China (38.9 million), US (19.2 million), Russia (9.6 million), and Germany (7.4 million). Currently, India is the diabetes capital of the world. Between 2010 and 2030, there might be a 69% increase in numbers of adults with diabetes in developing countries and a 20% increase in developed countries.

Pre-diabetes is a metabolic disorder in which there will be slight increase in the blood glucose levels from the normal levels but they are not said to be diabetic. If this pre-diabetes is left untreated, it will lead to type II diabetes with complications like Heart disease, Stroke, Kidney disease and Blindness. There is no treatment for pre-diabetes, but by following some preventive measures, like decreasing obesity, BMI, taking healthy diet etc., we can help to prevent or delay diabetes and its complications. So by early detection of this pre-diabetes can help to avoid its complications. Pre-diabetes is more likely to occur in the patients who are obese, at the age group over 45, people who are physically inactive, having family history of diabetes, patients with polycystic ovary syndrome, history of gestational pre-diabetes, giving birth to baby with weight of 4kg and hypertension patients. So the pre-diabetic people should regularly monitor their blood glucose levels. Further understanding of pre-diabetes, its symptoms, diagnostic tests have to be evaluated. Indian epidemiological studies should be conducted in different age groups, in different geographical locations.

KEY WORDS: Pre-diabetes, Type-2 Diabetes, prevention of pre-diabetes.

INTRODUCTION

Pre-diabetes is the condition in which the people have slight increase in blood glucose levels than the normal levels but they are not said to be diabetic. People with pre-diabetes will have impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). Some people may have both IFG and IGT. IFG is a condition in which the fasting blood sugar

level is elevated after an overnight fast but is not high enough to be classified as diabetes (100-125mg/dl). IGT is a condition in which the blood sugar level is elevated after a 2-hour oral glucose tolerance test, but is not high enough to be classified as diabetes (140-199mg/dl) ¹

If the muscle and fat is present in more amounts, it will lead to insulin resistance,

which leads to pre-diabetes ². Pre-diabetes patients will be at high risk for the development of type II diabetes, High blood pressure (A patient with systolic and/or diastolic blood pressures consistently above the normal range (120/80 mm Hg) is said to have high blood pressure), High cholesterol (more than 240mg/dl), Heart disease, Stroke, Kidney disease and Blindness. Those with pre-diabetes are likely to develop type 2 diabetes within 10 years, unless they take steps to prevent or delay diabetes.

Most of the patients now days that are diagnosed with cardiovascular diseases would be suffering from pre-diabetes or in any diabetic stage. Thus the patients with pre-diabetes are in high risk to develop cardiovascular diseases at any stage ³.

EPIDEMIOLOGY

In 2000 it was estimated that ⁴ 171 million people globally suffered from diabetes or 2.8% of the population suffered from diabetes. Type-2 diabetes is the most common type worldwide. According to the year 2007 show that ⁵the 5 countries with the largest amount of people diagnosed with diabetes were India (40.9 million), China (38.9 million), US (19.2 million), Russia (9.6 million), and Germany (7.4 million).

Currently, India is the diabetes capital of the world. The world prevalence of diabetes among adults (aged 20–79 years) was found to be 6.4%, affecting 285 million adults, in 2010, and it might be increase to 7.7%, and 439 million adults by 2030. Between 2010 and 2030 ⁶, there might be a 69% increase in numbers of adults with diabetes in

developing countries and a 20% increase in developed countries.

It is estimated that over 40 million of those with diabetes are currently in India and that by 2025 that number will grow to 70 million. Another 30 million Indians have pre-diabetes and are at high risk of developing type II diabetes mellitus (T2DM). T2DM is an economically costly disease and a major cause of mortality and morbidity⁷

Risk factors

The major risk factors for the development of pre-diabetes are

- Having family history of diabetes, any family members like mother, father, grandparents, sisters or brothers having diabetes history will be in high risk to develop pre-diabetes⁸.
- Undergoing treatment of Cardiovascular Disease, generally people who have cardiovascular diseases will be either in pre-diabetes or in diabetes conditions⁹.
- Being overweight or obese, obesity is the major risk factor for the development of pre-diabetes⁸.
- Sedentary lifestyle
- Inadequate sleep. Several recent studies have showed that a lack of sleep would lead to an increased risk of insulin resistance. Research suggests that regularly sleeping fewer than 5.5 hours a night might increase the risk of pre-diabetes or type 2 diabetes⁸.

- Non-white ancestry, African Americans, Hispanics, Native Americans, Asian Americans, and Pacific Islanders are at higher risk than whites for type 2 diabetes⁸.
- Previously identified IGT, IFG, and/or metabolic syndrome
- Having hypertension or undergoing treatment for B.P⁸
- Increased levels of triglycerides, low concentrations of high-density lipoprotein cholesterol, or both will produce pre-diabetic and diabetic conditions. Total cholesterol (less than 200mg/dl), low density cholesterol(less than 100mg/dl), triglycerides (less than 150mg/dl), high-density lipoprotein cholesterol (more than 40 mg/dl for men,50mg/dl for women) are the normal ranges⁹.
- History of gestational diabetes⁸
- Delivery of a baby weighing more than 9 lb (4 kg)⁸
- Polycystic ovary syndrome, a condition that may include lack of periods, infertility, and increased hair on the body⁸.
- Receiving antipsychotic therapy for schizophrenia and severe bipolar disease¹⁰.

SYMPTOMS¹¹

The symptoms which come up, are the ones that are prominent in case of type 2 diabetes. Frequent urination and excessive thirst are

the most common symptoms of type 2 diabetes. There are other type 2 diabetes symptoms which may show up during pre diabetes, like feeling hungry at all times and unexplained weight loss or weight gain. The person may show symptoms of weakness and fatigue; similar to having influenza. The person's visual perception may also be affected, making the vision blurred. Cuts or bruises take a longer time to heal and there is low sensitivity in the limbs. Infections of gum and skin infections are also common and these may keep on recurring. Apart from these infections, vaginal or bladder infections may also be noticed in pre diabetes.

The symptoms of pre-diabetes in women are similar to that of adults, except they experience others signs as well¹².

- Severe outbreak of acne.
- Excessive facial hair or on any other part of the body that seems unusual.
- Difficulty getting pregnant.
- Menstrual cycles are delayed and not regular.

Pre-diabetes can be identified only by some diagnostic tests, where there will be alteration in the Impaired Fasting Glucose or Impaired Glucose Tolerance¹³.

Person may have one or both conditions for several years without noticing anything. Person with a severe form of insulin resistance may have dark patches of skin, usually on the back of the neck. Sometimes people have a dark ring around their neck.

Other possible sites for dark patches include elbows, knees, knuckles, and armpits. This triggers melanin levels to increase due to high levels of insulin in the blood. This condition is called acanthosis nigricans¹⁴(Fig.1).

TREATMENT AND PREVENTION

There is no particular medication for the treatment of pre-diabetes, preventive measures will act as treatment. Some of the medications are prescribed by the doctors for the prevention of cardiovascular damage. Some of the drugs like metformin and acarbose, statins (to lower the blood cholesterol) and low-dose of aspirin are given to prevent further complications¹⁵. Moderate lifestyle changes like taking healthy diet, daily physical activities will act as main preventive measure for treating diabetes and preventing the occurrence of pre-diabetes.

Prevention of type II diabetes and its complication is possible if pre-diabetes is diagnosed in the early stage and certain precautions should be taken².

Number of dietary components may modulate risk. Some preventive measures like¹⁶:

- Losing 5% to 10% of body weight may help to prevent or at least delay type 2 diabetes. Losing weight can be hard, but it is the most serious factor for the cause of many diseases. The easiest way to start is by cutting calories and getting more active¹⁶.
- Weight control can be done by taking low fat and high caloric consumption with 30 minutes of regular physical activity most days provides the greatest benefit¹⁶.
- Sodium intake should be less than 2,300 mg per day for patients with diabetes and hypertensive patients¹⁷.
- Uncontrolled hypertension can lead to diabetic neuropathy. So optimum blood pressure should be maintained in diabetic patients.
- Incorporating 2 to 3 servings of plant stanols and sterols, which naturally occur in some fruits, vegetables, nuts, and cereals, into the daily diet will decrease total and LDL cholesterol¹⁷.
- Increased daily physical activity: Because muscles use sugar/glucose for energy, activities like walking, bicycling, doing regular works and gardening help to lower blood glucose¹⁶.
- Food intake: Low-calorie, low-fat food and foods that are high in fiber are best. Lots of vegetables, fruits and whole grains, will have the best shot at avoiding pre-diabetes.
- When we are active, our body uses glucose. The more active, the more glucose is utilized by the body as energy. This keeps the sugar from building up in blood. Exercise can also improve insulin resistance.
- Quitting smoking can help to reduce the risk of getting type 2 diabetes and other

health problems. Quitting can also reduce the risk of heart attack and stroke.

- Pre-diabetes patients are more likely to get heart disease than someone with normal blood sugar levels. High cholesterol also increases risk for type 2 diabetes. So it's important to keep blood pressure and cholesterol under control.
- Foods containing more fiber should be taken. This will help to reduce the absorption of glucose into the blood stream, thereby reducing the sugar level in the blood.
- Reductions in saturated fatty acids and increases in fiber can help to reduce the weight and can also reduce the risk factor for pre-diabetes patients to develop diabetes¹⁸.

who to be diagnosed for pre-diabetes

Many times, people with pre-diabetes don't even know they have it. Anyone who is overweight and 45 years of age or older should be checked for pre-diabetes. People at Risk factors for pre-diabetes and diabetes include high blood pressure, low HDL cholesterol and high triglycerides, a family history of diabetes, a history of gestational diabetes or giving birth to a baby over 9 pounds, or belonging to an ethnic or minority group should be regularly diagnosed at least once in 2 years¹⁹. More active persons are at less risk to develop pre-diabetes.

DIAGNOSIS

There are many symptoms which could indicate a pre-diabetes phase which include extreme thirst, nausea, tiredness, high blood pressure, high cholesterol, heart disease, fatty liver, excess production of urine, giddiness, visual disturbances and foot pain. When any of these symptoms are observed, then the diagnostic test for the presence of diabetes can be done.

The best approach to screening for pre-diabetes is to use blood tests in defined high-risk populations and to prescreen other populations using questionnaires and waist circumference measurements to identify high-risk individuals, who should then be screened by blood tests. IGT cannot be diagnosed without glucose tolerance testing; thus, the OGTT is the test of choice for identifying high-risk individuals²⁰. Some of the diagnostic tests followed now a day are:

FASTING PLASMA GLUCOSE TEST (FPG)

The person to be tested must be on usual diet, at least three days prior to the test. In fasting plasma glucose (FPG) test, blood glucose levels are tested, in a person who has not eaten anything for at least 8 hours. This test is used to detect diabetes and pre-diabetes. People with a fasting glucose level of 100 to 125 milligrams per deciliter (mg/dl) have a form of pre-diabetes called impaired fasting glucose (IFG). If a person has an increased level of impaired fasting glucose, risk of developing type 2 diabetes will be more. A level of 126 mg/dl or above, confirmed by repeating the test on another

day, means a person has diabetes²¹ (Table 1).

ORAL GLUCOSE TOLERANCE TEST (OGTT)

An OGTT may be considered in patients with impaired fasting glucose (IFG) to better define the risk of diabetes. In oral glucose tolerance test, test is started by taking the blood in fasting state i.e. person should not eat anything for at least 8 hours. Initially blood is drawn and then glucose is given orally. Generally 75 grams or 100 g of glucose is given. This oral glucose tolerance test is done to diagnose gestational diabetes. After drinking the high glucose, blood glucose levels are checked²³

In a person without diabetes, the glucose levels in the blood rise following drinking the glucose drink, but then they fall quickly back to normal (because insulin is produced in response to the glucose, and the insulin has a normal effect of lowering blood glucose)²⁴.

In a diabetic, glucose levels rise higher than normal after drinking the glucose drink and come down to normal levels much slower (insulin is either not produced, or if it is produced, it may not be used by the cells)²⁴ (Table 2).

If the blood glucose level is between 140 and 199 mg/dl 2 hours after drinking the liquid, the person has a form of pre-diabetes called impaired glucose tolerance (IGT). Having IGT, like having IFG, means a person has an increased risk of developing type 2 diabetes but does not have it yet. A 2-hour glucose level of 200 mg/dl or above,

confirmed by repeating the test on another day, means a person has diabetes. In those patients identified with pre-diabetes, and if appropriate, treatment for cardiovascular risk factors should be started (Fig.2)

RANDOM GLUCOSE PLASMA TEST²¹

A random plasma glucose test, also called a casual plasma glucose test, measures blood glucose without regard to when the person being tested last ate. This test, along with an assessment of symptoms, is used to diagnose diabetes. Test results indicating that a person has diabetes should be confirmed with a second test on a different day. A random, or casual, blood glucose level of 200 mg/dl or higher, plus the presence of the following symptoms, can mean a person has diabetes:

- increased urination
- increased thirst
- unexplained weight loss

Other symptoms can include fatigue, blurred vision, increased hunger, and sores that do not heal. The person's blood glucose level on another day using the FPG test or the OGTT to confirm the diagnosis.

REFERENCES

1. Richard E Pratley, Glenn Matfin. Review: Pre-diabetes: clinical relevance and therapeutic approach. *British Journal of Diabetes & Vascular Disease* 2007; 7: 120-9.
2. HerbalCare shop.com. 2007 – 2011; <http://herbalcareshop.com/Diabetes/Prediabetes/>

3. Lars Ryde'n et al., Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. *European Heart Journal* 2007; 28: 88–136.
4. Sarah wild, et al., Global Prevalence of Diabetes. *Epidemiology/Health Services/Psychosocial Research Diabetes Care* 2004; 27:1047–1053.
5. International Diabetes Federation. Diabetes facts. *Diabetes Atlas*. 4th edition. 12 oct 2009.
6. J.E. Shaw et al., Global estimates of the prevalence of diabetes for 2010 and 2030. *diabetes research and clinical practice* 2010; Volume 87: Issue 1, Pages 4-14.
7. Dr. Ranjit Unnikrishnan & Dr.V.Mohan. THE DIABETES EPIDEMIC IN INDIA. Public Health Foundation in India 2008-2009.
8. Risk factors by Mayo Clinic staff. 21 Jan 2011; <http://www.mayoclinic.com/health/prediabetes/DS00624/DSECTION=risk-factors>.
9. Gretchen scalpi. The everything guide to managing and reversing pre-diabetes. chapter 2. diagnosing pre-diabetes. published by Adams media. Jan 16 2011. pg 31.
10. American Diabetes Association. Standards of medical care in diabetes-2008. Clinical Practice Recommendations. *Diabetes Care*. 2008; 31 (suppl 1):S12-S54.
11. Tydskrif vir geneeskunde s a. danger signs and symptoms in diabetic mellitus. *MEDICAL JOURNAL* 1955; 59-61.
12. NaomiSarah. Symptoms of Pre Diabetes. 29 sep 2010; <http://www.buzzle.com/articles/symptoms-of-pre-diabetes.html>.
13. WebMD. 02 Feb 2011; <http://diabetes.webmd.com/prediabetes>.
14. Pre-Diabetes Risk Factors. <http://www.prediabetes.com/info/prediabetes-risks.html>
15. Ranlyn Oakes. *Prediabetes Prevention*. updated: 1 April 2010.
16. Wisconsin. Wisconsin Diabetes Strategic Plan 2010 – 2015. Department of Health Services. SECTION 13: IDENTIFICATION AND DIAGNOSIS OF PRE-DIABETES AND TYPE 2 DIABETES. dec 2010; <http://dhs.wisconsin.gov/health/diabetes/index.htm>
17. Shai Gavi MD. Jennifer Hensley MD. Diagnosis and management of type 2 diabetes in adults: A review of the ICSI guideline June 2009; Volume 64: Number 6.
18. Dr Susan Jebb. Dietary strategies for the prevention of pre-diabetes. *MRC Human Nutrition Research. Cambridge. UK*.
19. Alan L. Rubin MD. pre-diabetes for dummies. The Origins and Dangers of Pre-diabetes. 2nd ed. Nov 2010; Published by Wiley publications.
20. K. G. M. M. Alberti. Screening and diagnosis of pre-diabetes: where are we headed? The Author Journal Compilation. *Diabetes, Obesity and Metabolism*. 2007; 9 (Suppl. 1), 12–16.
21. National Institute of Health. Diagnosis of Diabetes. U.S. Department of Health and Human Services 1998; <http://diabetes.niddk.nih.gov/dm/publications/diagnosis/diagnosis.pdf>.

22. James Norman MD. endocrine web 12 oct 2010; <http://www.endocrineweb.com/conditions/diabetes/diagnosing-diabetes>
23. Khanh Cao et al., Sonoma County Indian Health Project. Inc. Diabetes Program. Diabetes Prevention Prog, 2010-2011; <http://healthytraditions.org/Services.html>.
24. Kesington Blog. blood test for diabetes diseases June 1 2009; <http://blood.health-tips-diseases.com/2009/06/blood-test-for-diabetes-diseases.html>.

TABLE 1: FPG test ²²

Plasma glucose test result (mg/dl)	Diagnosis
99 or below	Normal
100 to 125	Pre-diabetes (impaired fasting glucose)
126 or above	Diabetes

TABLE 2: Oral glucose tolerance test ²²:

2-hours plasma glucose result (mg/dl)	Diagnosis
139 or below	Normal
140 to 199	Pre-diabetes (impaired glucose tolerance)
200 or above	Diabetes

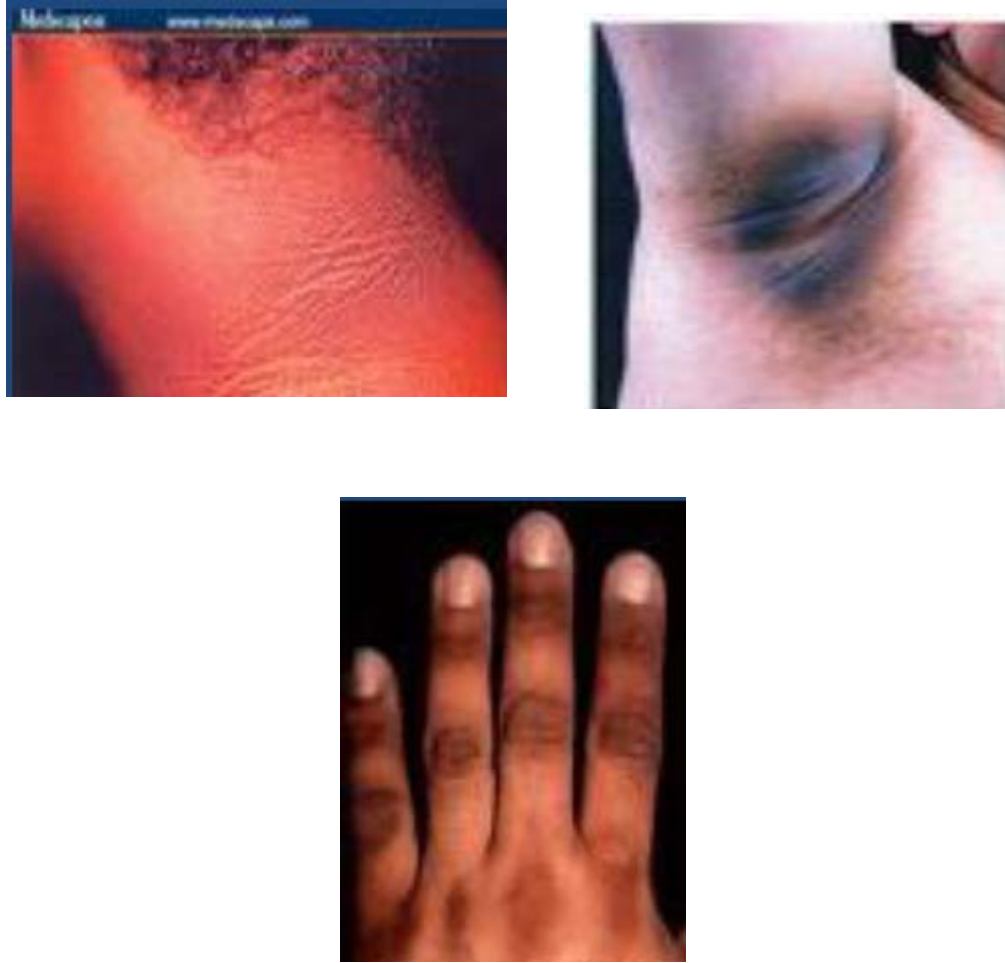


Fig 1. *acanthosis*

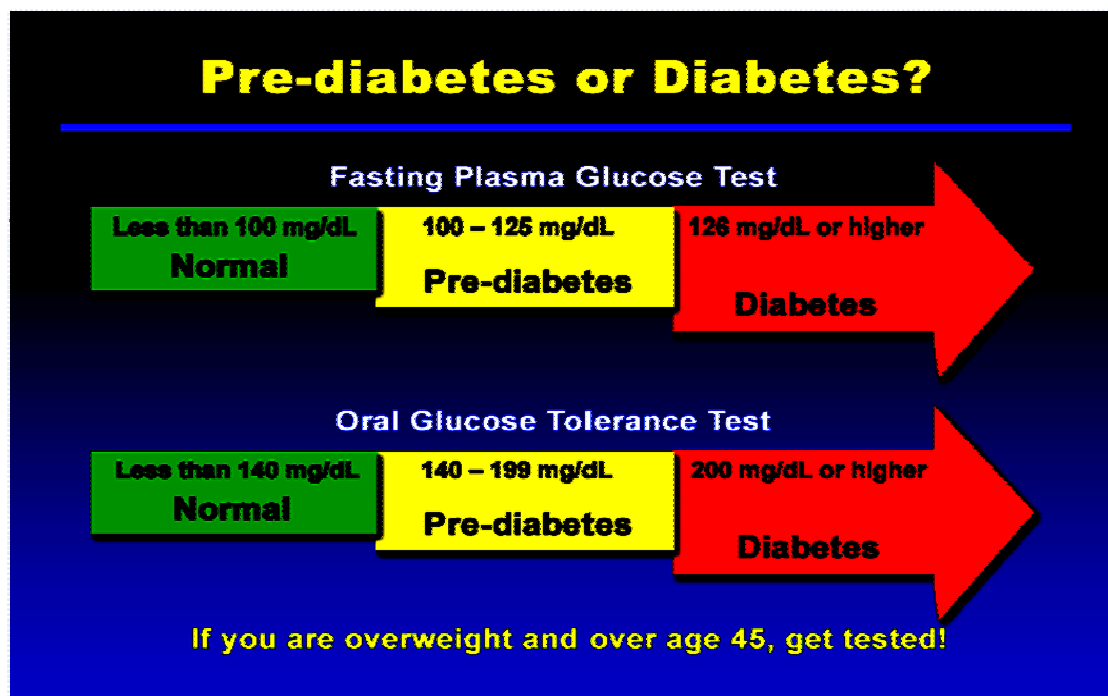


Fig. 2. Ranges of Pre-diabetes and diabetes ²