REVIEW ARTICLE

Medicine

PREDIABETES PRECURSOR TO TYPE 2 DIABETES ,ACT TODAY - BLOCK THE ROAD TO DIABETES

KEY WORDS: Prediabetes , Diabetes, HbA1C lifestyle modification , metformin

Bijaya Mohanty Consultant Medicine , Tata Main Hospital , Jamshedpur

ABSTRACT

Prediabetes is the precursor stage before diabetes mellitus sets in. This stage is often referred to as the "grey area."[1]. These people are at high risk of getting diabetes. There are an estimated 77.2 million people in India who are suffering from pre-diabetes .This increased incidence of prediabetes may be attributed towards rapid urbanization, demographic transition and maintainence of poor & unhealthy lifestyle which leads to increase in stress, anxiety & obesity all of which contributed to diabetes. Further, the ICMR study found that around 5 per cent of the adults are engaged in some form of physical activity. At least one out of every six adolescent in India is now overweight.

Therefore identifying people with prediabetes is a crucial step in preventing or delaying the development of diabetes. This can be achieved by creating awareness on lifestyle modification and developing a cost-effective strategy to address the issue.

Introduction

Prediabetes is not a disease . It is a "pre-diagnosis" of diabetes & considered as a warning sign . Infact it is the precursor stage before diabetes mellitus .This stage is often referred to as the "grey area."[1] .The American Diabetes Association says,[2] "Prediabetes should not be viewed as a clinical entity in its own right but rather as an increased risk for diabetes and cardiovascular disease (CVD). Prediabetes is associated with obesity especially abdominal or visceral, dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension."[2] .It is thus a metabolic syndrome usually with no symptoms and only high blood sugar as the sole sign. Diagnosis of prediabetes is based upon an impaired fasting glucose, impaired glucose tolerance, and/or an elevated glycosylated hemoglobin (A1C). The American Diabetes Association (ADA) defines a person to be pre diabetic if his value for IGT is between 140-199 mg/dL , IFG (100-125 mg/dL) and has additional hemoglobin A1c (HbA1C) level from 5.7% to 6.4%.

A systematic review of prospective studies confirms a strong, continuous association between HbA1C level and subsequent diabetes risk(3). Persons with an HbA1C value of 6.0% or above had a high risk for development of clinically defined diabetes. The 5-year risk of diabetes with baseline HbA1C value of 6% ranged from 25% to 50%. The relative risk of diabetes is 20 times higher if the HbA1C is greater than 6% compared with an HbA1C of 5% or less . HbA1C level appears to have a continuous association with diabetes risk(4). According to an American Diabetes Association expert panel, up to 70% of individuals with prediabetes will eventually have diabetes. If current trends continue, 1 in 3 adults will have diabetes by 2050 (5,6). Studies in India had shown that nearly 40-55% of the people with pre diabetic stage will develop to type 2 diabetes mellitus over a period of 3-5 years [7,8,9,10] . As per DPP (Diabetes Prevention Program) 11% of people with pre-diabetes develop T2DM each year. Other similar studies showed that majority with prediabetes develop T2DM in 10 years .Factors such as age above 40 years, males, higher WHR(Waist hip ratio) and BMI(Body mass index), systolic hypertension, and alcohol consumption, and less vegetable intake were higher among prediabetics. Thus, the target population for the intervention should be people with prediabetes and associated factors.

There is a long period of glucose intolerance that precedes the development of diabetes. Screening tests can identify persons at high risk for development of diabetes. There are safe, potentially effective interventions that can prevent the above modifiable risk factors such as lifestyle and pharmacologic interventions. Only diet modification reduce 58% risk of developing diabetes[11].

The diagnosis of diabetes is often delayed until complications are present.[12] Because current methods of treating diabetes do not prevent all the complications associated with the condition, prevention of diabetes and even prediabetes is preferable. The Diabetes Prevention Program Research Group has published several studies showing that Type 2 diabetes may be preventable by diet and exercise.[13,14,15]. In 2002, Knowler et al hypothesized that lifestyle intervention would prevent or delay the development of diabetes. The researchers randomly assigned patients with prediabetes to receive a placebo or a lifestyle modification program with the goals of at least a 7% weight loss and at least 150 minutes of physical activity per week. The lifestyle intervention reduced the incidence by 58% compared with placebo. Unless people with prediabetes change their lifestyle, most will have Type 2 diabetes within the next 10 years, according to the National Institute of Diabetes and Digestive and Kidney Diseases. Lifestyle changes such as weight loss (7% of body weight) and moderate physical activity (150 minutes per week) can reduce the risk of diabetes by as much as 58%.[16]. The Finnish Diabetes Prevention Study published in 2003 also shown reduction in diabetes risk with intensive lifestyle intervention . In 2012, Perreault et al reported that patients with prediabetes that did not progress to diabetes after they completed an intensive lifestyle intervention were still at high risk for the development of diabetes. They also discovered that reversion to normal glucose levels, even transiently, was associated with a 56% reduced risk of future diabetes.In 2013, Schellenberg et al compared the effectiveness of lifestyle interventions to standard care on minimizing progression of prediabetes to diabetes or reducing all-cause mortality in diabetes. This meta-analysis study identified 9 randomized, controlled trials with prediabetic patients who were at risk of diabetes and 11 randomized, controlled trials with patients who had diabetes. Seven of the 9 studies looking at patients who were at risk of diabetes reported that lifestyle interventions decreased the risk of diabetes up to 10 years after a lifestyle intervention. Results of multiple trials support a long-term reduction in diabetes risk or a delay in onset of the disease as a result of lifestyle and drug-based intervention. In the 20-year follow-up of the Da Qing Diabetes Prevention Study, those receiving a lifestyle intervention had a 51% lower incidence of diabetes.

Pharmacologic and Surgical Intervention

Evidence of potential benefits from pharmacotherapy to prevent diabetes in patients with prediabetes was reported by Knowler et al in 2002. Biguanides, such as metformin, were shown by the investigators to decrease the incidence of diabetes but not as much as lifestyle interventions. Metformin, which has a good safety profile, has beneficial effects on BMI and lipid concentrations[17]. In 2010, Lilly and Godwin concluded after a systematic review of the literature and meta-analysis that metformin lowers risk of Type 2 diabetes by 45%[18]. The beneficial effects of metformin were greater in people who were prediabetic with a higher baseline BMI than in the individuals with a lower BMI. Thiazolidinediones (troglitazone, rosiglitazone, and pioglitazone) have been shown to reduce the incidence of diabetes in patients at risk of diabetes. However, risks of this medication, which may include hepato toxicity, weight gain, edema, and heart failure, outweigh the benefit in preventing prediabetes from progressing to diabetes. Although inhibitors of the renin-angiotensin-aldosterone system may have a beneficial effect on reducing complications of prediabetes and diabetes, there is no evidence that they help in preventing prediabetes from progressing to diabetes. EDIT (Early Diabetes Intervention Study)

used both acarbose & metformin for prevention of diabetes also showed promo=ising results. STOP NIDDM study used Acarbose & recommend its use either as an alternative or in addition to changes in lifestyle, to delay development of type 2 diabetes in patients with impaired glucose tolerance.

ADA Consensus Statement says that preventive treatment to be given in high risk individuals with prediabetes. In addition to lifestyle modification the high risk individuals should be considered for treatment with metformin.They are those who have both IFG and IGT or with at least one additional risk factor like age above 60, BMI ≥35, Family H/o of diabetes, high triglyceride, HDL level & A1C level more than 6%.In morbidly obese people, bariatric surgery is associated with sustained weight loss and a substantial reduction in the two-year and ten-year incidence of diabetes[19,20].

Conclusion

To identify prediabetes early and intervention on war foot basis is the cornerstone in reducing type 2 diabetes load in future. This can be achieved by increasing awareness in the community on the prevention of diabetes by lifestyle modification specially targeting obesity and physical inactivity. Patients not responding to lifestyle interventions may be considered for pharmacologic interventions or surgery. The need of the hour is strategic planning & targeting interventions aimed at the entire population at risk of prediabetes.This is the time to act .Lets be proactive & block the road from prediabetes to diabetes.

References

1- "prediabetes" at Dorland's Medical Dictionary
2- American Diabetes Association (2017), "2. Classification and diagnosis of diabetes", Diabetes Care, 40 (Suppl 1): S11–24, doi:10.2337/dc17-S005, PMID 27979889.
3- Meigs JB, Muller DC, Nathan DM, Blake DR, Andres R, Baltimore Longitudinal Study of Aging. The natural history of progression from normal glucose tolerance to type 2 diabetes in the Baltimore Longitudinal Study of Aging. Diabetes 2003;52:1475-84.
4- Zhang X, Gregg EW, Williamson DF, et al. A1C level and future risk of diabetes: a systematic review. Diabetes Care. 2010 Jul;33(7):1665–73. DOI: http://dx.doi.org/10.2337/dc09-1939. [PMC free article] [PubMed]
5- Qian Q, Joushilahti P, Erikson J, Tuomilehto J. Predictive properties of impaired glucose tolerance for cardiovascular risks are not explained by the development of overt diabetes during follow up. Diabetes Care 2003;26:1910-4.
6- Heianza Y, Hara S, Arase Y, et al. HbA1C 5.7–6.4% and impaired fasting plasma glucose for diagnosis of prediabetes and risk of progression to diabetes in Japan (TOPICS 3): a longitudinal cohort study. Lancet. 2011 Jul 9;378(9786):147–55. DOI: http://dx.doi.org/10.1016/S0140-6736(11)60472-8. [PubMed]
7- Viswanathan V, Clementina M, Nair BM, Satyavani K. Risk of future diabetes is as high with abnormal intermediate post-glucose response as with impaired glucose tolerance. J Assoc Physicians India 2007;55:833-7.
8- Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V, et al. The Indian diabetes prevention programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia 2006;49:289-97.
9- Sushma N, Raju AB. Pre-diabetes: A review. Int J Biomed Res 2011;2:161-70
10- Mohan V, Deepa M, Anjana RM, Lanthorn H, Deepa R. Incidence of diabetes and pre-diabetes in a selected urban south Indian population (CUPS-19). J Assoc Physicians India 2008;56:152-7
11- The Finnish Diabetes Prevention Study-Tuomilehto et al. N Engl J Med. 2001;344:1343.Lifestyle Modifications only diet modification reduce 58% risk of developing diabetes
12- Harris MI, Eastman RC. Early detection of undiagnosed diabetes mellitus: a US perspective. Diabetes Metab Res Rev. 2000 Jul-Aug;16(4):230–6. DOI:
13- Knowler WC, Barrett-Connor E, Fowler SE, et al. Diabetes Prevention Program Research Group Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002 Feb 7;346(6):393–403. DOI: http://dx.doi.org/10.1056/NEJMoa012512. [PMC free article] [PubMed]
14. Diabetes Prevention Program Research Group. Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009 Nov 14;374(9702):1677–86. DOI: http://dx.doi.org/10.1016/S0140-6736(09)61457-4. [PMC free article] [PubMed]
15. Perreault L, Pan Q, Mather KJ, Watson KE, Hamman RF, Kahn SE, Diabetes Prevention Program Research Group Effect of regression from prediabetes to normal glucose regulation on long-term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study. Lancet. 2012 Jun 16;379(9833):2243–51. DOI: http://dx.doi.org/10.1016/S0140-6736(12)60525-X. [PMC free article] [PubMed]
16- Schellenberg ES, Dryden DM, Vandermeer B, Ha C, Korownyk C. Lifestyle interventions for patients with and at risk for type 2 diabetes: a systematic review and meta-analysis. Ann Intern Med. 2013 Oct 15;159(8):543–51. DOI: http://dx.doi.org/10.7326/0003-4819-159-8-201310150-00007. [PubMed]
17- Salpeter SR, Buckley NS, Kahn JA, Salpeter EE. Meta-analysis: metformin treatment in persons at risk for diabetes mellitus. Am J Med. 2008 Feb;121(2):149–57. e2. DOI: http://dx.doi.org/10.1016/j.amjmed.2007.09.016. [PubMed]
18-. Lily M, Godwin M. Treating prediabetes with metformin: systematic review and meta-analysis. Can Fam Physician. 2009 Apr;55(4):363–9. [PMC free article] [PubMed]
19- Sjöström L, Lindroos AK, Peltonen M, et al. Swedish Obese Subjects Study Scientific Group Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004 Dec 23;351(26):2683–93. DOI: http://dx.doi.org/10.1056/NEJMoa035622. [PubMed]
20- Sjöström L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. JAMA. 2012 Jan 4;307(1):56–65. DOI:
21- Viswanathan V, Clementina M, Nair BM, Satyavani K. Risk of future diabetes is as high with abnormal intermediate post-glucose response as with impaired glucose tolerance. J Assoc Physicians India 2007;55:833-7.
22- Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V, et al. The Indian diabetes prevention programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia 2006;49:289-97.
23- Sushma N, Raju AB. Pre-diabetes: A review. Int J Biomed Res 2011;2:161-70
24- Tuso P. Prediabetes and lifestyle modification: Time to prevent a preventable disease. Perm J. 2014 Summer; 18(3): 88–93.