

Original Research Article

Cross sectional study of microalbuminuria, C-peptide and fundal changes in pre-diabetics

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ABSTRACT

Background: Pre-diabetes is a mounting health problem occurring worldwide. Microvascular complications are prone to occur during this stage. Early diagnosis and treatment delay progression to diabetes mellitus and microvascular complications. Aims and objectives of the study was to determine the prevalence of microalbuminuria, c-peptide and fundal changes in pre-diabetics.

Methods: 125 pre-diabetic patients those who visited MGMCRI General Medicine OPD and admitted in wards were taken into the study after fulfilling the inclusion criteria and after obtaining written informed consent. All those study patient's urine and blood sample were sent for analysis of microalbuminuria and C-peptide respectively. Fundus was examined for retinopathic changes.

Results: Among 125 prediabetic participants, prevalence of microalbuminuria was 12.8%, c-peptide levels was elevated in 46.4 %, but none of the study participants had fundal diabetic retinopathy changes.

Conclusions: The microvascular complications like microalbuminuria starts in the pre-diabetic stage itself. Prevalence of increased c-peptide levels and microalbuminuria was more in individuals who had both IFG and IGT. Elevated C peptide level and microalbuminuria were found to appear much earlier than retinopathy in prediabetes. Hence its use can enhance for early diagnosis of prediabetes.

Keywords: C-peptide, Microalbuminuria, Prediabetes, Retinopathy

INTRODUCTION

Diabetes mellitus is a non-communicable disease which affects 150 million individuals worldwide. Diabetes mellitus has long been recognized as a major public health problem, not only for its adverse health impact on individuals, but also for its economic burden on the health care system and the society at large.¹ The International Diabetes Federation (IDF) in 2005 confirmed that diabetes is one of the most common non-communicable diseases globally and constitutes the

fourth or fifth leading cause of death in most developed countries as well as many developing countries. In India number of estimated case of diabetes is 79.4 million in 2030 compared to 31.7 million in 2000.²

In India, over 30 million people have been diagnosed with pre-diabetes.³ Pre-diabetes is a condition in which the glucose levels are higher than normal but not enough for the diagnosis of diabetes mellitus. It's often described as gray area between normal and diabetes glucose levels.⁴ The microvascular complications start in the pre-diabetic

state itself, so early diagnosis and treatment of this condition is important as this delay may cause the progression of microvascular complications and onset of diabetes mellitus. In India, prevalence of pre-diabetes is around 8.7 % in urban and 7.9% in rural areas. Around 35 % of pre-diabetes may progress to develop Type 2 diabetes mellitus. So, India is one among the countries which is facing a health care crisis on pre-diabetes.³

As per American Diabetes Association (ADA), Pre-diabetes refers to individuals who have Impaired Fasting Glucose (IFG) between 100-125 mg/dl or Impaired Glucose Tolerance (IGT) between 140-199 mg/dl or HbA1c levels between 5.7-6.4 %.⁵

Diabetes mellitus is vulnerable for multiple microvascular and macrovascular complications, such as nephropathy, retinopathy, cardiovascular events and stroke. Epidemiological evidence suggests that these complications begin early in the progression from normal glucose to overt diabetes.⁶ Early identification and treatment of pre-diabetes reduces both incidence of diabetes and its complications. Early diabetic nephropathy in the pre-diabetic state can be detected by micro-albuminuria and typical fundus changes.

C-peptide is a peptide which has 31 amino acids which connects A chain and B chain in proinsulin. Insulin and C-peptide is stored together co-secreted from secretory granules in the beta cells.⁴ C-peptide and insulin are produced in equal amounts and so can be useful to assess endogenous insulin secretion, including those who are treated with insulin.⁷ C-peptide is an important marker in diagnosis of early diabetes. It is likely to be increased in early or newly diagnosed diabetes.⁸ There were some reports that C-peptide-based indices were better indices than insulin based indices for the evaluation of pathophysiology of diabetes.⁹

According to National Kidney Foundation, microalbuminuria defined as "urine albumin excretion rate of approximately 30-300 mg/dl in at least two of three consecutive samples of non-ketotic sterile urine.

24-hour urine albumin excretion remains the gold standard test, but impractical for routine practice. Microalbuminuria can be diagnosed on the basis of three positive tests-Albumin creatinine ratio; urine albumin excretion rate or a combination of both.

Diabetic Retinopathy occurs as a result of microvascular retinal changes. Early fundus changes of diabetes is a marker of diabetic vascular 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.¹⁰

As microvascular complications are prone to occur in prediabetes, which leads researchers and experts to

reconsider occurrence of microvascular complications with respect to glucose threshold levels in diabetes.

METHODS

This cross sectional study was conducted at the Mahatma Gandhi Medical College and Research Institute, Pillayarkuppam, Puducherry, India. All participants who attended the General Medicine OPD/In patient who were fulfilling the inclusion/exclusion criteria were taken up for the study from December 2015-May 2017 by stratified random sampling.

Inclusion criteria

Patients who have Impaired Fasting Glucose (IFG) between 100-125 mg/dl or Impaired Glucose Tolerance (IGT) between 140-199 mg/dl or HbA1c levels between 5.7-6.4%

Exclusion criteria

Overt diabetics, Systemic Hypertension, Chronic Heart failure, Renal impairment, Previous history proteinuria, Patients on drugs as spironolactone, Angiotensin converting enzyme inhibitors and Angiotensin receptor blockers, Pregnant women, Patient with Urinary tract infections.

This study was done in compliance with declaration of Helsinki and it was approved by Institutional human committee of Mahatma Gandhi Medical College and Research Institute, Puducherry, India.

Procedure

After obtaining the written consent from the patient, 2ml blood sample was collected in plain (red tube) and sent for c-peptide analysis. 5ml midstream urine was collected in the early morning for analysis of microalbuminuria by nephelometry method. Fundus was examined to look for retinopathic changes by slit lamp biomicroscopy with +90 D lens and Indirect Ophthalmoscopy.

Data collection

All data was entered into a Data Collection Proforma Sheet and were entered into Excel (MS Excel 2011). The Sheet had a visual map for marking and divided into indications for both genders. Other biographical data had also been collected.

Statistical methods

Descriptive analyses were reported as mean and standard deviation of continuous variables. Chi square test was used to study the relationship between microalbuminuria and c-peptide levels with age, gender and sugar values. p value was calculated for all the variables which were compared.

RESULTS

The study included 125 pre-diabetic patients. Among 125 study participants, 28 participants (22.4%) were below 40 years, 61 participants (48.8%) were between 40-49years, 30 participants (24%) were between 50-59 years and 6 participants (4.8%) were between >60 years. The mean age was 45.5 years. Minimum age was 28 years and Maximum age was 66 years. (Table 1).

Table 1: Age distribution of study participants.

Age group (years)	Number	%
<40	28	22.4
40-49	61	48.8
50-59	30	24.0
>60	6	4.8
Total	125	100

Among 125 participants, 81 (64.8%) were males and 44(35.2%) were females (Figure 1).

In our study, among the 125 participants, 22 (17.6%) had IFG alone, 10 (8.0%) had IGT alone and 88 (70.4%) had

both IFG and IGT. The remaining 5 (4%) participants had HbA1c in Pre-diabetic ranges inspite of having normal IFG and IGT (Table 2).

Table 2: Classification of IFG, IGT and both among study participants.

Type	Number	%
IFG alone	22	17.6
IGT alone	10	8.0
IFG and IGT	88	70.4
Others (HbA1c 5.7-6.4%)	5	4.0
Total	125	100

Table 3: C-peptide levels in study participants.

C Peptide levels (ng/ml)	Number	%
<0.8	1	0.8
0.8-3.1	66	52.8
>3.1	58	46.4
Total	125	100

c-peptide normal range- 0.8-3.1 ng/ml.

Table 4: Comparison of microalbuminuria with IFT, IGT and others.

Microalbuminuria	Pre-diabetes groups				Total
	IFG	IGT	IFG and IGT	HbA1C	
Yes	3	2	10	1	16
No	19	8	78	4	108
Total	22	10	88	5	125

Table 5: Comparison of C-peptide and IFT, IGT and others.

C-Peptide	Pre-diabetes groups				Total
	IFG	IGT	IFG and IGT	HbA1C	
<0.8	0	0	1	0	1
0.8-3.1	19	5	40	2	66
>3.1	3	5	47	3	58
Total	22	10	88	5	125

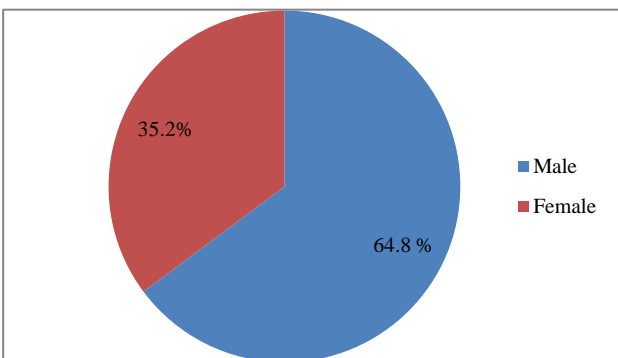


Figure 1: Gender distribution among study participants.

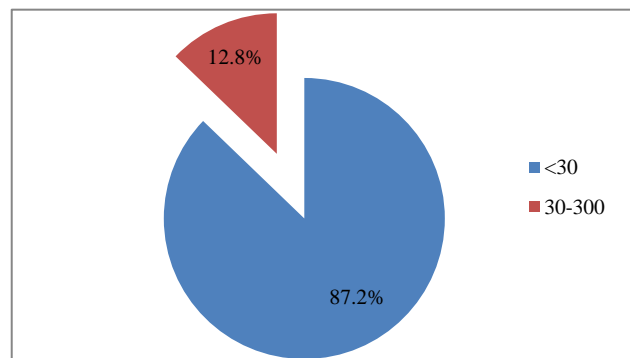


Figure 2: Prevalence of microalbuminuria.

Out of the 125 Prediabetic subjects the prevalence of microalbuminuria was 12.8% (Figure 2). On comparing microalbuminuria with blood glucose level of the participants, among 16 participants who had microalbuminuria, 3 participants (18.75%) had IFG alone, 2 participants (12.5%) had IGT alone and 10 participants (62.5%) had both IFG and IGT. 1 participant with microalbuminuria had HbA1c alone in pre-diabetic range. p value was 0.84 (Table 4).

The C-peptide levels among our study participants were found to be normal in 66(52.8%), participants the level were elevated in 58(46.4%) participants and lower in 1(0.8%) participant (Table 3). On comparing C-peptide with blood sugar values of the participants, out of 58 participants who had elevated C-peptide levels, 3 participants (5.1%) had IFG alone, 5 participants (8.6%) had IGT alone, 47 participants (81%) had both IFG and IGT. Among 66 participants who had normal C-peptide levels, 19 participants had IFG alone, 5 participants had IGT alone, 40 participants had both IFG and IGT. 1 participant who had low c-peptide had both IFG and IGT. p value was 0.06 (Table 5).

None of the study participants had retinopathic changes on fundus examination.

DISCUSSION

The mean age of pre-diabetic participants of our study was 45.5 years, which was similar to study done by Rao et al where the mean age was 48.3 years.¹¹ In our study, male population (64.8%) were more prone to develop pre-diabetes. The reason may be attributed to life style of males such as smoking and consumption of alcohol.

The prevalence of microalbuminuria was 12.8%. In comparison with IFG, IGT and both, microalbuminuria (62.5%) was prevalent in both who had IFG and IGT, which was similar to a study done in a private hospital in Andhra Pradesh and Iran.^{11,12}

In our study, c-peptide levels were elevated in 46.4% study participants. When compared with IFG, IGT and both, 50 % of the participants were found to have both IFG and IGT. Similar study done by Chailurkit et al in Thailand, C-peptide levels were elevated significantly in prediabetic people and on follow up, these individuals were found to develop diabetes.⁸ In a study done by Kim et al in Japan, C-peptide based index was found to be elevated in newly diagnosed diabetes and individuals with pre-diabetes significantly. That study concluded that elevated c-peptide was one of the important risk factor for diabetes.⁹ Study done by Thazin et al in Myanmar quoted that increased fasting c-peptide was significantly associated with prediabetes.¹³

Though microalbuminuria and elevated c-peptide were prevalent in our study population, none of the study participants had fundus retinopathic changes. Similar

studies done in Andhra Pradesh and Chennai showed, retinopathy was present in 8% and 6% respectively of the prediabetic population. Possible reason would be early screening for fundus, in case followed up months to years later could find significant fundal changes.¹¹ And this again clearly shows the possibility of early nephropathy related microvascular complication in the diabetes individual.

Limitation of the study: As the study size was small, we were not able to get significant results on comparing the variables. Even though we got significant results of prevalence of microalbuminuria and elevated c-peptide levels, Fundus didn't show any retinopathic changes. This can be due to early screening of participants. Following up the participants could have picked it up, whereas it's not the part of the study.

CONCLUSION

Pre-diabetes is a mounting health problem in the community. Early diagnosis and intervention delay the onset of diabetes and the development microvascular complications. The microvascular complications like microalbuminuria starts in the pre-diabetic stage itself.

Increased c-peptide levels are an important marker of prediabetes and a risk factor for diabetes. Prevalence of increased c-peptide levels and microalbuminuria was more in individuals who had both IFG and IGT. Hence, in our study, an elevated C peptide level and microalbuminuria were found to be prevalent in prediabetes than retinopathy.

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