

## Original Research Article

# Unmasking the diabetic population in pre-diabetic subset of population

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### ABSTRACT

**Background:** Identification of individuals with a high risk of developing diabetes and early diagnosis of diabetes is essential in prevention and early treatment of diabetes. Effective lifestyle and pharmacologic interventions to delay development of diabetes in people with high risk have been established.

**Methods:** This Prospective non-randomized interventional study was conducted in 100 Pre diabetic patients who came in OPD of MGM Medical College and MY Hospitals, Indore, MP, from December, 2017 to February, 2019.

**Results:** OGTT after 1hour was more than160mg/dl and OGTT after 2 hour was more than140mg/dl was found in 40 patients that is 40% of patients. The mean OGTT at 1 hour at presentation was  $189.60 \pm 28.89$  mg/dl and after 6 weeks (first follow-up) was  $150.90 \pm 14.29$ mg/dl. The difference was found to be statistically significant ( $p=0.001$ ), showing a significantly lower OGTT at 1 hour after 6 weeks (first follow-up). The mean OGTT at 1 hour after 6 weeks (first follow-up) was  $169.00 \pm 3.72$  mg/dl and after 6 weeks (second follow-up) was  $148.67 \pm 6.29$  mg/dl. The difference was found to be statistically significant ( $p=0.001$ ), showing a significantly lower OGTT at 1 hour after 6 weeks (second follow-up) in comparison to follow-up after 6 weeks (first follow-up).

**Conclusions:** Patients who were labelled as pre-diabetic on the basis of FPG and PPPG may have underlying diabetes which will remain unmasked due to less sensitivity of these tests individually.

**Keywords:** Diabetes, Fasting plasma glucose, Oral glucose tolerance test, Pre-diabetes, Post prandial plasma glucose

### INTRODUCTION

Identification of individuals with a high risk of developing diabetes and early diagnosis of diabetes is essential in prevention and early treatment of diabetes.<sup>1</sup> Effective lifestyle and pharmacologic interventions to delay development of diabetes in people with high risk have been established. It still remains inconclusive if screening of diabetes in general population is cost effective or improves health outcomes.

However, screening for pre diabetes and diabetes among high risk population with appropriate intervention is more effective than screening for diabetes alone.<sup>2</sup> To detect dysglycemia and diabetes, the ADA recommends at least

2 alternatives, namely, fasting plasma glucose (FPG) and 2 hour postmeal oral glucose tolerance test for detection of pre diabetes and diabetes with different pros and cons in practice. Normally, in a health care setting, FPG is used to identify diabetes among high risk groups because of the convenience and low cost compared with OGTT.<sup>3</sup>

Although OGTT has disadvantages in feasibility for mass screening, it is more sensitive than FPG to identify pre diabetes and diabetes. It is interesting and useful to explore which population was missed most by FPG.<sup>4,5</sup> High degree of discrepancy has been noted in previous studies in the classification of the two criteria and using FPG led to missing of lot of cases with diabetes. So, the purpose of our study is to unveil the hidden diabetes

mellitus in pre-diabetic and high risk population and to aware, alert, and sensitize the high risk population for future diabetes mellitus.

## METHODS

This Prospective non-randomized interventional study was conducted in 100 Pre diabetic patients who came in OPD of MGM Medical College and MY Hospitals, Indore, MP, from December, 2017 to February, 2019.

### Inclusion criteria

- Patients came from routine or yearly executive checkup.
- Patients having FPG between 100 and less than 126mg/dl (impaired fasting plasma glucose) or impaired glucose tolerance test as 2hr PPPG between 140 and less than 200 mg/dl

### Exclusion criteria

- Patient already labelled as DM T2.
- Patient having FPG more than equal to 126 or 2hr PPPG more than 200mg/dl.
- Type 1 DM
- Pregnancy
- Admitted or patients suffering from serious/chronic illness or comorbidity
- Patient taking oral hypoglycemic drugs
- Patient taking drugs causing hypoglycemia (eg. steroids)
- Alcoholic patients.

### Investigations

- Fasting blood sugar
- Post Prandial 2hr blood sugar
- 75gm Oral glucose tolerance test

### Data collection and methods

- Customized proforma was used for collecting data.
- Baseline FBS and PPBS.

### Statistical analysis

It was a descriptive study where results were presented in the form of numbers and percentage. Comparison of mean within the group was done by using paired 't' test and 'p' value of <0.05 was taken as statistically significant. The final data was presented in the form of tables and graphs. Statistical software "Mini Tab" version 17.0 was used for calculating 'p' value.

## RESULTS

In this study, maximum impaired fasting glucose was found in 100-105mg/dl in 28 patients, followed by 106-

110mg/dl in 24 patients, followed by 121-125mg/dl in 20 patients, followed by 111-115mg/dl in 16 patients. Mean of distribution of impaired fasting glucose (100-126mg/dl) in study population is  $111.72 \pm 7.14$  mg/dl. Maximum impaired glucose tolerance was found in 140-150mg/dl in 24 patients, followed by 171-180mg/dl in 21 patients. Mean of distribution of impaired glucose tolerance (100-126mg/dl) in study population is  $165.18 \pm 14.92$  mg/dl. Maximum number of patients in OGTT after 1 hour was in between 130-160mg/dl in 60, followed by 161-190mg/dl in 28.

Mean of distribution of OGTT after 1 hour in study population is  $162.64 \pm 29.13$  mg/dl. Maximum number of patients in OGTT after 2 hour was in between 110-140mg/dl in 60 patients, followed by 141-170mg/dl in 32 patients. Mean of distribution of OGTT after 2 hour in study population is  $140.48 \pm 21.66$  mg/dl.

After 1 hour of OGTT blood sugar was more than 160mg/dl and after 2 hour of OGTT blood sugar was more than 140mg/dl were found in 40 patients that is 40% of total patients. These 40% of patients were advised life style intervention by dietary modification, exercise, and stress reduction.

In our study population of 100 patients, out of 40 patients who were followed up after life style intervention maximum OGTT after 1 hour were found in 130-140mg/dl and 161-180mg/dl in 12 patients in each. Mean of distribution of OGTT after 1 hour in follow up population after 6 weeks of life style intervention population is  $150.90 \pm 14.297$  mg/dl (Table 1).

**Table 1: Distribution of OGTT after 1 hour in followed up (after life style intervention) in study population.**

OGTT after 1 hour	No. of patients	Percentage
130-140	12	30
141-150	08	20
151-160	08	20
161-180	12	30
Total	40	100

**Table 2: Distribution of OGTT after 2 hours in followed up (after life style intervention) in study population.**

OGTT After 2 Hour	No. of patients	Percentage
110-120	04	10
121-130	16	40
131-140	08	20
141-150	12	30
Total	40	100

In this study population of 100 patients, out of 40 patients who were followed up after life style intervention maximum OGTT after 2 hours were found in between

121-130mg/dl in 16 patients and between 141-150mg/dl in 12 patients. Mean of distribution of OGTT after 2 hour in follow up population after 6 weeks of life style intervention population is 132.50±10.36mg/dl (Table 2).

In our follow up population of 40 patients, 30% of patients have OGTT more than 160mg/dl after 1 hour and OGTT after 2 hour was more than 140mg/dl even after life style intervention (Table 3).

The mean OGTT at 1 hour at presentation was 189.60±28.89mg/dl and after 6 weeks (first follow-up) was 150.90±14.29mg/dl. The difference was found to be statistically significant (p=0.001), showing a significantly lower OGTT at 1 hour after 6 weeks (first follow-up). The mean OGTT at 1 hour after 6 weeks (first follow-up) was 169.00±3.72mg/dl and after 6 weeks (second follow-up) was 148.67±6.29mg/dl. The difference was found to

be statistically significant (p=0.001), showing a significantly lower OGTT at 1 hour after 6 weeks (second follow-up) in comparison to follow-up after 6 weeks (first follow-up) (Table 4).

**Table 3: Patients having blood glucose more than 160mg/dl after 1 hour of OGTT and blood glucose more than 140mg/dl after 2 hours of OGTT (after life style intervention) in follow up population.**

After 1 hour of OGTT(Blood Glucose>160) and after 2 hours of OGTT(Blood Glucose>140)	No. of patients	Percentage
Yes	12	30
No	28	70
Total	100	100

**Table 4: Comparison of mean OGTT level at 1 hour at different time intervals.**

Time interval	No.	OGTT(mg/dl) after 1 hour (Mean±SD)	't' value	p value
At presentation	40	189.60±28.89	7.819, df=39	0.001*
After 6 weeks (first follow-up)	40	150.90±14.29		
After 6 weeks (first follow-up)	12	169.00±3.72	12.134, df=11	0.001*
After 6 weeks (Second follow-up)	12	148.67±6.29		

Paired 't' test applied. p value <0.05 was taken as statistically significant

**Table 5: Comparison of mean OGTT level at 2 hour at different time intervals.**

Time interval	No.	OGTT(mg/dl) after 1 hour (Mean±SD)	't' value	p value
At presentation	40	161.20±19.51	8.265, df=39	0.001*
After 6 weeks (first follow-up)	40	132.50±10.36		
After 6 weeks (first follow-up)	12	146.00±2.56	22.983, df=11	0.001*
After 6 weeks (Second follow-up)	12	129.67±4.85		

Paired 't' test applied. p value <0.05 was taken as statistically significant

The mean OGTT at 2 hours at presentation was 161.20±19.51mg/dl and after 6 weeks (first follow-up) was 132.50±10.36mg/dl. The difference was found to be statistically significant (p=0.001), showing a significantly lower OGTT at 2 hours after 6 weeks (first follow-up). The mean OGTT at 2 hours after 6 weeks (first follow-up) was 129.67±4.85mg/dl and after 6 weeks (second follow-up) was 129.67±4.85mg/dl. The difference was found to be statistically significant (p=0.001), showing a significantly lower OGTT at 2 hours after 6 weeks (second follow-up) in comparison to follow-up after 6 weeks (first follow-up) (Table 5).

## DISCUSSION

The various parameters like age, sex, fasting plasma glucose level, post prandial plasma glucose level, oral glucose tolerance test were analyzed before and after the

life style modification and medical intervention. The findings and interpretations are discussed below.

In this study population of 100 pre-diabetic individuals having impaired fasting glucose oral glucose tolerance test was done with 75gm of glucose and we found that OGTT after 1 hour was more than 160mg/dl and OGTT after 2 hours was more than 140mg/dl was found in 40 patients that is 40% of patients. This concludes that 40% patients of our study population were converted to overt diabetes after OGTT. This unveils the hidden diabetes in 40% of our study individuals which were previously labeled as pre-diabetic on the basis of impaired fasting glucose.

This may be due to these 40% patients who were labeled as pre-diabetic on the basis of FPG level may already have underlying beta cell dysfunction which unveiled on

provocation of these beta cells by 75 gram glucose causing exhaustion of remaining beta cells.

A study conducted by Shailendra Kumar Manjhar et al shows that more than one-fourth of the subjects were found to have an impaired OGTT.<sup>6</sup> None of the subjects were aware of their OGTT. Total prevalence of impaired oral 75 gram glucose tolerance found in this study was 27.27%.

Another study done by Dong-Lim Kim et al suggests that performing additional OGTT for patients with FPG  $\geq 110$  mg/dL or HbA1c  $\geq 6.1\%$  is helpful to reclassify their glucose tolerance levels and evaluate the potential to progress to overt diabetes.<sup>7</sup>

### ***OGTT in patients with impaired glucose tolerance***

Patients who were labeled as pre-diabetic on the basis of 2 hour post meal plasma glucose level and our meal would contain lipid, proteins, minerals etc. along with carbohydrate which were interfere the result and the underlying diabetes remain unveiled. But when we took 2 hour plasma glucose level after 75 gram glucose it would convert this unveiled diabetes into overt diabetes.

In non-diabetic individuals, plasma glucose concentration peaks 60 min after the start of a meal, rarely exceeds 140 mg/dl, also, returns to pre-prandial levels within 2-3 hours. Even though glucose concentration returns to pre-prandial levels by 3 h, absorption of the ingested carbohydrate continues for at least 5-6 h after a meal. Because the absorption of food persists for 5-6 h after a meal in both diabetic and non-diabetic individuals, the optimal time to measure postprandial glucose concentration must be determined.

### ***1st Follow up (n=40)***

#### ***OGTT after life style intervention***

Suggest that in early screening of high risk individuals early life style intervention would defer the progression of underlying diabetes mellitus and also prevent the complications of diabetes and decrease their progression.

Knowler WC et al, hypothesized that lifestyle intervention would prevent or delay the development of diabetes.<sup>4</sup> The lifestyle intervention reduced the incidence by 58% compared with placebo. Participants assigned to the lifestyle intervention had more weight loss and greater increase in physical activity than did participants in the placebo group.

The average weight loss was 0.1 kg and 5.6 kg in the placebo and lifestyle intervention groups, respectively ( $p < 0.001$ ). Further analysis of the study showed that if patients with pre-diabetes received no intervention, diabetes would develop in approximately 37% in 4 years. The lifestyle modification program decreased the

percentage of persons with pre-diabetes in whom diabetes developed in 4 years to approximately 20%.

Toshikazu Saito et al conducted a study on 641 overweight Japanese individuals and concluded that lifestyle modifications can prevent type 2 diabetes among overweight Japanese with impaired fasting glucose levels.<sup>8</sup>

Glenn Matfin et al concluded that obesity and physical inactivity are important risk factors for T2DM, lifestyle interventions, emphasizing modest weight loss and increases in physical activity, should be recommended for most patients with pre diabetes.<sup>9</sup> Such interventions are safe and effective and also reduce risk factors for cardiovascular diseases. In our study results were also significant which suggest that early life style intervention would defer the progression of diabetes mellitus in high risk individuals, prevent complications of diabetes and its progression and also reduces risk factors for cardiovascular diseases.

In our study 12 individuals that is 30% of follow up patients have OGTT after 1 hour was more than 160mg/dl and OGTT after 2 hours was more than 140mg/dl after Life Style Intervention, this could be due to these individuals are nit stringent and compliant to the diet and exercise advised to these individuals as a part of life style modifications, may be because they do not have control over their hunger and not so much of dedication to continue the diet and exercise advised as a part of life style intervention.

In these 12 that is 30% of patients we advised medical along with life style intervention and follow up again after 6 weeks.

### ***2nd Follow up (n=12)***

#### ***OGTT after medical intervention along with life style intervention***

In our study population 12 that is 30% of patients having significantly impaired OGTT even after 6 weeks of life style intervention were advised medical intervention (tab metformin 500mg BD) and were reassessed after 6 weeks. After reassessing these 12 that is 30% of individuals by repeating OGTT none of the patient out of 100 patients in our study population have OGTT after 1 hour more than 160mg/dl and OGTT after 2 hour more than 140mg/dl after medical along with life Style intervention that is all of these 12 patients have OGTT after 1 hour was less than 160mg/dl and OGTT after 2 hour was less than 140mg/dl.

In our study, the mean OGTT at 1 hour after 6 weeks (first follow-up) was  $169.00 \pm 3.72$  mg/dl and after 6 weeks (second follow-up) was  $148.67 \pm 6.29$  mg/dl. The difference was found to be statistically significant ( $p = 0.001$ ), showing a significantly lower OGTT at 1 hour

after 6 weeks (second follow-up) in comparison to follow-up after 6 weeks (first follow-up).

Similarly the mean OGTT at 2 hours after 6 weeks (first follow-up) was  $129.67 \pm 4.85$  mg/dl and after 6 weeks (second follow-up) was  $129.67 \pm 4.85$  mg/dl. The difference was found to be statistically significant ( $p=0.001$ ), showing a significantly lower OGTT at 2 hours after 6 weeks (second follow-up) in comparison to follow-up after 6 weeks (first follow-up).

Significant results of our study suggests that metformin works well in early diabetes and when implemented early in diabetes patients would defer the progression of diabetes and prevent its complications and also decrease the further progression of its complications. Glenn Matfin et al concluded that both lifestyle and metformin therapy subsequently reduced the development of metabolic syndrome in the remaining participants without the syndrome at baseline.<sup>9</sup> Pharmacologic interventions may be appropriate for patients at particular risk for developing diabetes, but the benefits of treatment need to be balanced against the safety and tolerability of the intervention.

Shruthi Kulkarni et al, conducted a pilot randomized control trial of total 103 participants were randomized into three arms standard care (STD), intensive lifestyle modification (ILSM) or ILSM and metformin (ILSM+Met) and followed up for six months.<sup>10</sup> At six months, there was a reduction from baseline in weight and fasting blood sugar (FBS) ( $p<0.01$ ) in all three arms and a reduction in HbA1c ( $p=0.03$ ) only in the ILSM+Met arm. Our results were significant and consistent with this study.

## CONCLUSION

Patients who were labeled as pre-diabetic on the basis of FPG and PPPG may have underlying diabetes which will remain unmasked due to less sensitivity of these tests individually.

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