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Article received on:

12/09/2017

Accepted for publication:

18/11/2017

Received after proof reading:

29/11/2017

INTRODUCTION

According to the International Diabetes Federation (IDF) the number of adults with impaired glucose tolerance (IGT) is expected to increase globally, reaching 472 million by 2030.¹ The greatest rises are expected in South-East Asia and the Western Pacific Region.¹ Impaired glucose tolerance prevalence for South-East Asian region for 2015 among 20-79 years old is 6.2% and is expected to go upto 7.2% by 2040.² Prediabetes is the term used for non diabetic hyperglycemia associated with the simultaneous presence of insulin resistance and β -cell dysfunction, abnormalities that start before glucose changes are detectable. Interventions that improve insulin sensitivity can typically slow the progression to diabetes.^{3,4}

PRE-DIABETES; PREVALENCE OF PRE-DIABETES IN OUR LOCAL POPULATION.

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ABSTRACT... Introduction: Early intervention among patients with prediabetes can prevent or delay diabetes. Moreover, regression from prediabetes to normal glucose regulation has been associated with reduction in cardiovascular disease (CVD) risk. Estimate of prevalence of this condition is vital as diabetes is now a global epidemic requiring steps towards its prevention. **Study Design:** Descriptive study. **Setting:** Fatima Memorial Hospital & Medical & Dental College Lahore. **Period:** 1st February 2016 till 1st February 2017. **Objective:** To determine the prevalence of pre-diabetes and associated risk factors and demographic features in our local population using HbA1c as a screening test. **Material and Methods:** The study population includes adults 18 years and above who reported in hospital outdoor as well as employees, faculty members and students. Subjects were included in the study after taking written consent. The statistical analysis was performed on SPSS version 23. **Results:** The number of subjects included was 400. 138(34%) had HbA1c value in prediabetic range (5.7-6.4%) and 56 (14%) in diabetic range (>6.4%). Mean age of prediabetics was 41 ± 13 , 34% were males and 66% were females, 27% were in age group less than 30 years. Their mean HbA1c was 5.9%. Above normal body mass index (BMI) was reported in 128 (93%) and positive family history of diabetes mellitus (DM) in 135 (98 %) subjects (P value: 0.00). All females with history of Polycystic Ovarian Syndrome and Gestational Diabetes showed prediabetes. **Conclusion:** The prevalence of prediabetes is significant in our studied population. It has strong association with family history of diabetes and above normal BMI values. There are also a significant number of undiagnosed asymptomatic diabetics in our population.

Key words: Prediabetes, Hb A1c, Prevalence, BMI.

Article Citation: Kitchlew R, Chachar AZK, Haider M, Saleem AR, Mirza MS, Latif S, Afzal U. Pre-Diabetes; Prevalence of pre-diabetes in our local population. Professional Med J 2017;24(12):1860-1866. DOI:10.17957/TPMJ/17.4310

Prediabetes is a high risk state for diabetes with an annual conversion rate of 5%–10%; with similar proportion converting back to normoglycaemia. Data from observational studies suggest that 25–40% of individuals with pre-diabetes will develop diabetes over the next 3–8 years.^{4,5} Prediabetes is associated with an increased risk of composite cardiovascular events, coronary heart disease, stroke, and all cause mortality.⁶⁻⁸ Evidence is accumulating on increased prevalence of idiopathic polyneuropathy among prediabetic individuals.^{9,10} Moreover, regression from prediabetes to normal glucose regulation has been associated with long-term reduction in diabetes and CVD risk.¹¹

According to American Diabetes Association

(ADA), prediabetes is defined as HbA1c levels 5.7-6.4%, Fasting Plasma Glucose (FPG) of 100-125mg/dl or an Oral Glucose Tolerance Test (OGTT) 2 hour blood glucose of 140 mg/dl – 199 mg/dl.¹²

According to National Center for Chronic Disease Prevention and Health Promotion Division of Diabetes Translation- 2016, about 86 million US adults have prediabetes¹³, and 90% of them are unaware of it. About 69 % of the pre-diabetes population lives in low- or middle-income countries.¹⁴

Pakistan is a country with 7th highest diabetic population in the world and it is expected to rise to 4th highest place by 2030.^{14,15} Data from 2011 WHO statement indicates that in Pakistan, 12.9 million people are suffering from diabetes (10% of total population). Of them, 9.4 million are properly diagnosed while undiagnosed cases are believed to be as much as 3.5 million and 38 million people (29%) are with Pre- diabetes (20.5% women and 15.9% men).¹⁴⁻¹⁵

Serious efforts are required to prevent this exponent rise in diabetes cases. An important step would be to identify the burden of prediabetes in our population and then to implement steps towards reversing it or preventing progression. Very few studies using HbA1c levels criteria in this respect have been done locally. The current study was done as a pilot study in a tertiary care setup in Lahore. To our knowledge no other study has been published using HbA1c as criteria for estimating prediabetes prevalence in this area. HbA1c measurement does not require patients to be fasting, has greater preanalytical stability, and is less affected by acute physiological perturbations, and hence is more convenient to use in clinical practice than other diabetes tests such as fasting glucose or glucose tolerance test.

MATERIAL & METHODS

This descriptive study was conducted from 1st February 2016 till 1st February 2017 in the medical unit of Fatima Memorial Hospital (FMH) Lahore. Approval was taken from the institute's ethical committee.

Adults above 18 years of age with family history of diabetes mellitus, BMI above normal or history of gestational diabetes who reported in hospital outdoor or were employees in the hospital and the FMH medical and dental college including faculty members and students were enrolled.

Exclusion criteria was diagnosed Diabetes, Renal failure, Haemoglobinopathies, blood transfusion in last 3 months, pregnancy and use of steroids (ongoing or in last three months). Subjects qualifying inclusion criteria after interview were examined, height and weight recorded and advised HbA1c level test after taking their written consent. All tests were performed at Fatima Memorial Hospital (FMH) laboratory by chemiluminescent micro particle immunoassay (CMIA) for the quantitative determination of percentage HbA1c in human whole blood on the ARCHITECT Plus system (Architect HbA1c 4P72 Abbott Laboratories). BMI of enrolled individuals was calculated. They were interviewed for associated medical conditions including hypertension, dyslipidemia, coronary artery disease, Polycystic ovarian syndrome, Cushing syndrome and Acromegaly.

The statistical analysis was done using SPSS version 23. Continuous variables like age, BMI and HbA1c values were expressed as mean \pm SD. Frequency and percentages were expressed for categorical variables like gender, comorbidities. Chi-square test was applied and P-value < 0.05 taken as significant.

RESULTS

The number of study participants was 400. There were 148 (37%) males and 252 (63%) females. The mean age of study population was 36 \pm 12 years.

The mean value of HbA1c was 5.8%. The prediabetic range (5.7-6.4%) was found in 138 (34%) and diabetic range (>6.4%) in 56(14%). Family history for diabetes was positive in 391(98%). The mean BMI was 29(kg/m²) there were 318 (79%) individuals who had BMI above normal. According to world health organization (WHO) Asian specific criteria 134 (33%) were

overweight and 184 (46%) obese.

Mean age of prediabetics was 41± 13. Among these 47 (34%) were males and 91 (66%) were females. Their mean HbA1c was 5.9%. 135 (98%) had family history of DM. They had mean BMI of 29 kg/m² and 128 (93%) had BMI above normal and 69(50%) were obese. Hypertension was present in 54 (39%), IHD in 8 (6 %) and dyslipidemia in 11(8%). History of Polycystic ovarian syndrome in 1 participant and gestational DM in 3. All later four were less than 30 years of age. Demographic features per various age groups is shown in Table-I.

There was strong association between prediabetes and obesity and family history of DM (P=0.00). The prevalence of prediabetes increased among females with increasing age as shown in Table-II.

Majority of our subjects were in age group of less than 30 years. Their demographic parameters are shown in Table-III. Number of males was 64 and female 107 and prediabetics 21 and 17 respectively i.e. more males in this age group had prediabetes.

Age Group (years)	Total Patients	Number of Prediabetics	Gender		Obese/ overweight	Family History of DM	Comorbidities (HTN/IHD/Dyslipidaemia /PCOD/GDM)
			M	F			
<=30	171	38(22.2%)	21(55.3%)	17(44.7%)	35 (92%)	38(100%)	12(31.5%)
31-40	94	34(36.1%)	11(32.4%)	23(67.6%)	33(97%)	33(97%)	19(55.8%)
41-50	79	37(46.8%)	9(24.3%)	28(75.7%)	34(91.9%)	37(100%)	25(67.5%)
51-60	37	22(59.4%)	5(22.7%)	17(77.3%)	19(86%)	20(91%)	15(68.1%)
>60	19	7(36.8%)	1(14.3%)	6(85.7%)	7(100%)	7(100%)	7(100%)

Table-I. Demographic features of pre- diabetics

Age in years			Gender			Total	
			Male	%	Female		%
<=30	HBA1Cc	Normal	40	32%	85	68%	125
		Pre DM	21	55.3%	17	44.7%	38
		DM	3	37.5%	5	62.5%	8
	Total		64	37.4%	107	62.6%	171
31-40	HBA1Cc	Normal	19	40.4%	28	59.6%	47
		Pre DM	11	32.4%	23	67.6%	34
		DM	7	53.8%	6	46.2%	13
	Total		37	39.3%	57	60.7%	94
41-50	HBA1Cc	Normal	9	37.5%	15	62.5%	24
		Pre DM	9	24.3%	28	75.7%	37
		DM	8	44.4%	10	55.5%	18
	Total		26	32.9%	53	67.1%	79
51-60	HBA1Cc	Normal	3	42.8%	4	57.2%	7
		Pre DM	5	22.7%	17	77.3%	22
		DM	4	50%	4	50%	8
	Total		12	32.4%	25	67.6%	37
>60	HBA1Cc	Normal	1	33.3%	2	66.7%	3
		Pre DM	1	14.3%	6	85.7%	7
		DM	7	77.8%	2	22.2%	9
	Total		9	47.4%	10	52.6%	19

Table-II. Gender based prevalence of prediabetes among age groups

Age (years)	Number	Gender		BMI Category		Family History of DM	HbA1c Criteria			Co- morbidities
		M	F	Overweight	Obese		Normal	Pre DM	DM	Hypertension (54)
≤30	171	64	107	74 (43 %)	57 (33%)	165 (96 %)	125 (73%)	38 (22 %)	8 (5%)	Gestational Diabetes (3) PCOS (1)

Table-III. Characteristics of participants ≤ 30 years of age

DISCUSSION

In this study, prevalence of prediabetes was calculated among the participants using HbA1c. To best of our knowledge no other study of this kind had been performed in our region. We report the prevalence of prediabetes as 34% among study participants indicating a rising number. As data from 2011 WHO statement indicates that in Pakistan, 38 million people (29%) are with Pre-diabetes (20.5% women and 15.9% men).¹⁴⁻¹⁵ A study from Rawalpindi reports prediabetes prevalence as 37.4%.¹⁶ National diabetic survey conducted by Shera et al. has shown that the overall impaired glucose tolerance (IGT) was 22% in urban and 17% in rural areas.¹⁷ However, they used OGTT as a measure. Other studies done in various countries in Asia report figures less than these. Suhad M, et al¹⁸ reported prevalence of prediabetes in the Adult Population of Jeddah, Saudi Arabia as 9.0% (95% CI 7.5–10.5); 9.4% in men and 8.6% in women using fasting plasma glucose and glycated hemoglobin (HbA1c) based ADA criteria whereas we report as 32% and 36% respectively. Study conducted in urban slums of Bangalore by Hemavathi Dasappa et al¹⁹, reported prevalence as 11.57%. However study from Ningbo, China²⁰ using OGTT identified the age-standardized prevalence for pre diabetes as 30.53%.

In the overall 2011-2012 US population estimated prevalence for prediabetes was 38.0% (95% CI, 34.7%–41.3%).²¹ Prevalence rate of prediabetes also increased from 11.6% to 35.3% from 2003 to 2011 in England.²²

The prevalence of prediabetes increased with age in both genders but more among the females. Our study showed statistically significant association between prediabetes and family history of diabetes, overweight, obesity and hypertension.

Same has been reported in earlier studies.¹⁸⁻²²

In our study all 4 participants with history of gestational diabetes qualified the criteria for prediabetes. A study done among American women with history of Gestational Diabetes showed, 24.4% (95% CI, 18.3%–31.7%) of women had undiagnosed prediabetes and 6.5% (95% CI, 3.7%–11.3%) had undiagnosed diabetes.²³ Thus we suggest further studies in such females in our country as Asian population has their own characteristics regarding the dysglycemic metabolic states.

In our study group only one female had PCOS and she had prediabetes. In prospective trials, Moran et al. showed a prevalence of prediabetes of 35%, prevalence of Type 2 diabetes mellitus (T2DM) of 10%, and 5-10 fold risk of progression from prediabetes to diabetes in PCOS patients.²⁴ Velija-Asimi et al showed prevalence of (18%) in the women with PCOS with elevated BMI.²⁵ We recommend special focus on this young group of females in future studies.

Interestingly our study showed 22 % prevalence of prediabetes among young (age ≤30 years). Majority of these had family history for diabetes and had BMI above normal. Therefore we strongly recommend screening for pre-diabetes in such young adults. DM is irreversible once established. It is a slowly progressive condition; and it can take many years to progress from prediabetic to diabetic state without interventions.^{26,27} Therefore identifying prediabetes in younger age group become vital.

We also identified 14% enrolled participants as asymptomatic diabetics previously undiagnosed. So we recommend enhancement of public awareness efforts regarding screening for

diabetes.

Previous studies for prediabetes were mostly based on fasting blood sugar or OGTT levels. American Diabetes Association (ADA) approved HbA1c as diagnostic tool for DM and Prediabetes in 2010. Mann DM et al reported that if an alone HbA1c criterion is used, 8.9 million people who would have been considered normal by fasting glucose will be classified as having pre-diabetes. However, 37.6 million people will also be reclassified as not having pre-diabetes by HbA1c who would have been labeled as having pre-diabetes by the IFG criteria.²⁸ This discordance is in contrast to a relatively good agreement between HbA1c and fasting glucose when applied to the diagnosis of diabetes.²⁸ Lipska et al did study with objective to examine performance of HbA1c in comparison with FPG in diagnosing dysglycemia in older adults. They reported sensitivities and specificities of HbA1c compared with FPG as 47.0 % and 84.5% respectively for prediabetes.²⁹ Afro-Americans and women were more likely to be identified with dysglycemia by HbA1c than FPG. They found considerable discordance between FPG and A1c-based diagnosis of diabetes and prediabetes, with differences accentuated by race and gender. Broad implementation of HbA1c to diagnose dysglycemic states may substantially alter the epidemiology of these conditions.

For prediabetes, HbA1c testing should be used only as a screening tool; FPG measurement or an OGTT should be used for definitive diagnosis.³⁰ Measurement of HbA1c is convenient for the patients as no special preparation is required except the cost of the test. In our study small sample size and the sample collected, may not be true representative of Pakistani population. Secondly our study is based on sole HbA1c levels criteria. We therefore recommend further studies to establish the utility of this test as screening or diagnostic tool. Till that time we recommended fasting sugar levels and postprandial sugar level testing subsequent to positive screening for prediabetes by HbA1c testing.

Estimation of prevalence of prediabetes is important to identify the burden of this metabolic

state in our country which is already struggling with limited health resources. Creating awareness through seminars and involving electronic and print media on preventing or delaying the progression of prediabetes to diabetes should be prioritized as cost-effective health strategy rather than only attempting to manage the disease after it is established.

CONCLUSION

The prevalence of prediabetes in our studied population was significant which is almost same as in many other Asian countries. This state has strong relation to family history of diabetes and above normal BMI values. There are also a significant number of young prediabetics and undiagnosed diabetics in our population.

ACKNOWLEDGEMENTS

We thank SAMI pharmaceuticals, Getz Pharma, SciLife Pharma and High-Q Intl for funding our research project.

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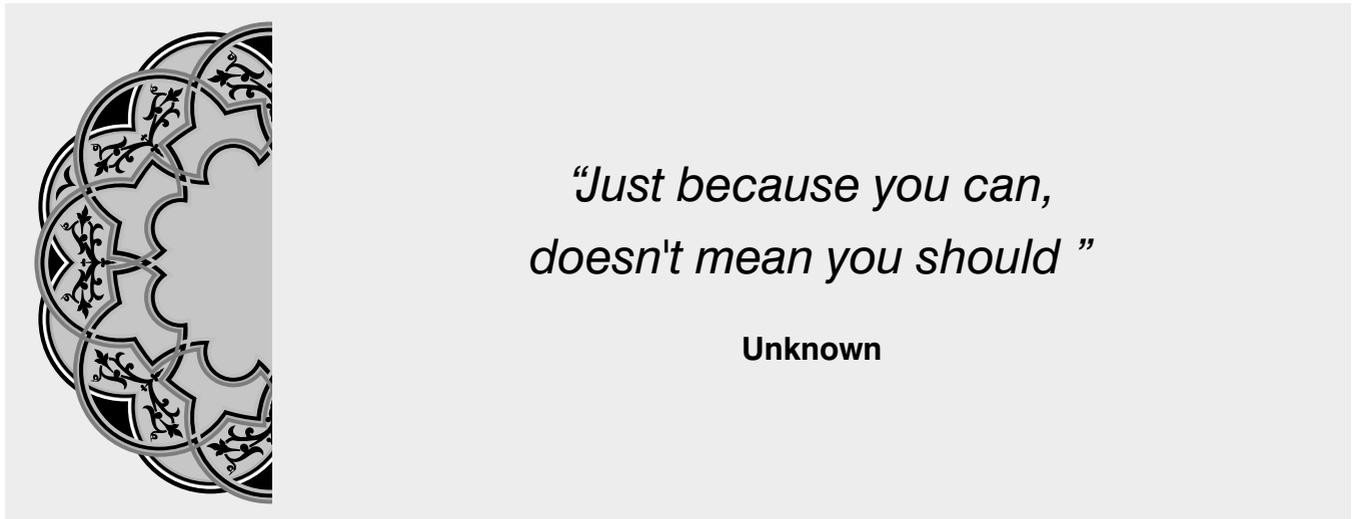
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3	Miqdad Haider	Data collection, Review of literature, Data analysis & drafting article.	
4	Abdul Rehman Saleem	Data collection & assembly	
5	M. Shahjehan Mirza	Data collection & assembly	
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