ORIGINAL ARTICLE

Evaluation of random plasma glucose for assessment of glycaemic control in type 2 diabetes mellitus

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Abstract

Objective: To evaluate the accuracy of random plasma glucose in outpatients with type 2 diabetes mellitus for assessing glycaemic control.

Methods: This comparative, cross-sectional study was conducted at the chemical pathology department of PNS Shifa Hospital, Karachi, from August 2015 to March 2016, and comprised data of subjects with type 2 diabetes mellitus who reported for evaluation of glycaemic control in non-fasting state. All blood samples were analysed for random plasma glucose and glycated haemoglobin. Random plasma glucose was compared as an index test with glycated haemoglobin considering it as reference standard at a value of less than 7% for good glycaemic control. SPSS 20 was used for data analysis.

Results: Of the 222 subjects, 93(42%) had good glycaemic control. Random plasma glucose showed strong positive correlation with glycated haemoglobin (p=0.000).Area under curve for random plasma glucose as determined by plotting receiver operating characteristic curve against glycated haemoglobin value of 7% was 0.89 (95% confidence interval: 0.849-0.930). Random plasma glucose at cut-off value of 150 mg/dl was most efficient for ruling out poor glycaemic control among patients with type 2 diabetes mellitus with 90.7% sensitivity and69.9% specificity and Youden's index of 0.606.

Conclusion: Random plasma glucose may be used to reflect glycaemic control in adults with type 2 diabetes mellitus in areas where glycated haemoglobin is not feasible.

Keywords: Random plasma glucose, RPG), Type 2 diabetes mellitus, T2DM, Long-term glycaemic control, Glycated haemoglobin, HbA1c. (JPMA 67: 1353; 2017)

Introduction

Type 2 diabetes mellitus (T2DM) is the most challenging health care problem of the 21st century that poses great threats to economy and quality of life due to very high rate of complications.[1] Global burden of the disease is about 415 million with 9.1% regional prevalence for Pakistan.[1] The Asian population, due to the onset of diabetes at early age and longer duration, are at greater risk of long-term complications.[2,3]

Glycaemic control is the cornerstone in the management of T2DM.[4] Several randomised clinical trials and observational studies have revealed that good glycaemic control considerably reduce the microvascular and macrovascular complications of T2DM.[5] Glycated haemoglobin (HbA1c) is well recognised as an index of long-term blood glucose concentrations and has analogous correlation with development of complications in T2DM.[4,5] However, due to limited resources in developing countries like Pakistan, standardised HbA1c assay is either not available or not affordable due to its high cost.[6] High prevalence of T2DM and more risk of complications in our population increase the need for consideration of alternative tests like random plasma glucose (RPG), 2-hour postprandial glucose and fasting plasma glucose for monitoring of glycaemic control.[7] RPG is the most feasible test because of untimed sampling, easy availability of standardised assay and being inexpensive.[6] Various studies have shown acceptable correlation between HbA1c and RPG levels.[6,8,9] However, Bleyer et al. revealed ethnic differences in relationship between HbA1c and RPG among Caucasians and Africans, thus making it worth to establish such association in other populations.[10] Another well-appreciated and documented controversy associated with RPG is the use of various cut-offs to define glycaemic control.[6,11,12] The current study was conducted to assess the diagnostic accuracy of RPG as a reliable indicator of good glycaemic control and to evaluate the performance of RPG at various cut-offs considering HbA1c< 7.0% as a reference indicator of good glycaemic control.

Patients and Methods

This comparative cross-sectional study was conducted at the Department of Chemical Pathology and Endocrinology, PNS Shifa Hospital, Karachi, from August 2015 to March 2016. Formal approval from the

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institutional review board was obtained. Sensitivity and specificity sample size calculator by Lin Naing was used to estimate sample size using 9% prevalence for T2DM in Pakistan,[1] 77% sensitivity and 71% specificity of RPG against HbA1c[6] while keeping error probability at 0.05 and statistical power at 0.80. All individuals who reported at laboratory reception for laboratory evaluation of glycaemic control were targeted for further inclusion in the study. The subjects of either gender aged more than 18 years and diagnosed cases of T2DM were included. Subjects with pregnancy, any acute illness, hypoglycaemia, haemoglobinopathies and anaemia were excluded. Individuals reporting in fasting state were also excluded. Informed consent was taken from each individual.

Three ml of blood sample was taken by venipuncture in sample tube with sodium fluoride (NaF) /ethylenediaminetetraacetic acid (EDTA) for RPG and HbA1c. RPG was analysed within 2 hours of sample collection by hexokinase method while HbA1c was analysed using Tina-quant method on a fully automated chemistry analyser (Roche Modular P800). SPSS 20 was used for data analysis. Descriptive statistics for qualitative variables like gender were shown in percentages. All data was checked for normality using Kolmogorov-Smirnov test. Mean and standard deviation (SD) were calculated for parametric quantitative variables like age. Median and range were calculated for non-parametric variables like RPG and HbA1c. The correlation analysis between RPG and HbA1c was carried out by Spearman's correlation coefficient (rs). Using American Diabetes Association (ADA) criteria of HbA1c, i.e. less than 7% as indicator of good glycaemic control,[4] area under the curve (AUC) was calculated through receiver operating characteristic (ROC) curve analysis and different cut-offs of RPG were evaluated against the reference standard. This included calculation of diagnostic accuracy parameters like sensitivity, specificity, predictive values, likelihood ratios and Youden index. P<0.05 was considered significant.

Results

Of the 222 participants, 85(38%) were females and 137(62%) were males. The overall mean age of patients was53±13.6 years. Median values for RPG and HbA1c were137.7mg/dl (interquartile range [IQR]: 134.6-230.4) and 7.5% (IQR: 6.0-9.4), respectively. Moreover, 93(41.9%) subjects had good glycaemic control as per the results of reference standard HbA1c according to the ADA criteria (Table-1).

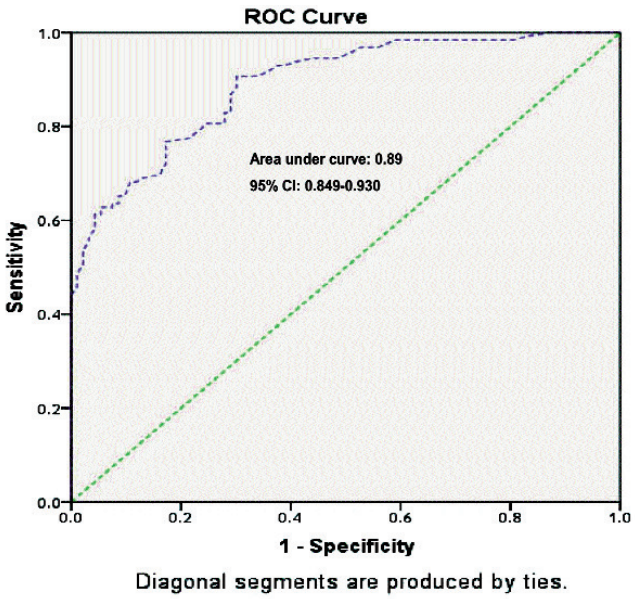
There was significant positive correlation between RPG and HbA1c (r_s = 0.75, p<0.001). ROC curve analysis showed RPG to have an AUC of 0.89 (95% confidence interval (CI): 0.849-0.930) (Figure).

Table-1: Demographic and clinical characteristics of study population (N=222).

Characteristics	Mean	SD
Age (years)	53	13.6
	Frequency	**Percentage**
Gender Male	137	62
Female	85	38
Good glycaemic control (HbA1c < 7%)	93	42
	Median	**Interquartile range**
RPG(mg/dl)	173.7	134.6-230.4
HbA1c (% of total Hb)	7.5	6 -9.4

RPG: Random plasma glucose
HbA1c: Glycated haemoglobin
Hb: Haemoglobin.

Comparison of RPG at different cut-offs showed that a cut-off of 150 mg/dl had better sensitivity and negative predictive value (NPV) with optimum specificity (sensitivity = 90.7%; specificity = 69.9%; positive predictive value (PPV) = 80.7%; NPV = 84.4%, positive likelihood ratio [LR+]= 3.013, negative likelihood ratio [LR-]= 0.133). Employing a lower cut-off, i.e. 140 mg/dl, improved sensitivity to 94.6%, but it markedly reduced specificity to 55.9%. On the other hand, the results of RPG at the International Diabetes Federation (IDF)-recommended cut-off, i.e. 160 mg/dl, showed marginally



ROC: Receiver operating characteristic
CI: Confidence interval.

Figure: ROC analysis of random plasma glucose keeping glycated haemoglobin as reference standard.

Table-2: Diagnostic performance characteristics of random plasma glucose at different cut-offs.

RPG mg/dl	Sensitivity %	Specificity %	PPV %	NPV %	LR+ %	LR- %	Youden's index
140	94.6	55.9	74.8	88.1	2.145	0.096	0.505
150	90.7	69.9	80.7	84.4	3.013	0.133	0.606
160	82.9	72.04	80.5	75.3	2.960	0.237	0.549

RPG: Random plasma glucose
PPV: Positive predictive value
NPV: Negative predictive value
LR+: Positive likelihood ratio
LR-: Negative likelihood ratio.

better specificity but with moderately reduced sensitivity and low NPV(sensitivity = 82.9%; specificity = 72.04%; PPV = 80.5%; NPV= 75.3%, LR+= 2.96, LR-= 0.237). Youden's index was used to define maximum potential effectiveness of RPG and it revealed that 150 mg/dl with a value of 0.606 was the optimal cut-off for good glycaemic control among patients with T2DM (Table-2).

Discussion

Diabetes mellitus is the most prevalent chronic metabolic disease that has affected 415 million people with 75% of its victims residing in low- and middle-income countries. About 91% of the diabetics are suffering from T2DM.[1] The chronic hyperglycaemia of T2DM affects all major body organs like heart, kidneys, eyes, nerves and blood vessels, leading to increased morbidity and mortality.[3] The landmark study of diabetes control and complication trial (DCCT) clearly revealed that glycaemic control is the cornerstone in reducing the microvascular and macrovascular complications of the disease. Moreover, this large randomised control trial also specified that HbA1c >7.0% is associated with a considerably increased risk of both microvascular and macrovascular complications, irrespective of underlying treatment.[13] After strenuous efforts at standardisation of HbA1c, it is now recommended as the gold standard marker for long-term monitoring of glycaemic control and is being widely used in developed countries for this purpose.[4,14] However, facilities for standardised HbA1c assay are either not available or not affordable in low-income countries like Pakistan owing to its high cost and limited resources. Recently, the IDF recommended use of post-meal plasma glucose measurement with a target value of 160 mg/dl for monitoring of glycaemic control in resource-poor setting.[15] However, there are ethnic differences in relationship between HbA1c and RPG as revealed by Bleyer et al. and data from various countries also emphasises the fact that the cut-off value of RPG may differ from the one suggested by the IDF.[10-12]

Kazmi et al. reported significant positive correlation between RPG and HbA1c (p= 0.000) in Pakistani adults with T2DM.[9] However, the RPG has not yet been evaluated for monitoring of glycaemic control in Pakistan. This study investigated the diagnostic accuracy of RPG in assessing glycaemic control in our adult patients with T2DM and has revealed significant findings. First, RPG levels have significant correlation with HbA1c. Second, RPG can be used as a good predictor of HbA1c< 7.0% as shown by AUC of 0.89(95% CI: 0.849-0.930). Third, the overall efficiency of the RPG remained superior at cut-off value of 150 mg/dl with higher Youden's index than at other selected cut-offs.

Various studies from developing countries have evaluated association of 2-hour PPG with HbA1c.[16-18] Recently, a meta-analysis by Ketema E. B. summarised that PPG has a closer association with HbA1c than FPG, and a better predictor of overall glycaemic control in the absence of HbA1c.[19] In our study, we selected RPG for evaluation because being untimed sample it is more convenient than 2-hour PPG. But data is very scarce regarding evaluation of RPG as a tool for monitoring glycaemic control. A study conducted in the United Kingdom (UK) by Gill et al. revealed that a target value of 180 mg/dl of RPG measured by point-of-care testing (POCT) device has 96% sensitivity for HbA1c <10%.[11] Otieno et al. from Kenya reported that RPG level of 126 mg/dl has 92.7% sensitivity and 59.8% specificity for good glycaemic control at HbA1c $\leq$ 7.8%.[12] Recently, J.B. Rasmussen et al. revealed that RPG level of 135 mg/dl could be used in Sub-Saharan Africa for monitoring of glycaemic control with 76.7% sensitivity, 70.8% specificity and 82.9% NPV at HbA1c <7.0%.[6] The discordant results of these studies and our data can be explained by the racial difference of the participants, heterogeneity in the analytical methods for RPG and HbA1c and use of different cut-off of HbA1c as a reference standard for good glycaemic control. The IDF in 2012 recommended RPG level of 160 mg/dl to be used for monitoring of glycaemic control, but we found that

adopting RPG at a lower cut-off of 150 mg/dl will prove more beneficial in our population due to enhance sensitivity and NPV for identifying patients with poor glycaemic control as demonstrated in this study.

The current study also had a few limitations. First, it was a hospital-based, cross-sectional study. Second, we had limited information about the duration of DM, treatment modalities used and existing complications in our subjects. In future, we plan to have a more comprehensive prospective study with a detailed analysis of demographic and clinical variables.

Conclusion

RPG may be used to reflect glycaemic control in adults with T2DM in areas where facility for standardised HbA1c test is not available. A target value of 150 mg/dl was found to be more suitable for monitoring of glycaemic control in Pakistani adults.

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Conflict of Interest: None.

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