

## MICROVASCULAR COMPLICATIONS IN PREDIABETES



### Medicine

**KEYWORDS:** pre diabetes, impaired fasting glucose, impaired glucose tolerance

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### ABSTRACT

**Background:** Pre-diabetes is a condition in which the glucose levels are higher than normal but not enough for the diagnosis of diabetes mellitus. Epidemiologic evidence suggests that the complications of diabetes begin early in the progression from normal glucose tolerance to frank diabetes. Microvascular complications start in the pre-diabetic state itself. Based on previous studies, almost 8% of individuals with pre-diabetes have detectable early diabetic retinopathy. Between 25% and 62% of patients with idiopathic peripheral neuropathy are reported to have prediabetes. **Methods:** We conducted an observational cross sectional study of 100 pre diabetic patients in a tertiary care centre to study the prevalence of microvascular complications in pre diabetics, to study the prevalence of microalbuminuria, retinopathy and neuropathy in prediabetics according to sex, age group and blood sugar level and to study the association between microalbuminuria, retinopathy and neuropathy in prediabetics. **Results:** The prevalence of microalbuminuria in this study was 7%, retinopathy was 4%, and neuropathy was 8%. The prevalence of microalbuminuria is more in impaired glucose tolerance (IGT) compared to impaired fasting glucose (IFG). When the blood sugar rises in the prediabetic range in IFG and IGT the prevalence of microalbuminuria also rises. The prevalence of retinopathy was also more in IGT compared to IFG. The prevalence was higher in those with higher blood sugar both in IFG and IGT. Out of 100 patients were studied, 60% were overweight, 11% were obese, and 29% have normal body mass index (BMI). Prevalence of overweight is seen more in IGT rather than IFG. **Conclusions:** The microvascular complications like neuropathy, retinopathy and microalbuminuria starts in the pre-diabetic stage itself. Prevalence of microalbuminuria, retinopathy and neuropathy was more in IGT when compared to IFG. There is significant association between microalbuminuria and retinopathy in pre-diabetic patient.

### INTRODUCTION

Diabetes Mellitus is one of the most common endocrine disorders. Pre-diabetes is a condition in which the glucose levels are higher than normal but not enough for the diagnosis of diabetes mellitus. Epidemiologic evidence suggests that the complications of diabetes begin early in the progression from normal glucose tolerance to frank diabetes<sup>1</sup>. Microvascular complications start in the pre-diabetic state itself. Pre-diabetes currently refers to people who have impaired fasting glucose (IFG) i.e. fasting glucose levels between 100-125mg/dl or impaired glucose tolerance (IGT), i.e. two hours post glucose load between 140-199 mg/dl or both. Pre-diabetes raises short-term absolute risk of Type 2 diabetes five to six fold, and in some populations this may be even higher<sup>2</sup>.

Early identification and treatment of persons with pre-diabetic conditions has the potential to reduce both the incidence of diabetes and related complications. Early diabetic nephropathy in the pre-diabetic state can be detected by micro-albuminuria, retinopathy by typical fundus changes and neuropathy by Monofilament test.

Recognition of micro-albuminuria Stemmed from Diabetes research decades ago. According to National Kidney Foundation Microalbuminuria is defined as a Urine Albumin Excretion Rate (UAER) of approximately 30-300 mg/d in at least two of three consecutive samples of non-ketotic sterile urine. Microalbuminuria possibly reflects state of increased renal endothelial permeability and is an easily measured marker of rather diffuse endothelial dysfunction, low grade inflammation and vascular disease burden<sup>3</sup>. There are data supporting that this programme would have beneficial effects in detecting individuals at high risk for cardiovascular atherosclerotic disease.

Almost 8% of individuals with pre-diabetes have detectable early diabetic retinopathy, according to research presented June 12 at the 65th Scientific Sessions of the American Diabetes Association (ADA) in San Diego.

Between 25% and 62% of patients with idiopathic peripheral neuropathy are reported to have prediabetes, and among individuals with prediabetes 11–25% are thought to have peripheral neuropathy, and 13–21% have neuropathic pain<sup>4</sup>. Population-based studies

suggest a gradient for the prevalence of neuropathy, being highest in patients with diabetes mellitus, followed by individuals with impaired glucose tolerance then impaired fasting glucose and least in those with normoglycemia.

Based on the evidence from the previous studies, we decided to conduct a study to determine the prevalence of microvascular complications of prediabetics in our population.

### MATERIALS AND METHODS

The aims of the study were to study the prevalence of microvascular complications in prediabetic patients, to study the prevalence of microalbuminuria, retinopathy and neuropathy in prediabetics according to sex, age group and blood sugar level and to study the association between microalbuminuria, retinopathy and neuropathy in prediabetics. It was an observational cross-sectional study. 100 Patients above the age of 45 attending outpatient unit of a tertiary care center were enrolled, during the period of one year from April 2011—March 2012, with prediabetes, fulfilling inclusion and exclusion criteria were studied. The inclusion criteria were patients aged 45 years and above, detected to have pre diabetes. The exclusion criteria were patients already on treatment for diabetes, patients on treatment for hypertension, patients with history of liver disease, patients with urinary tract infections, pregnant females and patients with any critical illness. These patients were examined to study the Clinical profile and complications at the time of presentation. The diagnosis of Prediabetes was made by checking plasma glucose, i.e. Fasting plasma glucose (FPG) between 100-125 or 2 hr Post prandial plasma glucose 140-199 after oral glucose tolerance test (OGTT). FPG was taken 8 hr over night fasting. Oral glucose tolerance test (OGTT) was done using 75 gram of glucose. Routine laboratory investigations like blood routine, urine routine, blood urea, serum creatinine, urine microalbumin estimation done by using Immuno-turbidimetry kit. Optic fundus examination and Monofilament test done to check for retinopathy and neuropathy respectively.

Study population was divided into two categories impaired fasting glucose (IFG) (Fasting plasma sugar 100-125) OR impaired glucose tolerance (IGT) (post prandial plasma sugar 140-199). Both of them were sub divided into three categories according to the level of plasma sugar.

## RESULTS

The study group had 100 prediabetic patients. There were 46 females and 54 males. The maximum number of patients belonged to the age group 45- 54 years. Out of 100 patients were studied, 60% were overweight, 11% were obese, and 29% have normal BMI. Out of 54 male patients, 4 patients had microalbuminuria (7.4%). Out of 46 female patients, 3 patients had microalbuminuria (6.5%). There was no statistically significant difference in the prevalence of microalbuminuria in male & female pre-diabetics ( $p=0.59$ ). There is increased prevalence of microalbuminuria in IGT when compared to IFG. It was observed that as the age advances, there is no significant increase in microalbuminuria. The prevalence of microalbuminuria increases as the blood sugar rises in the pre-diabetic range in IFG. Out of 54 male patients, 1 patient had retinopathy (1.9%). Out of 46 female patients, 3 patients had retinopathy (6.5%). It was observed that there was no statistically significant difference in prevalence of retinopathy in male and female pre-diabetic ( $P=0.25$ ). As the age advances there is no significant increase in prevalence of retinopathy. The prevalence of retinopathy increase as the blood sugar rises within the pre-diabetic range in IFG. There is increase in prevalence of retinopathy as the blood sugar rises within pre-diabetic range IGT. A higher proportion of patients with early diabetic retinopathy had microalbuminuria compared to those without retinopathy changes. The association between the two were statistically significant. [ $P<0.00083$ ]. Out of 54 male prediabetes 5 patients had neuropathy (9.3%). Out of 46 female prediabetes 3 patients had neuropathy. It was observed that there was no statistically significant difference in prevalence of neuropathy in male and female pre-diabetics ( $P=0.45$ ). As the age advances there is increase in prevalence of neuropathy. The prevalence of neuropathy increase as the blood sugar rises within the pre-diabetic range in IFG. There was an increase in prevalence of neuropathy as the blood sugar rises within pre-diabetic range in IFT. There was no statistically significant association between neuropathy and microalbuminuria in patients with pre-diabetes [ $P<0.096$ ]. There was no statistically significant association between retinopathy and neuropathy in patients with pre-diabetes. [ $P=0.29$ ]. On fundus examination, 4 patients had the changes of Diabetic Retinopathy, 89 patients had normal fundus, and in 7 patients fundus was not visualized due to hazy media.

## DISCUSSION

The present study evaluated the prevalence of microalbuminuria, retinopathy, and neuropathy in pre-diabetic patients and correlation between microalbuminuria, retinopathy, neuropathy with age, sex, levels of fasting plasma sugar and post prandial plasma sugar.

The prevalence of microalbuminuria in this study was 7%, retinopathy was 4%, and neuropathy was 8%. The prevalence of microalbuminuria is more in IGT compared to IFG. A similar study by Wang XL et al showed a prevalence of microalbuminuria more in IGT than in IFG<sup>5</sup>. When the blood sugar rises in the prediabetic range in IFG and IGT the prevalence of microalbuminuria also rises. The prevalence of retinopathy was also more in IGT compared to IFG. The prevalence was higher in those with higher blood sugar both in IFG and IGT. The DPP Outcome Study (Diabetes Prevention Program) Showed a prevalence of retinopathy as 7.6% in those with pre-diabetes using Fasting blood glucose. A higher proportion of patients with retinopathy had microalbuminuria and its association was statistically significant. The prevalence of neuropathy is more in IGT compared to IFG. There was no statistically significant association between neuropathy and microalbuminuria, and neuropathy and retinopathy.

In the present study, for microalbuminuria, retinopathy, and neuropathy there was no significant difference of prevalence in men and women.

The prevalence of microalbuminuria and retinopathy was not significantly higher in the older age groups. In the case of neuropathy, there was increase in prevalence with increase in age.

Out of 100 patients were studied, 60% were overweight, 11% were obese, and 29% have normal BMI. Prevalence of overweight is seen more in IGT rather than IFG. Obese people with a BMI of 30.0 and above are five times as likely to develop pre-diabetes when compared with people in the normal weight range. Risk starts to increase at a BMI of 25<sup>6</sup>.

## CONCLUSION

In this study prevalence of microalbuminuria, retinopathy and neuropathy were 7%, 4% and 8% respectively. The microvascular complications like neuropathy, retinopathy and microalbuminuria starts in the pre-diabetic stage itself. Prevalence of microalbuminuria, retinopathy and neuropathy was more in IGT when compared to IFG. There is significant association between microalbuminuria and retinopathy in pre-diabetic patient. Further studies including large population are needed to know the prevalence of retinopathy, neuropathy and microalbuminuria in pre-diabetic individuals.

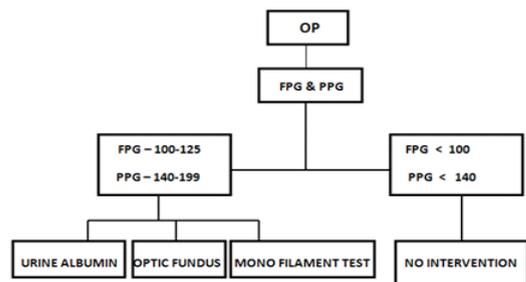


Figure 1: showing the study design

## REFERENCES

1. The DECODE Study group, Age and sex-specific prevalences of IGT and DM in European Cohorts, *Diabetes Care* 26:61-69, 318: 2003
2. Lillioja S, Mott DM, Howard BV, et al. Impaired glucose tolerance as a disorder of insulin action: longitudinal and cross-sectional studies in Pima Indians. *N Engl J Med* 1988; 121:712-25
3. S.M. Haffner, C.Gonzales, R.A. Valdez, L. Mykkanen, H.P. Hazuda, B.D. Mitchell, A. Monterrosa and M.P. Stern Is microalbuminuria part of the prediabetic state? *The Mexico City Diabetes Study journal diabetologia springer berlin vume 36, November 10, 1993*
4. Lindstrom J, Lianne-Parikka P, Ppeltonen M, et al; Finnish Diabetes Prevention Study Group. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow up of the Finnish Diabetes Prevention study *Lancet*. 2006; 368: 1673-1679.
5. Wang XL, Lu JM, Pan CV; Comparing the prevalence of urinary albumin excretion and microalbuminuria in prediabetic subjects; *Zhghuaneikezazhi* 2004 march 43(3): 170-3
6. American Diabetes Association: Nutrition recommendation and intervention for Diabetes; *Diabetes care*: 30 suppl: (2007) 742-749