

Evaluation of Random Plasma Glucose with Lowered Cutoff Limits for Screening of Diabetes and Prediabetes

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ABSTRACT

Objective: To evaluate whether random plasma glucose (RPG) can be used as predictive marker and to determine lower cut off limits for screening of undiagnosed diabetes and prediabetes.

Study Design: Cross-sectional study

Place and Duration of Study: Department of Chemical Pathology, Rehman Medical Institute, Peshawar, Pakistan from 1st July, 2020 to 31st December, 2020.

Methodology: Two hundred and sixty four subjects having RPG less than 200mg/dl were selected and then OGTT was done according to ADA guidelines. Enzymatic hexokinase method (reference method) using Cobas c501 ® analyzer was used for measurement of plasma glucose.

Results: Mean age of patients was 39.92±12.49 years. There was significant difference ($p < 0.001$) between mean values of RPG in non-diabetics and diabetics at 95% confidence interval. Post-hoc analysis showed statistically significant difference between these groups. On applying ROC curve for prediabetics, it showed AUC of 0.777 while for diabetes it showed 0.922 at 95% CI. Diagnostic efficacy of RPG for prediabetics and diabetics at different cut off values was evaluated and it was found that sensitivity and specificity for prediabetics was good and for diabetics was excellent at cut off of 136mg/dl.

Conclusion: Random plasma glucose can be used as a reliable screening tool for initial diagnosis of diabetes and prediabetes. A random cut off value of 136 mg/dl can be used as a reliable limit for screening purposes and can be confirmed by using OGTT.

Keywords: Oral glucose tolerance test, Random plasma glucose, ROC curve, Diabetes, Prediabetes

INTRODUCTION

Diabetes mellitus “especially” type II (T2D) is a significant medical issue that affects millions of people around the world which necessitates a variety of diagnostic strategies to be adopted in addition to routine glycemic regulation. It is a leading cause of micro and macro vascular complications, so an early diagnosis of condition can prevent further progression, comorbidities and complications of disease and can also increase life expectancy of individuals.¹ Diabetes affected 463 million people worldwide in 2019, with 80 percent of those living in low- and middle-income countries. Diabetes decreases life expectancy by 4–10 years in people aged 40–60 years and raises the risk of death.² Pakistan is ranked in top five all over the world and 2nd amid twenty-one countries for having the largest number of diabetes in the Middle East and according to the Pakistan National survey of Diabetes, the prevalence of prediabetes in Pakistan is 10.91 percent and 16.98 percent for diabetes.³

Diabetes affects about half of the global community of adults, moreover, the number of people with prediabetes is on the rise.^{4,5} Diabetes and its complications are expensive to manage, and they cause significant morbidity and mortality early in life. The prediabetes has affected 352 million people worldwide, with 35-50% progressing to overt diabetes within five years. The prediabetes has been linked to coronary artery disease⁶ and heart failure⁷, its prevention is most successful if started before diabetes develops.⁶ Screening of healthy individuals through monitoring, healthy lifestyle and education can prevent advancement of risk factors which lead to development of prediabetes and diabetes mellitus.⁸

Targeted screening programs can help in early detection of prediabetes and undiagnosed diabetes.⁹ Screening of patients with high risk factors might not be costly.¹⁰ Diagnosis of diabetes in today's world is based on estimating glycosylated hemoglobin (HbA1C), fasting plasma glucose (FPG); or performing oral glucose tolerance test (OGTT) and measuring 2hour post glucose load plasma glucose.¹¹ Although HbA1c requires no preparation, but it has the lowest diagnostic prevalence, moreover standardized measurement is not available.¹² Fasting plasma glucose is more convenient but requires fasting for more than 8 hours and needs

more than one result or another test along with FPG for confirmation. On the other hand; OGTT is the gold standard test and is more sensitive in the diagnosis of diabetes and prediabetes¹³, but the process is much lengthier and also requires fasting leading to poor reproducibility of the test.¹¹

We need much easy and inexpensive way to screen undiagnosed cases of diabetes and prediabetes. RPG appears to be such test which is usually done in emergency and outpatient visits and can detect these conditions which when augmented by OGTT, FPG or HbA1c can help in their confirmation.¹⁴ RPG appears to be very helpful in testing especially in times of Covid-19 pandemic and can also help in confirmation of gestational diabetes mellitus in addition to HbA1c.¹⁵ The role of RPG in screening of undiagnosed cases of diabetes and prediabetes is evident from a study conducted in 2013 by Friedman et al¹⁶ showing 12.5% of screened patients suffering from DM. Other studies in support of the former statement conducted in 2012 by Barasch et al¹⁷ and Qurat-ul-Ain et al¹⁸ in 2021 show occurrence of diabetes and prediabetes in 12.2%, 24.46% and 5.7%, 13.6% respectively. The study was conducted to check if RPG can diagnose diabetes and prediabetes as our primary goal and establishing the appropriate cutoff at which diagnostic testing can be performed as our secondary goal.

MATERIALS AND METHODS

This was a cross-sectional study, carried out in Peshawar, Khyber Pakhtunkhwa Pakistan. The study was approved by the Rehman Medical Institute Ethics board in June 2020 for a period of 6 months under the study reference number RMI/RMI-REC/Approval/65. This study was started in July 2020 and ended in December 2020. Sample size was calculated through WHO sample size calculator considering margin of error of 5% and frequency of 16.98%.³ A total of 264 participants of age 18-60 years were required for the study and were selected through non-probability convenient sampling technique. The study was explained to all participants in local language. Written informed consent was signed by all the participants. Participants less than 18 years of age, diagnosed diabetic, with history of cardiovascular disease, hospitalization, associated drug history of corticosteroids,

immunosuppressant or chemotherapy, acute illness and pregnancy were excluded.

Participants with RPG less than 200 mg/dl (11.11 mmol/l) were included in the study. Oral glucose tolerance test (OGTT) of every participant was carried out according to the guidelines of American Diabetic Association (ADA).¹⁹ The study participants were divided into diabetic and non-diabetic groups. Non diabetics were then further sub divided into normoglycemics and prediabetics.

Gray top blood collection tube (potassium oxalate/sodium fluoride) was used for sample collection. The blood samples were transported within half an hour to processing room. Enzymatic hexokinase reference method using Cobas c501 ® (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim) was used for the measurement of plasma glucose levels. The rate of NADPH formation during the reaction is photometrically determined which is equivalent to glucose concentration. The Kit has lower limit of detection of 2mg/dl (0.11 mmol/l), linearity of 750mg/dl (41.6mmol/l) and CV of repeatability/intermediate precision of 0.7%/1.1% respectively.

All the data were arranged and organized on Excel sheet from both the groups, which were then analyzed by using SPSS version 23.0. Independent sample t-test was used for evaluating difference between mean RPG and OGTT values in diabetics and non-diabetics. ROC curves were plotted and AUC was calculated. P-value <0.05 was considered statistically significant. On the basis of ROC curve analysis, sensitivity and specificity for different cut off values of RPG were evaluated. Mean, Standard deviation and frequency were calculated for age and gender in both groups.

RESULTS

The number of females was more than those of males in both diabetic and non-diabetic categories with mean age of diabetic subjects were more as compared to non-diabetic individuals (Table 1).

On applying independent sample t-test there was significant difference (p<0.001) between mean values of RPG in non-diabetics and diabetics (Table 2).

On applying one-way Anova, mean RPG values based on OGTT showed highly significant difference (p=<.001) among the groups (Table 3). Post-hoc analysis showed that there was highly significant difference between prediabetics and normoglycemics (p=.001), a highly significant difference between diabetics and normoglycemics (p=.001) and a significant difference between diabetics and prediabetics (p=.001) [Table 4].

Table 1: Demographic information of the patients in both groups

Variable	Non-Diabetic	Diabetic
Gender		
Male	96 (40%)	10 (41.7%)
Female	144 (60%)	14 (58.3%)
Age (years)	39.32±12.74	45.92±7.35

Table 2: Mean random plasma glucose in both diabetic and non-diabetic groups

RPG (mg/dl)	N	Mean±SD	p-value
Non-Diabetic	240	123.92±17.87	<0.001
Diabetic	24	152.08±8.62	

Table 3: Mean RPG vs OGTT in different groups

	N	(Mean±SD)	p-value
Normoglycemia (<140mg/dl)	188 (71.21%)	119±17.13	<.001
Prediabetics (140-200mg/dl)	52 (19.69%)	138.46±12.06	
Diabetes (>200mg/dl)	24 (9.09%)	152.08±8.62	

ROC curve analysis of RPG for prediabetics (52/264) yielded an AUC of 0.777 (Fig. 1). ROC curve for diabetics (24/264) showed an AUC of 0.922 which was greater than that of prediabetic individuals (Fig. 2). Upon ROC curve analysis optimal

RPG cut-off value was found to be 136mg/dl for prediabetics (AUC 0.777 at 95% CI) as fair diagnostic test with sensitivity and specificity of 76.9% and 79.8% while same cut-off value for diabetics showed AUC 0.922 at 95% CI as excellent diagnostic test with sensitivity and specificity of 91.7% and 66.7% respectively (Table 5).

Table 4: Post Hoc analysis on comparison of different groups

Group comparison	P value	95% Confidence Interval
Prediabetics normoglycemics	<.001	12.78- 24.35
Diabetics normoglycemics	<.001	24.19- 40.19
Diabetics prediabetics	.001	4.51-22.73

Table 5: Diagnostic efficacy of prediabetics vs diabetics at different cut-offs

Cut-offs of RPG (mg/dl)	Prediabetics		Diabetics	
	Sensitivity	Specificity	Sensitivity	Specificity
120	92.3%	61.7%	100%	50%
130	80.8%	72.3%	100%	60.8%
136	76.9%	79.8%	91.7%	67.5%
140	50%	79.8%	83.3%	67.5%

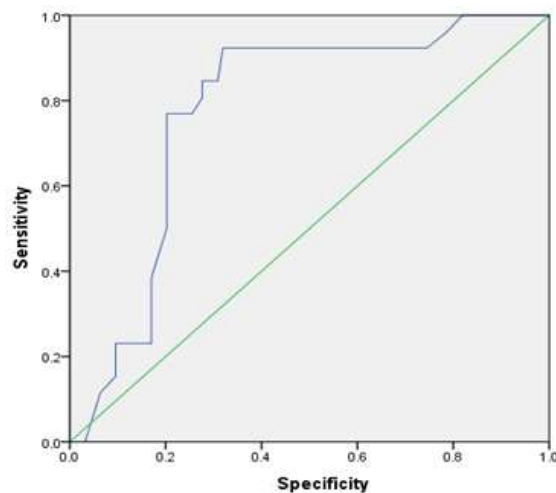


Fig. 1: ROC curve showing AUC of RPG for pre-diabetes

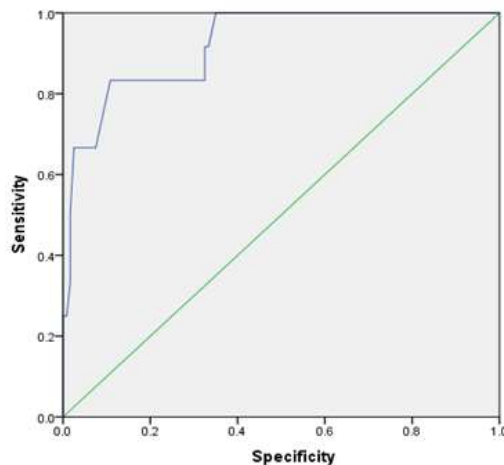


Fig. 2: ROC curve showing AUC of RPG for diabetes

DISCUSSION

Diabetes mellitus is the most prevalent metabolic disease. The prevalence of prediabetes and undiagnosed diabetes is increasing day by day. There is a need for rapid screening test which can detect such cases and can be further evaluated through confirmatory test. RPG can be done at any time not requiring

fasting and can be done along-with routine blood tests. ADA recommends that testing for prediabetes and undiagnosed diabetes should be done in early age.²⁰

Our study showed high levels of RPG, which are different from the values reported by Rhee et al.¹⁴ Similarly the current study also demonstrates that normoglycemics (NG) were 188 (71.21%) while prediabetics and diabetics was 52 (19.69%) and 24 (9.09%) respectively, these findings are almost consistent with the findings of Qurat-ul-Ain et al¹⁸ in which the number of individuals with NG were 173 (61.8%), prediabetics were 69 (24.6%) and diabetics were 38 (13.6%) respectively. On post hoc analysis there was found a statistically significant difference between different groups of patients based on results of OGTT and these findings are again in accordance with the results illustrated by Qurat-ul-Ain et al.¹⁸ ROC curve analysis of RPG levels against OGTT in diabetic patients in this study yielded an AUC of 0.922 which is much higher than 0.856, demonstrated by Rhee et al, while ROC curve analysis for prediabetics yielded an AUC of 0.777 which is comparable to the value of 0.771 reported by Qurat-ul-Ain et al.¹⁸ The current study also highlighted the sensitivity of and specificity of RPG levels. The levels of RPG derived for the screening purpose was comparable with the levels of 135 mg/dl reported by Meek et al²¹ with a sensitivity of 70% and specificity of 90% which does not align with our study. A study conducted by Steven et al¹⁶, in which RPG levels of >126 mg/dl were suggested for screening of the patients presenting in emergency department of tertiary care hospital. These levels were lower than the levels derived from our study. Similarly Ziemer et al²² derived RPG levels of 125 mg/dl with a sensitivity of 40% and specificity of 93%, these value were not consistent with the current study. Ginde et al²³ reported that sensitivity and specificity for different cut off levels of RPG for predicting abnormal HbA1C were similar to our study. Our study also demonstrated sensitivity and specificity of RPG for predicting abnormal OGTT. The sensitivity of our study for each cut off levels was much higher while specificity was lower than that of Ginde et al.²³ Our study deduced the levels of >120 mg/dl with sensitivity of 100% and specificity of 60.8% and levels of >130 mg/dl had sensitivity of 91.7% and specificity of 67.5 % while levels of 140 mg/dl had sensitivity of 83.3 % and specificity of 67.5 %. Ginde et al²³ reported that glucose threshold >120 mg/dL had 89% specificity and 26% sensitivity for predicting abnormalHbA1c,>130 mg/dL had 95% specificity and 18% sensitivity and >140 mg/dL had 98% specificity and 14% sensitivity. Ginde et al²³ also described that in USA in emergency department raised RPG levels were overlooked and not communicated to the patients by physicians. The problem in using the RPG levels in outpatient and emergency department for screening of diabetics is the need for follow-up of patients by their physicians. A lack of patient follow-up has been found in other studies as well.²³⁻²⁵

CONCLUSION

Random plasma glucose can be used as a reliable screening tool for initial diagnosis of diabetes and prediabetes in outpatient or emergency departments. Random plasma glucose levels of 136 mg/dl can be used as a reliable cut off limit for further evaluation of the patient. Furthermore, the confirmation of diabetes or prediabetes can be done by using OGTT.

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