Clinical utility of point of care glucose in the assessment of gestational diabetes: Prospective cohort study.

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Abstract

Objective: To assess the clinical utility of point of care (POC) capillary blood glucose (CBG) in the assessment of gestational diabetes (GDM) during oral glucose tolerance test (OGTT). Design: Prospective cohort study. Setting: Antenatal clinics at King's Collage Hospital. Population: Women screening for GDM between March and June 2020. Methods: CBG was measured using POC-StatStrip® (Nova) and venous plasma glucose (VPG) was measured by Roche (Cobas 8000 c702) analyser. GDM was diagnosed based on NICE-2015 criteria. The two methods were compared statistically using Analyse-It (v 5.40.2) Main outcome measures: Diagnostic sensitivity, specificity, positive and negative predictive values (PPV and NPV) for POC-StatStrip® compared to reference laboratory method. Results: 230 women were included. The number and the percentage of women with glucose concentration above the GDM thresholds using POC-StatStrip® vs. Lab-VPG measurement was 15 (6.5%) vs. 8 (3.4%) at fasting and 105 (45%.6) vs. 72 (31.1%) at 2-hour respectively. Sensitivity and specificity for POC-StatStrip® were 88% and 97% at fasting and 97% and 79% at 2-hour respectively. However, the specificity and the NPV for POC-StatStrip® concentrations [?]5.0 mmol/L at fasting or <7.5mmol/L at 2-hour were 100% and the sensitivity and the PPV for concentration >9.5mmol/L at 2-hour was 100 %. Conclusion: In our cohort POC-CBG measurement cannot entirely replace laboratory method in OGTT, however, it can be used to rule out/rule in GDM when the glucose concentrations are [?]5.0mmol/L at fasting or <7.5/>9.5mmol/L at 2-hour. Funding: not applicable. Key Words: Gestational Diabetes Mellitus (GDM), point of care (POC).

Introduction

Gestational Diabetes (GDM) is a significant complication during pregnancy. It is associated with an increased risk of adverse outcomes including preeclampsia; macrosomia growth; caesarean section birth; shoulder dystocia and neonatal hypoglycaemia.(1) GDM is also a predictor for later development of type 2 diabetes mellitus (T2DM) in the mother.(2) The risk of adverse pregnancy outcomes can be reduced by treatment directed at reducing blood glucose concentrations.(3, 4)

The proportion of pregnancies affected by GDM vary according to the diagnostic criteria and the demographic characteristics of the studied population.(5) The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) Consensus Panel's assessment of the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study reported prevalence of 17.8%.(6) This is expected to further increase with the rise of obesity and increasing number of pregnancies at older maternal age.(7)

It is widely accepted that healthcare organisations should screen for GDM, since it is an asymptomatic condition in which appropriate interventions can improve pregnancy outcomes. However, there is disagreement on both the screening approach and the diagnostic cut-offs.(7) NICE recommend screening by assessing the

risk factors, with higher risk women being offered 75g 2-hour OGTT with VPG measured at fasting and 2-hours.[8]

POC uses whole blood, rather than plasma for analysis of glucose concentrations. VPG measured by reference laboratory methods are 10 to 15 % higher than that of whole blood, due to the difference in the water content between red blood cells in comparison to plasma.[9] To avoid clinical misinterpretations, POC devices report glucose as plasma equivalent, rather than whole blood, by multiplying the measured concentration by a conversion factor to adjust for the haematocrit.[9]

POC is an effective tool in aiding management of glycaemic control diabetes. However, despite offering advantages over laboratory testing including: rapid turnaround time and lower cost, POC devices are not routinely recommended for screening/diagnosis of GDM due to insufficient accuracy and precision.[10, 11]

The Nova StatStrip® Glucose Hospital Meter (Nova Biomedical) is approved by the food and drug administration (FDA) for glucose monitoring in hospital/healthcare settings, including in those critically unwell,[12] and it is also acceptable for the diagnosis of T2DM.[13] Nova StatStrip® directly measures the haematocrit and uses a corrective algorithm for reporting glucose concentrations resulting in minimal interference from haematocrit between 20 to 70%, across a wide analytical range of glucose (3-33mmol/L).[14]

Our study objective was to assess the clinical utility of POC-StatStrip® meter in screening for GDM.

Methods

Study Population:

All women who attended for an OGTT as part of standard antenatal care between March and June 2020, during the first National lockdown in England in response to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic (COVID-19). The study is reporting on data from routine clinical practice so no ethical approval was needed.

At the time of this study, our GDM screening protocol was to offer 75-gram OGTT as follows:

those with previous GDM were offered an OGTT at 16-20 weeks and a second OGTT at 28 weeks if the first is normal.

those with a BMI $> 40 \text{kg/m}^2$ were offered an OGTT at 28 weeks.

all other pregnant women were routinely screened for GDM with a post meal VPG at 28 weeks gestation. If the random VPG was [?] 6.7mmol/L an OGTT was offered. We continued the same pathway throughout the UK COVID-19 lockdown, however in 2020, as part of efforts to minimise clinical contact due to concerns around COVID-19, we introduced measurement of POC-StatStrip(r) testing at the same time as the 2-hour VPG. This allowed us to identify women likely to have GDM and provide them with a GDM kit, including written information and a blood glucose meter, before they left the clinic. If the diagnosis of GDM was confirmed on laboratory VPG measurement, women could be taught self-monitoring of glucose immediately via online videos without having to return for a second visit to collect a glucose meter or wait for a postal delivery.

Standard procedure for OGTT and blood collection:

Our standard procedure for OGTT in pregnancy was followed. Women were instructed to fast from 10 pm the night before the test (water was allowed). Trained staff in the antenatal department carried out the OGTT. At 0-minute (fasting) and 120-minutes post 75-gram glucose load, VPG samples were collected by venepuncture into sodium fluoride oxalate (BD Vacutainer(r)) tubes and sent to the laboratory. For POC-StatStrip(r), capillary whole blood was obtained from finger prick or earlobe prick.

Glucose analysis :

VPG was measured in the main hospital laboratory using Roche (Cobas 8000 c702, Burgess Hill, UK) chemistry analyser. It employs the enzymatic hexokinase method. The laboratory (Synnovis) is accredited

by the United Kingdom Accreditation Service (UKAS) for the international medical laboratory standard ISO15189.

POC-CBG was measured using Nova StatStrip(r) Glucose Hospital Meter which uses a modified glucose oxidase method. The StatStrip(r) Internal Quality Control (IQC) was performed daily with level 1 and level 3 Nova StatStrip(r) control solution, according to our standard practice. The External Quality Control (EQC) of the meter was performed bimonthly by WEQAS (the largest provider of External Quality Assessment services for POC tests in the UK).

OGTT interpretation :

NICE (2015) criteria for diagnosis of GDM were used: fasting glucose concentration [?] 5.6 mmol/L or 2-hour post-75g oral glucose load glucose concentration [?]7.8 mmol/L.

Statistical Analysis :

Data were analysed using Analyse-It (version 5.40.2) and are reported as median and inter-quartile range (IQR). Pearson correlation, Bland Altman plot and Passing Bablok regression analysis were used to assess the agreement between the two methods. A p value of <0.05 was considered statistically significant. Results are presented for all data and for fasting and 2-hour concentrations. For each time-point, concordance in meeting GDM diagnostic threshold, sensitivity, specificity, false positive (FP) rate, false negative (FN) rate, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Receiver Operating Characteristic curve (ROC) was used to compare the diagnostic sensitivity and specificity. Sub-analysis was performed to compare fasting POC-StatStrip(r) concentrations [?]5mmol/l and 2-hour <7.5mmol/l or >9.5mmol/l with the corresponding Lab-VPG concentrations.

Results

In total 230 pregnant women were included. The age and gestation were 34 (30-37) years and 28 (20-35) weeks respectively. Our hospital serves a large ethnically diverse catchment area. The reported ethnicities were; Black 41% (n=94), White 28% (n=63), Asian 8% (n=19), other/Mixed 9% (n=22) and undisclosed 14% (n=31).

Paired fasting and 2-hour glucose data were available for all women. The glucose concentrations in the entire cohort at fasting were 4.7 (4.3-5.0) mmol/L using POC-StatStrip(r) and 4.5 (4.2-4.8) mmol/L with Lab-VPG. Glucose concentrations at 2-hour were 7.6 (6.6-8.7) mmol/L using POC- StatStrip(r) and 7.0 (5.8-8.3) mmol/L with Lab-VPG.

The correlation (R) of all glucose concentration from both methods was 0.905. For glucose concentrations at fasting r = 0.871 and for concentrations at 2-hour r = 0.919. However, the correlation between 2-hour POC-StatStrip(r) concentrations in the range of 7.5-9.5 mmol/L with the corresponding Lab-VPG concentrations was weaker (r=0.72) (Figure 1a, 1b, 1c and 1d).

Bland Altman Plot showed good agreement between the two methods. However, it demonstrated a positive bias of 0.35 mmol/L for POC- StatStrip(r) with most values scattered within a tight limit of agreement (LoA) (95% LoA from-0.74 mmol/L to +1.44 mmol/L). Bland Altman plot was applied to fasting and 2-hour glucose concentrations separately and showed a positive bias of 0.14 mmol/L at fasting (95% LoA -0.44 to +0.73) and 0.55 mmo/L (95% LoA -0.76 and +1.82) at 2-hours (Figure 2a, 2b and 2c).

Passing Bablok regression analysis showed good agreement between the two methods. Regression equation:POC-StatStrip(r) (mmol/l) = -0.2182 + 1.091 Lab-VPG, (intercept=- 0.22 and 95% Confidence Interval (CI) -0.44 to -0.04, slope -1.01 and 95% CI 1.06 to 1.13) (figure 3). However, the agreement was less pronounced when the POC-StatStrip(r) glucose concentration within the range of 7.5 to 9.5 mmol/L was considered separately: POC-StatStrip(r) mmol/l = 3.829 + 0.5714 Lab-VPG.

NICE, 2015 diagnostic thresholds for GDM were used to compare diagnostic performance between POC-StatStrip(r) and VPG-Lab. The number (n) and the percentage of women with glucose concentration above

the GDM diagnostic thresholds using POC-StatStrip(r) versus Lab-VPG for the whole test, at fasting and 2-hour OGTT, sensitivity, specificity, FP and FN rates are listed in table (1).

The specificity and NPV for fating POC-StatStrip(r) glucose [?] 5.0 mmol/L and 2-hour glucose $<$ 7.5 were 100% while the sensitivity and PPV for fating POC-StatStrip(r) glucose $>$ 9.5 mmol/L were 100%.

The Youden Index for POC-CBG thresholds were 0.86 and 0.76 for fasting and 2-hour respectively.

ROC curve analysis for fasting and 2-hour POC-StatStrip(r) glucose are shown in figure 4a and 4b. For fasting glucose, the area under the curve (AUC) was 0.97 (95%: CI 0.96 to 0.99) and for 2-hour, AUC was 0.97 (95% CI: 0.99 to 0.99). The diagnostic accuracy for POC-StatStrip(r) in our cohort for GDM diagnosis was 84%.

Discussion &Conclusion

Main Findings

In our cohort, the diagnostic performance of POC-StatStrip(r) was generally good at both fasting and 2-hour time points. It provided a good diagnostic yield as evidenced by ROC-curve and Youden index analysis. However, on statistical analysis for method comparison, POC-StatStrip(r) showed a positive bias in both fasting (0.13 mmol/L) and 2-hours (0.55 mmol/L) compared to Lab-VPG. This resulted in a low PPV (68%) and moderate specificity (77.8%) for POC- StatStrip(r) in OGTT.

If POC StatStrip(r) were to replace all Lab-VPG measurements, it would increase the proportion of women in our cohort diagnosed with GDM by 15.3% (from 32 % to 47.3%), which would have implications for the pregnant women and for health resources.

An alternative approach that can safely utilise the advantages of POC testing is to identify samples within a specific glucose range with acceptable specificity and sensitivity that will not require laboratory confirmation. We therefore tested the utility of POC- StatStrip(r) in replacing conventional Lab-VPG testing when fasting POC-StatStrip(r) [?] 5.0mmol/L and 2-hour glucose POC-StatStrip(r) is $<$7.5 or $>$9.5 mmol/L (7.5 to 9.5 mmol/L being around the diagnostic threshold and our analysis showed weaker correlation between the two methods within this range). The specificity and the NPV for fasting POC-StatStrip(r) [?] 5.0 mmol/L and for 2-hour POC-StatStrip(r) $<$ 7.5 mmol/l were 100% which means that we can confidently exclude GDM when POC-StatStrip(r) glucose concentrations are below these concentrations. The sensitivity and the PPV for 2-hour POC $>$9.5 mmol/L was 100% which means that we can confidently diagnose GDM when POC-StatStrip(r) glucose is $>$ 9.5 mmol/L. We cannot comment on the threshold for fasting glucose because in our cohort very few women were above diagnostic threshold.

Based on the above we propose an OGTT protocol in which POC-StatStrip(r) is performed first, with immediate venous sampling only required at fasting time-point if POC-StatStrip(r) [?]5.1 mmol/L and at 2-hour time-point if POC-StatStrip(r) is in the range of 7.5-9.5 mmol/L . This would, in our cohort, reduce the requirement for venepunctures and laboratory glucose testing by 75% for fasting samples and by 48 % for 2-hour samples.

The protocol could improve patient experience and reduce the cost of laboratory tests. Furthermore, as a proportion of women can be given a definitive diagnosis of GDM/no GDM immediately, this would improve staff productivity by reducing time spent on phoning patients to provide results and will allow those with a diagnosis of GDM to receive equipment and counselling sooner.

Strength and Limitation

A main strength of our study is the relatively large sample size with 230 women from different ethnic backgrounds. Both fasting and at 2-hour time-points of OGTT were available for all patient and performed by competent staff which minimises operator errors. It is the first study to use NICE 2015 diagnostic thresholds for POC and Lab-VPG comparison. To our knowledge this is the only study using the POC-StatStrip(r) meter on an antenatal cohort, with its unique haematocrit measurement, which is particularly

important due to the effect of pregnancy on haematocrit. We acknowledge that the proposed protocol of checking POC- StatStrip(r) first with the result determining the need for venous sampling and laboratory testing can increase complexity so staff training and support prior to implementing this protocol would be essential.

Interpretation

OGTT remains the gold standard test for diagnosing GDM. With the pressure on health care resources, anxiety associated with the diagnosis, and the need to start management in timely manner, providing accurate, precise and rapid results for OGTT is beneficial. The advancing technology of POC devices can help achieve these goals.

Several studies have investigated the use of a variety of variable POC glucometers using different diagnosis criteria. Summary of these studies are included in table 2. The studies used a variety of VPG reference measurements: from sending samples to the hospital laboratory without special arrangements as we have done here, which has the advantage being a comparison to usual clinical practice; through sending to the hospital laboratory paying strict attention to The National Association of Clinical Biochemist (NACB) for the diagnosis of GDM guidelines to minimise impact of pre-analytical factors; through to use of Isotope Dilution Gas Chromatography Mass Spectrometry. Most studies showed good agreement between POC testing and VPG with acceptable diagnostic performance, but no study has advocated for completely replacing laboratory testing with POC-testing for GDM screening. Other studies comparing POC with Lab-VPG methods in 50g OGGT also reported satisfactory performance for POC in GDM diagnosis.[15-17] However, the case for comparing POC testing to laboratory testing is far from straightforward due to multiple factors including clinical and analytical factors.

Clinically, the diagnostic performance is partly depending on the diagnostic thresholds. The HAPO study showed there is a linear relationship between increasing glucose concentrations at OGTT and adverse pregnancy outcomes, such as macrosomia, neonatal hypoglycaemia and caesarean birth, with no threshold effect.[1]Health care systems impose diagnostic thresholds: those at or above threshold are managed as GDM and those below are labelled as no GDM. This is relatively easy to administer and allows healthcare resources to be directed for those at higher risk of adverse pregnancy outcomes. However, in this situation, when a linear parameter is converted into a binary outcome, when different systems are used to measure the linear parameter there will be diagnostic disagreement, particularly when close to the diagnostic threshold.

Analytically, POC glucometer performance is subjected to analytical interferences from variation in haematocrit, pH and oxygen and sample matrix effect.[9] However, the laboratory methods, against which POC devices are compared, have inherent analytical and pre-analytical errors, of which the effect of in-vitro glycolysis is particularly significant. Uninhibited in-vitro glycolysis can result in 5-10% reduction in VPG[18] and GDM misclassification. To prevent this, NACB guidelines recommends collecting samples in sodium fluoride additive tubes, transferring them on slurry ice to be centrifuged with 30 minutes of collection. Alternatively, citrate tubes can immediately inhibit the glycolysis.[19] In routine practice adherence to these guidelines is suboptimal.[20-22] So the discrepancy in diagnostic performance might be partly attributed to the negative bias with lab methods rather than positive bias with POC. Generally, studies that compared POC without strict measures to control in-vitro glycolysis, like our study, have reported positive analytical bias,[23, 24] high sensitivity and NPV[25-29] for POC with potential for over-diagnosis. While some studies that religiously applied NACB guidelines have reported negative analytical bias and potential for misdiagnosis.[30, 31]

Conclusion

We propose that POC is included in a protocol for GDM screening that reserves VPG for when CBG-StatStrip fasting glucose [?]5.1 mmol/L or 2-hour CBG-StatStrip is 7.5-9.5 mmol/L. This would reduce the requirement for venous sampling and laboratory measurements by 75% for fasting samples and by 48% for 2-hour samples. This approach may allow to focus resources on measures to mitigate pre-analytical factors in samples that do need to be sent to the lab.

It may also improve patient experience with fewer venous blood samples and quicker results for some women, reduce the overall costs of laboratory tests and save staff time. Our study is population specific and applied using POC-Statstrips(r) in a specific health care setting so further studies in different cohorts using locally validated POC/lab analysers are recommended before similar protocols can be implemented in different healthcare settings.

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Contribution to authorship:

Wiaam Al-Hasani: Data collection, statistical analysis and interpretation, literature review, writing of the manuscripts , main corresponding author.

Ruvini Ranasinghe: Data collection, contribution to statistical analysis.

Helen Rogers: patients review, POC test performance and venous blood sampling.

William Spanier: Data collection.

Katie Spears: Review of the final manuscript, scientific and clinical feedback.

Carol Gayle: Review of the final manuscript, scientific and clinical feedback.

Lisa Long: Review of the final manuscript, scientific clinical feedback.

Georgios K Dimitriadis: statistical analysis and interpretation.

Katharine F Hunt and Royce P Vincent: Joint senior authors, designed the study with the first author, approved the scientific statistical analysis.

All co-authers reviewed and approved the final manuscript following the feedback.

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Table 1: Number (n) Percentage % of pregnant women meeting GDM diagnostic thresholds (fasting [?] 5.6 mmol/L, 2-hour [?] 7.8 mmol/L) with each method, sensitivity and specificity, FP FN rates, PPV and NPV for POC-StatStrip(r).

	POC-Stat-Strip® n (%)	**Lab-VPG n (%)**	**Sensitivity**	**Specificity**	**FP rate**	**FN rate**	**PPV**	**NPV**
Fasting	15 (6.5%)	8 (3.4%)	88%	97%	3.2%	6.6%	53%	99%
2-hour	105 (45.6%)	72 (31.1%)	97%	79%	26.4%	1.9%	68%	98%
Total	109 (47.3%)	75 (32%)	97%	77.8%	28%	1.8%	68%	98%

Table 2: Summery of studies compared POC glucose testing with laboratory methods in the diagnosis of GDM. WHO: world health organisation, ADA: American Diabetes Association, FIGO: International Federation of Gynaecology and Obstetrics, DIPSI: Diabetes in Pregnancy Study Group India. NDDG: National Diabetes Data Group. CBG: capillary blood glucose. VPG: Venous plasma glucose. VBG : venous whole blood glucose

Studies & Country	**Number of participants**	**Sample timing**	**POC sample type**	**POC device/Method**	**Reference method/ platform**	**Control of Pre-analytical factors***	**Method Agreement statistics**	**GDM Diagnosis Criteria**	**Diagnostic performance Statistics**
O'Malley EG (30)et al. Ireland	202	0-h 1h 2-h	CBG	Bayer Contour XT meter/Gluocse dehydrigenase	Beckman Coulter AU640 (hexokinase)	Yes	Correlation R >0.9. Linear Regression: 0-h lab-VPG= 0.893 + (0.877 × 0-h POC) 2-h Lab-VPG = -0.352 + (1.031 x 2-h POC)	IADPSG diagnostic criteria	Sensitivity= 80.4% specificity= 86.4% PPV=88.2% NPV =77.6% Accuracy= 83%

Studies & Country	Number of participants	Sample timing	POC sample type	POC device/Method	Reference method/ platform	Control of Pre-analytical factors*	Method Agreement statistics	GDM Diagnosis Criteria	Diagnostic performance Statistics
Van den Berg et al. Netherlands (32)	80	0-h 2-h	CBG	Roche Accuchek Inform II/ glucose dehydrogenase	Not mentioned	Yes for 30 participants	Demming regression best fit 1.03 for 0-minute and 0.9 for 120 -minute (Bias0.06 mM versus 0.90 mM at 0 and 120, respectively,	WHO 1991	sensitivity: 100%, specificity: 98% FPR :2%
Daly et al. Ireland(20)	108	0-h 1-h 2-h	CBG	Bayer CONTOUR® XT Meter.	Beckman Coulter AU640 (hexokinase)	Yes	*Correlation R=0.8 fasting R=0.85 1-hour R=0.91 2-hour	0-h: adjusted to [?]4.8 mol/l from 5.1mmol/l) 1-h:10.0 mmol/l and 2-h: 8.5 mmol/l	Sensitivity:9 Specificity:76.% PPV: 69.8%, NPV: 94.5% Accuracy: 94.5%,
Balaji, V., et al.(26)	500	2-h	CBG	One touch Select Simple/ Oxidase	Hitachi aqua (Oxidase-Peroxidase)	No	Correlation R=0.907 Linear regression equation VPG=0.968x+CBG	2-h[?]7.8 mmol/l for	Sensitivity: 93.8% Specificity: 97.4% FPR:2.6% FNR:6.2% ROC:0.993

Studies & Country	Number of participants	Sample timing	POC sample type	POC device/Method	Reference method/ platform	Control of Pre-analytical factors*	Method Agreement statistics	GDM Diagnosis Criteria	Diagnostic performance Statistics
Gallardo et al. Mexico (33)	328	0-h	CBG (172 Measures) VBG (156 measures)	ACCU-CHEK instant® Glucose dehydrogenase	Not mentioned	No	POC-CBG R =0.4 at fasting, R[?]0.5 at 1,2-hour POC-VPG R=0.6 at fasting, R >0.9 at 1,2 hour	ADA 2020	**POC-CBG** Sensitivity: 78.5% Specificity: 74.1 % **POC-VB** Sensitivity: 100% Specificity :62%
Krinstein et al. Sweden (34)	135	0-h 1-h 2-h	VPG	HemoCue Glucose 201+ . HemoCue Glucose 201RT modified glucose dehydrogenase	ID-MS as reference and routine lab Cobas 8000 er (Roche) (Hexokinase) as comparator	Yes	R=0.87 at 0-h R=0.95 at 1-h R=0.97 at 2-h HC201RT bias: -1.8) HC201+ Bias: +4.2% Routine lab bias+6.1%	WHO 2013	Not mentioned

Studies & Country	Number of participants	Sample timing	POC sample type	POC device/Method	Reference method/ platform	Control of Pre-analytical factors*	Method Agreement statistics	GDM Diagnosis Criteria	Diagnostic performance Statistics
Landberg et al. Sweden (35)	175	0-h 1-h 2-h	VPG	AccuChek Inform II (glucose dehydrogenase)	EQA using ID/MS as a ref and Local Cobas c701 (hexokinase) as comparator	Yes	R=0.98 Between POC and Comparator lab method. Cobas c701 has higher positive bias than POC when compared with EQA	WHO 2013	Not mentioned
Adam and Rheeder. South Africa(31)	594	0-h 1-h 2-h	CBG	Roche Accuchek Activ (hexokinase)	Beckman DXc (hexokinase)	Yes	Bland Altman showed bias +0.3 mmol/l at 0-h, negative bias -0.68 mmol/l at 1-h, -0.45 mmol/l at 2-hr	FIGO	Sensitivity: 27.0% specificity: 89.4% Accuracy: 72.8%
Bhavadharini, Mahalakshmi et al. India(23)	1031	0-h 1-h 2-h	CBG	(One Touch Ultra-II, LifeScan) (oxidase)	AU2700 Beckman, Fullerton, CA (hexokinase)	No	R for fasting =0.43 R for 1-hour=0.65 R for 2-hour=0.74 Bias 0-h: minimal 1-h: 1mmol/l 2-h:1.1 mmol/l	2 analyses based on *IADPSG or *2-hour 6.1 or 6.6 mmol/l	2-h IADPSG Sensitivity: 62.3% Specificity 80.7%. 2-hour 6.1 mmol/l cut-off Sensitivity: 92.5 %

Studies & Country	Number of participants	Sample timing	POC sample type	POC device/Method	Reference method/ platform	Control of Pre-analytical factors*	Method Agreement statistics	GDM Diagnosis Criteria	Diagnostic performance Statistics
Balaji, Madhuri et al.India(25)	819	2-h	CBG	Accu-Chek®(dehydrogenase)	Hitachi (Oxidase-Peroxidase)	No	linear regression VPG=0+0.974×CBG	DIPSI =>7.8 mmol/l 2-hours	Sensitivity: 80.2%= specificity: 98.5% FPR: 19.8% FNR:1.5% AUC:0.991
Garcia et al. Spain(24)	109	0-h 1-h 2-h 3-h	CBG	Accu-Chek (Dehydrogenase) (57 participants) Contour Next (dehydrogenase) (52 participants)	AU5800-Beckman Coulter (Hexokinase)	No	Accu-Chek R [?] 0.70 0-h bias: +0.15 2-h bias: +1 Contour Next R [?] 0.75 0-h bias: -0.19 2-h bias: +1.49	NDDG	Accu-Chek FP(n):3 FN(n): 1 Contour Next FP(n): 9 FN(n):1
Hossain et al. Pakistan (27)	1030	2-h	CBG	Accu-check (dehydrogenase)	Dimension (Oxidase-Peroxidase)	No	R= 0.76	(DIPSI),2-hr [?] 7.8 mmo/l	Sensitivity: 94.8% Specificity: 79% PPV: 27.1 % NPV: 99.4 % ROC: 0.93

Studies & Country	Number of participants	Sample timing	POC sample type	POC device/Method	Reference method/ platform	Control of Pre-analytical factors*	Method Agreement statistics	GDM Diagnosis Criteria	Diagnostic performance Statistics
Afzal et al. Pakisatn(28)	713	0-h	CBG	On Call EZ II (Oxidase)	Roche c501 (hexokinase)	No	R=0.9 Linear regression CBG-POC=0.922 Lab-VPG + 1.055 1	0-h [?] 5.1 mmol/l ADA	Sensitivity: 96.9%, specificity: 78.2%, PPV :17.7%, NPV: 99.8%
Jadhav et al. India (29)	1000	2-h	CBG	Not mentioned	Not mentioned	No	Not mentioned	DIPSI),2-hr [?] 7.8 mmol/L	Sensitivity: 100% specificity 99.4%
Elkheir et al. Egypt (36)	500	2-h	CBG	Accu-Chek Active (Dehydrogenase)	Oxidase-peroxidase method	No	R=0.92	DIPSI),2-hr [?] 7.8 mmol/L	Sensitivity: 90.9% Specificity: 96.6% PPV:76.9% NPV: 98.8% ROC:0.99

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