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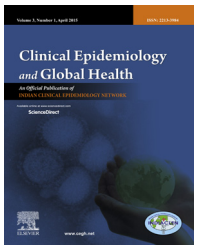

Original article

Comparison of venous plasma glucose and capillary whole blood glucose in diagnosis of gestational diabetes: Study from Karachi, Pakistan

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ABSTRACT

Objective: To determine accuracy of venous plasma glucose (VPG) and capillary blood glucose (CBG) in Gestational diabetes (GD) detection using Diabetes in Pregnancy Study Group India criteria.

Methods: It was a prospective single arm intervention study. One thousand thirty pregnant women, in second and third trimesters, recruited between June 2014 to March 2015 were included in the study. Seventy-five gram oral glucose was given, irrespective of last meal; venous and capillary blood samples were collected at 2 h. Using World Health Organization (WHO) criteria, 2 h VPG level ≥140 mg/dl but <200 mg/dl were labeled as GD; ≥200 mg/dl diabetes mellitus (DM), <140 mg/dl as normal. Correlation between VPG and CBG, sensitivity, specificity and predictive values of either for abnormal glycemic profile (GD or DM) were assessed.

Result: Mean maternal age was 25.8 ± 5.2 years, mean gestational age was 28.9 ± 4.4 weeks and mean body mass index was 25.8 ± 5.1 kg/m^2. By WHO criteria, 78 (7.6%) had GD, 14 (1.4%) had DM. Pearson's correlation between VPG and CBG was 0.761 ($p < 0.0001$). CBG value at 2-h plasma glucose level of ≥140 mg/dl had a sensitivity of 94.87% and specificity of 79.10% with area under receiver operative curve (ROC) 86%.

Conclusion: Non fasting CBG is useful for screening of abnormal glucose homeostasis in pregnancy.

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1. Introduction

Diabetes during pregnancy is the most common metabolic disorder.[1] Its prevalence during pregnancy has been reported to be around 13%.[2] Prevalence in a set of population depends upon ethnicity, dietary influence, life style, family history of diabetes and other factors.

Gestational diabetes (GD) has been associated with adverse pregnancy outcome. Globally, prevalence of GD is on rising trend. Increased prevalence of GDM has been reported from Asian population. This has been described in studies conducted in Europe, America and Australia.[3]

Prevalence of gestational diabetes mellitus (GDM) in Pakistan is largely unknown. In a hospital based study from a private University, prevalence of GDM was 3.3%. Small hospital based studies have shown a varying prevalence of 3.3–8%.[4,5] The estimated prevalence from neighboring country India, with population characteristics similar to ours, the prevalence has been found to be as high as 17%.[6]

Risk factors for GDM include increased body mass index (BMI), family history of diabetes mellitus, past history of GDM or macrosomic baby and past history of intrauterine demise or stillbirth. American Diabetes Association (ADA) and ACOG (American College of Obstetrician & Gynecologist) also recommends risk factor based screening for all women to diagnose GDM through a two-step procedure first sampling and then diagnosis.[7] If GCT is found positive, oral glucose tolerance test (OGTT) is performed. This two-step procedure has its advantages and disadvantages as well. A one step procedure to diagnose GDM has also been recommended by many societies.[8]

World Health Organization (WHO) also recommends a 2 step procedure for diagnosis of GDM. With a positive OGCT, 2 h glucose tolerance test with 75 g is recommended. A cut-off value >140 mg/dl at 2 h is taken as diagnostic for GDM. Pitfalls of test include recall, and fasting state. It is commonly observed that drinking large amount of glucose in an empty stomach is un-physiological and excites nausea and vomiting. A number of alternatives have also been suggested to replace glucola.[9] Diabetes in pregnancy study group of India (DIPSI), recommends performing 75 g OGTT in non-fasting state[10] and a single 2 h value of >140 mg/dl is taken as diagnostic of GDM. It is believed that a normal woman will respond with adequate insulin response to have normal glucose values, whereas a woman with impaired insulin response will behave abnormally, first with meal, and then with 75 g glucose ingestion. This cascading effect will decrease the risk of false positive diagnosis of GDM. Moreover, high risk women will not be lost from diagnosis, as lost to follow up is a common practice.[11] The above method of diagnosis and follow up has been adequately reported in literature as well.[10,12] This one step procedure is suitable for our set up where compliance is a major issue. Venous sampling on multiple occasions in low resource settings is also not feasible from logistics and economic point of view. Studies have been done to see if capillary glucose sampling, which is far simpler and easier, can replace venous sampling.[13]

We aimed to determine the diagnostic accuracy of CBG for detecting abnormal glucose homeostasis, as defined by Venous Plasma Glucose (VPG) levels using the DIPSI criteria, in a cross-sectional sample of Pakistani women.

2. Methodology

This prospective study was undertaken at the Department of Obstetrics & Gynecology Unit II, Civil Hospital and Dow University of Health Sciences, Karachi – Pakistan between June 2014 to March 2015. The study was approved by the ethical review board of the University.

The study population included pregnant women in the second and third trimesters, seeking antenatal care at the outpatient antenatal clinic demographic details, including height, weight and details of previous pregnancy on a predesigned questionnaire were filled by the research officers. Women with established diabetes mellitus, multiple gestation and chronic liver disease (hepatitis B &C) were excluded. Family history of diabetes included parents, siblings, first and second degree relatives. After informed verbal consent, 75 g glucose dissolved in a 100 ml of water was given to drink, in non-fasting i.e. irrespective of last meal. Diabetes in pregnancy study group of India (DIPSI), recommends performing 75 g OGTT in non-fasting state[9] and a single 2 h value of >140 mg/dl is taken as diagnostic of gestational diabetes mellitus (GDM). Blood glucose levels were collected both for capillary blood glucose (CBG) and venous plasma glucose (VPG); CBG levels were checked on Accu check (Roche) glucometer, after calibration VPG levels were measured by oxidase-peroxidase method, using analyzer (Dimension). The 2-h VPG value by the intravenous method glucose oxidase method and 2-h PG value by CBG were obtained simultaneously in all women. Women with blood glucose levels ≥140 mg/dl were given dietary advice along with exercise. A diet chart was given and follow up scheduled after 2 weeks with assessment of fasting blood glucose levels. In event of blood glucose levels >200 mg/dl, treatment with either oral hypoglycemic agent or insulin was started.

3. Statistical analysis

Statistical Package for Social Sciences (SPSS) version 17.0 was used for data analysis. Descriptive analyses were used for the mean values and percentage. Bland and Altman graph was used to find agreement between Venous oral glucose tolerance test (VOGTT) and Capillary oral glucose tolerance test (COGTT). Univariate and multivariate logistic regression analysis were utilized to predict the relationship between VOGTT (DIPSI) and risk factors. Sensitivity (specificity, positive and negative predictive values were computed to validate the COGTT (DIPSI) in detecting GDM. ROC was used to the predictive power of the constructed equation. $P < 0.05$ were considered statistically significant.

4. Results

In this study a total of 1030 pregnant women were recruited. The mean age of participants was 25.8 ± 5.2 years, mean gestational age was 28.9 ± 4.4 weeks and the mean body mass

Table 1 – Clinical characteristic of normoglycemic and gestational diabetes subjects identified by DIPSI.

Variables	Normoglycemic (VOGTT < 140 mg/dl)	Gestational diabetes (VOGTT ≥140 mg/dl)	p-value	Overall
n	952	78	–	1030
Age (years)	25.57 ± 5.12	28.45 ± 5.70	<0.001	25.79 ± 5.22
Gestational age (weeks)	28.96 ± 4.45	29.32 ± 3.80	0.490	28.99 ± 4.40
Weight (kg)	61.37 ± 11.59	66.21 ± 12.81	<0.001	61.74 ± 11.75
Height (cm)	154.95 ± 3.87	155.54 ± 6.23	0.219	154.99 ± 4.10
BMI (kg/m^2)	25.58 ± 4.75	27.37 ± 5.14	0.002	25.72 ± 4.80
Number of parity				
None	310 (32.6%)	17 (21.8%)	0.050	327 (31.7%)
One or more	642 (67.4%)	61 (78.2%)		703 (68.3%)
History of macrosomia	18 (1.9%)	7 (9%)	<0.001	25 (2.4%)
History of GDM	9 (0.9%)	6 (7.7%)	<0.001	15 (1.5%)
Family history of DM	229 (24.1%)	31 (39.7%)	0.002	260 (25.2%)

Data presented as Mean ± SD or *n* (%). $p < 0.05$ was considered statistically significant. VOGTT, Venous oral glucose tolerance test; BMI, Body Mass Index; GDM, Gestational Diabetes Mellitus; DM, Diabetes Mellitus; DIPSI, Diabetes in pregnancy study group of India.

index was 25.8 ± 5.1 kg/m^2. By using the DIPSI criteria (VPG ≥140 mg/dl),78 (7.6%) women were diagnosed as having gestational diabetes (GD). Out of 78 GD, 64 (6.2%) had VPG 140–200 mg/dl and 14 (1.4%) had VPG >200 mg/dl. Table 1 shows the clinical characteristics along with crude odds ratios fornormoglycemic and gestational diabetic participants. A statistically significant positive correlation was noted between CBG and VPG levels following DIPSI ($r = 0.761$, $p < 0.0001$) and interclass correlation coefficient (ICC) was 0.391 ($p < 0.0001$). Bland and Altman graph was shown for the agreement between VPG and CBG in Fig. 1. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CBG in detecting abnormal glucose response are presented in Table 2. CBG cut point of 140 mg/dl provide the optimum sensitivity and specificity of 94.87% (CI: 87.0–98.3) and 79.10% (CI: 78.4–79.4) respectively. PPV was 5.1% and NPV was 20.9% at the same cutoff. Area under the curve by using the Receiver operator characteristic analysis (ROC) was 90.3% which shows the high prediction power of the constructed equation (Fig. 2).

Univariate and multivariate logistic regression were used to predict the relationship between VPG and risk factors. All significant variables ($p < 0.25$ at univariate analysis) were considered for multivariate analysis. The final multivariate model shows the highly significant i.e. age, positive history of macrosomia and family history of diabetes are strongly associated with VPG ($p < 0.05$) (Table 3).

Table 2 – Multivariate logistic regression adjusted for age, BMI, parity, past history of macrosomia, history of GDM and family history of DM.

Variables	Gestational diabetes (VOGTT ≥140 mg/dl)	Normoglycemic (VOGTT < 140 mg/dl)	p-value	Odds ratio
Age				
<26 years	51 (65.4%)	395 (41.5%)	<0.001	2.664 (1.642–4.322)
≥26 years	27 (34.6%)	557 (58.5%)		
BMI				
≥25	50 (64.1%)	455 (48.3%)	0.007	1.911 (1.183–3.089)
<25	28 (35.9%)	487 (51.7%)		
Parity				
≥1	61 (78.2%)	642 (67.4%)	0.050	1.733 (0.995–3.016)
0	17 (21.8%)	310 (32.6%)		
History of macrosomia				
Yes	7 (9%)	18 (1.9%)	<0.001	5.116 (2.068–12.65)
No	71 (91%)	934 (98.1%)		
History of GDM				
Yes	6 (7.7%)	9 (0.9%)	<0.001	8.731 (3.024–25.21)
No	72 (92.3%)	943 (99.1%)		
Family history of DM				
Yes	31 (39.7%)	229 (24.1%)	0.002	2.082 (1.292–3.356)
No	47 (60.3%)	723 (75.9%)		

$p < 0.05$ was considered statistically significant. VOGTT, Venous oral glucose tolerance test; BMI, Body Mass Index; GDM, Gestational Diabetes Mellitus; DM, Diabetes Mellitus.

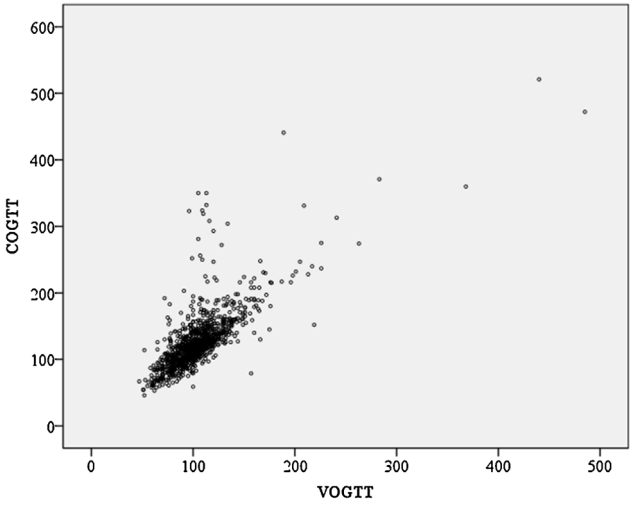

Fig. 1 – Scatter plot between COGTT and VOGTT. VOGTT, Venous oral glucose tolerance test; COGTT, Capillary oral glucose tolerance test.

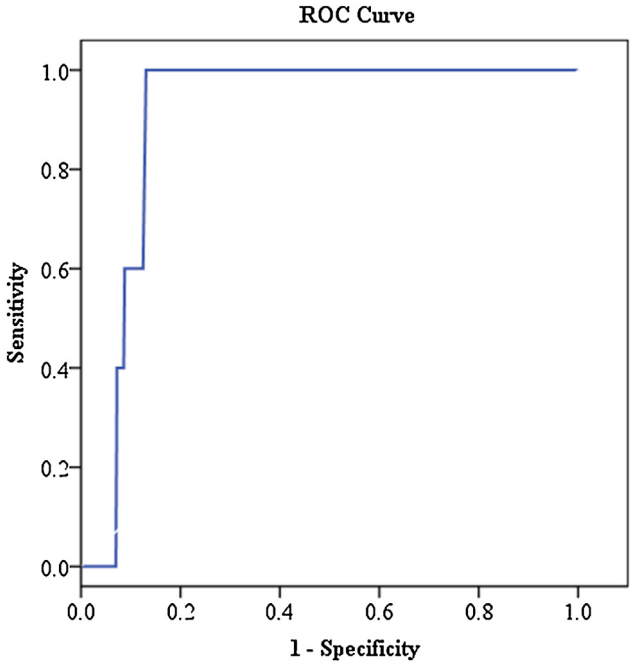

Fig. 2 – Receiver Operating Characteristic (ROC) curve. Area under the curve (AUC) = 0.903. Venous oral glucose tolerance test (VOGTT) was considered state variable with cut off ≥140 mg/dl. Capillary oral glucose tolerance test (COGTT)was considered as test variable

5. Discussion

In this study we compared the values of capillary blood glucose (CBG) with venous plasma glucose (VPC) using DIPSI criteria for the diagnosis of gestational diabetes.

This is the first study in Pakistan, using the DIPSI criteria for diagnosis of gestational diabetes (GD). All previous studies have been conducted in India, Srilanka and Nepal.[12–14] In a study from India, where universal screening was done for antenatal women, the prevalence was as high as 23%. The investigators included women in all three trimesters of pregnancy, and used WHO criteria of 75 g glucose in fasting state.[15] In our study, we included women in second and third trimesters only. Although the current recommendation is to screen for GDM with 75 g oral glucose and subsequent measurement of venous plasma glucose.[16] This procedure is not practical in many instances where trained personnel are not available to collect venous plasma glucose and may not be applicable for universal screening purposes at community level for the diagnosis of GDM. Therefore, estimation of CBG may be a convenient alternative method for screening purpose, especially in developing countries like Pakistan.[12] We used DIPSI criteria for diagnosis of GD, as it involved administering glucose load in non-fasting state. This results in better compliance in pregnant women. Risk based assessment need recall of patient for glucose tolerance test in fasting state to make a diagnosis of GDM.[15] This has been accepted universally that may result in loss of patients to follow up. This has been observed in both developing and developed countries.[11] DIPSI appears patient friendly, as it does not require fasting state of pregnant women. Considering our population being at high risk for diabetes mellitus, capillary blood glucose testing with a calibrated glucometer can be of enormous help. Technical facilities for venous blood glucose levels using oxidase-peroxidase method may not be available always and everywhere in our set up.

Dacus et al., in their study on subject with GDM, found sensitivity of 82% and specificity of 98% of CBG, when compared with VPG.[13,17,18] For low income countries, like Pakistan where a facility of venous blood glucose levels is not available everywhere, capillary testing of blood glucose levels can be recommended.

Increased body mass index, family history of diabetes and low socioeconomic status have been identified as risk factors for GDM in the previous studies.[4,5] The mean body mass index of the women in our study group was 26 kg/m^2. Recent WHO cut off of obesity is 25 kg/m^2 for Asian population,[19] hence majority of the women in the study were obese. In a study from Pakistan Northern Province, women with GDM were also found to have mean body index of 28 (kg/m^2).[20] Association between increased body mass index and gestational diabetes mellitus is well established. A positive family history of diabetes mellitus was found in 23%. Family history of diabetes mellitus increases the susceptibility to GDM, as high as nine times compared to control group with no positive family history.[21] In a study from Iran, positive family history was

Table 3 – Agreement between diagnosis of GDM by COGTT and VOGTT.

Test	Value	*p*-value/95% CI
Kappa	0.344	>0.001
Sensitivity	94.87%	87.39–98.59%
Specificity	79.09%	76.37–81.64%
Positive predictive value	27.10%	21.92–32.79%
Negative predictive value	99.47%	98.65–99.86%

$p < 0.05$ was considered statistically significant. VOGTT, Venous oral glucose tolerance test; COGTT, Capillary oral glucose tolerance test; GDM, Gestational Diabetes Mellitus; CI, Confidence Interval.

found in 42% of women diagnosed with GDM.[22] Though we did not take socioeconomic status into consideration, the hospital mainly caters to the women belonging to low socioeconomic class.

The predictive power of the constructed equation in our study evaluated by the area of the receiver operator characteristic curve was 86% which shows high prediction power.

6. Limitation

There are limitations of above study. Longitudinal follow up was not planned as the focus of the study was to assess predictive value of CBG for abnormal glucose homeostasis. With adequate resources and follow up, maternal and perinatal outcomes in women with GD will help in formulating national policy and guidelines for above group of women. Also since this was done in an institution, the prevalence of GD in community may not be same. But this study, do give an idea of GD in our set up. The rate is high enough to warrant population based studies in the country.

7. Conclusion and recommendation

A non- fasting, one step OGTT procedure with venous and capillary blood glucose can be helpful for screening the subject with gestational diabetes.

Conflict of interest

The authors have none to declare.

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