# Possibility to predict early postpartum glucose abnormality following gestational diabetes mellitus based on the results of routine mid-gestational screening

Vendula Bartáková*[1], Denisa Malúšková[2], Jan Mužík[2], Jana Bělobrádková[3], Kateřina Kaňková[1]

[1]Department of Pathophysiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic
[2]Institute of Biostatistics and Analyses, Masaryk University, Brno, Czech Republic
[3]Diabetes Centre, Department of Internal Medicine - Gastroenterology, University Hospital Brno, Czech Republic

*Corresponding author: vbartak@med.muni.cz

**Abstract**

**Introduction**: Women with previous gestational diabetes mellitus (GDM) have increased risk of developing glucose abnormality, but current diagnostic criteria are evidence-based for adverse pregnancy outcome. The aims of our study were: (i) to ascertain a frequency of early conversion of GDM into permanent glucose abnormality, (ii) to determine predictive potential of current GDM diagnostic criteria for prediction of postpartum glucose abnormality and (iii) to find optimal cut-off values of oral glucose tolerance test (oGTT) to stratify GDM population according to postpartum risk.

**Materials and methods**: Electronic medical records of an ethnically homogenous cohort of women diagnosed and treated for GDM in a single medical centre during the period 2005–2011 who completed postpartum oGTT up to 1 year after the index delivery were retrospectively analysed (N = 305).

**Results**: Postpartum glucose abnormality was detected in 16.7% subjects. Mid-trimester oGTT values, respective area under the curve and HbA1c were significantly associated with early postpartum glucose abnormality ($P < 0.05$, Mann-Whitney) and exhibited significant predictive potential for postpartum glucose abnormality risk assessment. Optimal cut-off values for discrimination of at-risk sub-population were identified using ROC analysis and their comparison with WHO and IADPSG criteria exhibited superiority of IADPSG for risk-stratification of GDM population.

**Conclusion**: Risk-based stratification at the time of GDM diagnosis could improve efficiency of the post-gestational screening for diabetes. IADPSG criteria seem to optimally capture both perinatal and maternal metabolic risks and are therefore medically and economically justified.

**Key words**: gestational diabetes; oral glucose tolerance test; postpartum period; glucose intolerance; diagnosis

*Received: February 19, 2015* *Accepted: July 02, 2015*

## Introduction

Gestational diabetes mellitus (GDM), a common complication of pregnancy, is defined as any degree of glucose intolerance with the onset or the first recognition during the pregnancy (most often during the second trimester of gestation) which then typically normalizes after the delivery (or puerperium) (1). Pregnancy is a relatively short period marked by dramatic changes of hormone profile and body composition with profound effects on metabolism. While the initial phase is usually characterized by increased insulin sensitivity, later marked insulin resistance develops (2), which, in a subset of women with latent defect of insulin secretion, manifests as a GDM.

Although the reported prevalence of GDM varies considerably between countries mainly due to different diagnostic criteria used, the incidence of GDM is reported to rise worldwide (3). Hypergly-

caemia and Adverse Pregnancy Outcomes study (HAPO) (4) prompted an important shift in the GDM paradigm since it provided grounds for the evidence-based modification of GDM diagnostic criteria showing that perinatal morbidity (high birth weight leading to complications during delivery such as shoulder dystocia, birth injury, hyperbilirubinemia, neonatal hypoglycaemia, foetal hyperinsulinemia reflected by increased cord-blood serum C-peptide levels) is proportionately related to maternal glycaemia. Recently International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed new criteria for GDM reflecting HAPO results (5). Applying IADPSG diagnostic criteria on HAPO study population the GDM incidence would reach 17.8% (6).

GDM elicits a complex medical situation affecting yet two people - mother and child - in the short-term as well as in the long-term perspectives. Timely diagnosis of GDM (esp. when applying evidence-based criteria) should improve short-term pregnancy and perinatal outcomes and newly proposed IADPSG diagnostic criteria are dominantly pregnancy risk-based. However, the extent of risk reduction is often regarded as minor (oral glucose tolerance test (oGTT) cut-off values calculated for "only" 75% reduction of adverse pregnancy outcomes) and disproportionate to the extra health care cost related to increased GDM prevalence when using more stringent criteria. Since recommendations issued by IADPSG will have major implications for the health care systems this stimulates an intense debate among relevant authorities in many countries (7) including Czech Republic. While Czech Diabetes Society adopted the IADPSG diagnostic criteria in April 2014, Czech Gynaecology and Obstetrics Society remains reluctant to their universal adoption and no official statement has yet been issued (8). One of the possible reasons for this hesitation in obstetric community (worldwide though) might be a paucity of data available on long-term consequences of GDM.

GDM is an established lifelong risk factor for the development of diabetes in women with GDM history. The estimation of the prevalence of permanent postpartum dysglycaemia (prediabetes or diabetes) was the subject of several studies during the past 20 years, part of them were included in a systematic review (9) or in a meta-analysis comprising about 675,000 of women with GDM diagnosis (10). In spite of limitations of this approach (such as variable follow-up, study design, actual GDM diagnostic criteria, definition of end-points and ethnicity) women with previous GDM had at least 7-fold increase of risk of developing type 2 diabetes mellitus (T2DM) in the future compared with those with normoglycaemia during pregnancy (10). Furthermore, cumulative incidence of T2DM was shown to increase steadily during the first 5 years after the delivery, reaching a plateau in 10 years postpartum (9).

We therefore hypothesize that documented early reoccurrence or even postpartum persistence of glucose abnormality gives a very good chance for an early postpartum screening to detect a largest proportion of at-risk women. Furthermore, being able to stratify GDM population according to the risk of subsequent glucose metabolism abnormality as soon as possible (ideally already during the pregnancy), the generally unsatisfactorily low compliance in postpartum diabetes screening (11,12) could improve thanks to more persuasive arguments and possibly increased motivation of at-risk subgroup. Therefore, given that women with previous GDM have significantly increased risk of postpartum glucose abnormality and screening for GDM is very well developed and widespread, however, none of the current diagnostic criteria are evidence-based for prediction of postpartum maternal risks, the aims of our study were: (i) to ascertain a frequency of early postpartum (up to 12 months post-delivery) conversion of GDM into permanent diabetes or prediabetes, (ii) to determine a predictive potential of national modification of the World Health Organisation (WHO) diagnostic criteria used at the time of subject's enrolment and currently recommended IADPSG diagnostic criteria for prediction of postpartum glucose abnormality and (iii) to find optimal cut-offs of oGTT values capturing mother's metabolic risks to stratify GDM population according to postpartum risk of glucose abnormality.

## Materials and methods

### Study design and subjects

Study was designed as a retrospective, electronic health records (EHR) based study of ethnically homogenous cohort of GDM subjects (Caucasian origin, geographically derived from South Moravia region of Czech Republic) who underwent their mid-gestational GDM screening by oGTT and were subsequently diagnosed and followed for GDM in outpatient clinics (Diabetes Centre of the University Hospital Brno, Czech Republic) from January 2005 till December 2011. University Hospital Brno is a public non-profit tertiary medical centre, one of the largest in Czech Republic, serving the area of Brno city and South Moravia district with approximately 1.2 million inhabitants. EHRs organizes digitalised patient-level data shared among multiple facilities, outpatient and inpatient clinics of three units of the University Hospital Brno (i.e. Hospital Brno-Bohunice, Children Hospital Brno and Centre for Reproductive Medicine) that are accessible real-time. Data are available either in codified form (demographic and anthropometric data, codes of diagnoses and procedures, list of chronological visits to health care professionals, images and laboratory test results, insurance and billing data etc.) or as a clinical narrative notes (family and patient's medical history, medications, treatment plans, records of hospitalization etc.). Data were retrieved from EHRs based on the following inclusion criteria: (i) GDM diagnosis classified by International Classification of Diseases (ICD)-10 code O24.4 or O24.9, (ii) GDM diagnosed by 3-point 75 g of glucose 2-h oGTT between 24$^{th}$ and 28$^{th}$ week of pregnancy at the University Hospital Brno, (ii) completed postpartum oGTT 6 weeks up to 1 year after the indexed delivery. Exclusion criteria were: (i) pre-gestational type 1 diabetes mellitus (T1DM), T2DM or abnormal glucose tolerance (i.e. O24.0–O24.3 or R73) and (ii) GDM diagnosed by oGTT outside the University Hospital Brno. Following data mining, extensive data checks and quality control were performed incl. cross-checking the GDM ICD-10 code and the results of the mid-gestational oGTT to finalise the study sample. A total of N = 305 GDM subjects were included in the study. The data mining and analysis were fully anonymised. Study was approved by the Ethical committee of the University Hospital Brno and Ethical committee of Faculty of Medicine, Masaryk University and its conduct was in compliance with the Helsinki Declaration.

### Methods

According to the current practice in Czech Republic screening for GDM is offered to all pregnant women (with exception of pre-existing diabetics) in second trimester. In case of the presence of at least two risk factors (positive family history, previous delivery of new-born with weight above 4000 g, obesity, diabetes mellitus in previous pregnancy, glycosuria, previous stillborn delivery, hypertension or preeclampsia in previous pregnancy, repeated abortions, age above 30 years) it should be performed during the first trimester. Diagnosis of GDM in the cohered diagnosed and followed in 2005–2011 period was based on the consensus criteria of Czech Diabetes Society and Czech Society for Clinical Biochemistry (13) derived from WHO criteria for subjects with impaired fasting glucose (IFG) / impaired glucose tolerance (IGT) (14) using a 3-point oGTT with 75 g glucose with threshold values (any value above cut-off diagnosing GDM): FPG $\geq$ 5.6 mmol/L, 1-hr after 75 g load glucose $\geq$ 8.8 mmol/L and/or 2-hr after 75 g load $\geq$ 7.8mmol/L (sample 60 minutes after challenge optional but recommended). Glycaemia was measured by hexokinase-based enzymatic method using Cobas 8000 analyser and commercial reagents (Roche) in venous plasma. HbA1c (cut off 39 mmol/mol) was measured in all subjects by ion-exchange high-performance liquid chromatography (HPLC) using D-10 analyser and commercial reagents (Bio-Rad) in whole blood. Additionally, area under the curve (AUC, mmol/L/hour) was calculated from a 3-point oGTT using the trapezoid rule (15). Cut-offs of newly recommended IADPSG criteria are as follows: FPG $\geq$ 5.1mmol/L, 1-hr post-load glucose: $\geq$ 10.0 mmol/L, 2-hr post-load glucose: $\geq$ 8.5 mmol/L.

Postpartum diagnosis of diabetes/prediabetes was based on the WHO criteria: FPG $\geq$ 7mmol/L alone or 2-hr after 75 g load glucose $\geq$ 11.1mmol/L for

DM, FPG 5.6–6.9mmol/L or 2-hr after 75 g load glucose 7.8-11.0 mmol/L for prediabetes. In the case of postpartum diagnosis of manifest diabetes urinary ketone bodies, C-peptide and antibodies (anti-glutamic acid decarboxylase (anti-GAD), anti-tyrosine phosphatase (antiIA-2), insulin auto-antibodies (IAA)) were measured to identify an eventual T1DM.

### Statistical analysis

Data are expressed as medians and interquartile ranges (IQR) or proportions for between group comparisons. Differences between groups were compared using non-parametric Mann-Whitney or Pearson chi-square tests for continuous or categorical variables, respectively, using Statistica for Windows (Statsoft Inc., Tulsa, OK, USA) software. $P \leq 0.05$ was considered statistically significant unless correction for multiple comparisons were applied ($P_{corr}$). Univariate and multivariate logistic models were constructed to determine an eventual statistically significant effect of any relevant variable and Receiver Operating Characteristic (ROC) analysis was applied to test the final models. Areas under the ROC curve ($AUC_{ROC}$) were compared by Delong paired test (16). Optimal cut-off of selected glycaemic indices for prediction of postpartum GDM conversion into permanent glucose abnormality within 12 month were selected by the highest Youden indices (17), i.e. single statistic capturing diagnostic test performance (J = sensitivity + specificity – 1) with value ranging from 0 to 1 (a zero value for the test giving the same proportion of positive results for groups with and without the disease and a value of 1 for no false positives or negatives).

## Results

### Incidence of postpartum glucose abnormality

Incidence of any disorder of glucose metabolism (i.e. diabetes or prediabetes) up to 1 year postpartum was 16.7% (N = 51/305). Of those, 62.7% had prediabetes (N = 32, 14 had IFG and 18 had IGT), 37.3% (N = 19) had manifest diabetes. Based on the examination of urinary ketone bodies, C-peptide and antibodies (anti-GAD, antiIA-2, IAA) 31.4% (N = 16) had T2DM and 5.9% (N = 3) had T1DM.

### Relationship between mid-trimester parameters and postpartum glucose intolerance

Characteristics of subjects at the time of GDM diagnosis with respect to their postpartum GDM normalization or persistence are shown in Table 1. Glycaemia in all three time-points of mid-trimester oGTT, $AUC_{oGTT}$ and mid-trimester HbA1c were significantly higher in the group of GDM women with the postpartum disorder compared to those with normal glucose tolerance (NGT) postpartum. Using categorial approach, i.e. comparing number of oGTT values under/above threshold, highly significant difference was found ($P < 0.001$) with the obvious trend towards the more frequent postpartum abnormality the higher the number of mid-trimester oGTT values above threshold. About 8% (16 from 203) of GDM patients with one oGTT value above threshold were diagnosed with glucose abnormality 1 year postpartum, 27% (22 from 82) with two oGTT values (OR for post-partum glucose intolerance 4.3-times higher than for those with one value above the threshold [95% CI = 2.1-8.7], $P < 0.001$) and 65% (13 from 20) with all three oGTT values (OR 21.7-times higher than for patients who have only one value oGTT above the threshold [95% CI = 7.6-62.1], $P < 0.001$ and 5.1-times higher than for patients who had two oGTT values above the threshold [95% CI = 1.8-4.3], $P = 0.002$).

### Predictive potential of routine mid-trimester parameters for postpartum glucose intolerance

Series of uni- and multivariate logistic regression models were constructed for both continuous (i.e. oGTT values, $AUC_{oGTT}$ and HbA1c) and categorial data (respective below/above-threshold values). Upon exclusion of mutually correlated variables final multivariate models identified (A) all three oGTT values above threshold, i.e. FPG (OR = 6.32, [95% CI = 2.96-13.78], $P < 0.001$), 1-hr post 75 g load glucose (OR = 4.33, [95% CI = 1.84-12.02], $P = 0.002$) and 2-hr post 75 g load glucose (OR = 3.88, [95% CI = 1.95-7.91], $P < 0.001$) as significant predictors of

**Table 1.** Characteristics of study subjects at the time of GDM diagnosis (24-28th gestational week) and postpartum.

| Parameters | GDM subjects with postpartum NGT (N = 254) | GDM subjects with postpartum glucose abnormality (N= 51) | $P_{corr}$ |
|---|---|---|---|
| Mid-gestation parameters | | | |
| Age (years) | 32 (29–35) | 32 (30–37) | 0.155 |
| Parity | 2 (1–2) | 2 (1–3) | 0.161 |
| Week of gestation* | 28 (26–28) | 28 (25–28) | 0.595 |
| Pre-gestational BMI | 27.9 (24.8–31.6) | 28.4 (24.3–32.2) | 0.997 |
| Total cholesterol (mmol/L) | 5.3 (4.7–6.3) | 4.8 (4.2–5.8) | 0.139 |
| Family history of DM (%) | 75 | 68 | 0.328 |
| Pregnancy after IVF (%) | 4 | 7 | 0.224 |
| HbA1C (mmol/mol) | 33 (31–36) | 36 (33–38) | < 0.001 |
| **Mid-gestation oGTT (24-28$^{th}$ week of gestation)** | | | |
| FPG (mmol/L) | 4.7 (4.3–5.1) | 5.2 (4.7–5.9) | < 0.001 |
| 1-h post 75 g load | 9.4 (8.8.–10.1) | 10.6 (9.2–11.7) | < 0.001 |
| 2-h post 75 g load | 7.5 (6.3–8.2) | 8.0 (7.0–9.3) | 0.003 |
| $AUC_{oGTT}$ (mmol/L/hour) | 15.2 (14.4–16.2) | 17.1 (15.3–18.5) | < 0.001 |
| **Postpartum oGTT (6 weeks -12 months after delivery)** | | | |
| FPG (mmol/L) | 4.7 (4.5–5.0) | 5.7 (4.7–6.1) | < 0.001 |
| 1-h post 75 g load | 7.5 (6.4–8.5) | 10.5 (8.8–11.6) | < 0.001 |
| 2-h post 75 g load | 5.4 (4.5–6.4) | 8.0 (6.3–11.0) | < 0.001 |
| $AUC_{oGTT}$ (mmol/L/hour) | 10.2 (9.3–11.1) | 12.8 (12.2–16.4) | < 0.001 |

Data expressed as a median (IQR) or proportions. Differences evaluated by nonparametric Mann-Whitney or chi-square test, respectively. Considering multiple comparisons involved Bonferoni correction ($P_{corr} \leq 0.05$ / number of tests) was applied and only $P_{corr} \leq 0.004$ should be considered significant.
*Week of gestation at the time of GDM diagnosis.
$AUC_{oGTT}$ – area under oGTT curve; BMI – body mass index; DM – diabetes mellitus; FPG – fasting plasma glucose; HbA1c – glycated haemoglobin; IVF – *in vitro* fertilisation; NGT – normal glucose tolerance; oGTT – oral glucose tolerance test.

postpartum glucose abnormality applying categorial approach. Analogical multivariate logistic model constructed for (B) continuous variables identified HbA1c (OR = 2.31, [95% CI = 1.01-5.39], P = 0.048), FPG (OR = 2.00, [95% CI = 1.18-3.42], P = 0.011) and 1-hr post 75 g load glucose (OR = 1.42, [95% CI = 1.13-1.81], P = 0.004) as significant predictors of postpartum glucose abnormality.

Finally, using ROC analysis combined with Youden statistics we attempted to find optimal cut-off values of parameters evaluated at mid-trimester best reflecting postpartum risk in our study population (see Table 2) and to determine to which extent they differ from the newly proposed IADPSG criteria. Following cut-off values for the prediction of postpartum glucose abnormality in our study population were identified (current WHO/recommended IADPSG diagnostic thresholds for GDM diagnosis according to Czech Diabetes Society are shown in brackets): FPG ≥ 5.1mmol/L, (≥ 5.6mmol/L / ≥ 5.1mmol/L), 1-hr post 75 g load glucose ≥ 10.7 mmol/L (≥ 8.8 mmol/L / ≥ 10 mmol/L) and 2-hr post 75 g load glucose 7.8 mmol/L, (≥ 7.7 mmol/L / ≥ 8.5 mmol/L).

**Table 2.** ROC analysis combined with Youden statistics identifying optimal cut-off values of parameters evaluated at mid-trimester best reflecting postpartum risk in our study population.

| Parameters | Cut-off according to Youden index | AUC | 95 % CI | P |
|---|---|---|---|---|
| HbA1c (mmol/mol) | ≥ 36 | 0.675 | 0.619–0.728 | < 0.001 |
| FPG during oGTT | ≥ 5.1 | 0.692 | 0.637–0.743 | < 0.001 |
| oGTT 1-h post 75 g load glucose | ≥ 10.7 | 0.694 | 0.639–0.745 | < 0.001 |
| oGTT 2-h post 75 g load glucose | ≥ 7.8 | 0.630 | 0.573–0.684 | 0.006 |

AUC – area under the curve; CI – confidence interval; FPG – fasting plasma glucose; HbA1c – glycated haemoglobin; oGTT – oral glucose tolerance test.

## Discussion

In this report, using a cohort of 305 metabolically well characterized GDM subjects we ascertained incidence of post-GDM glucose abnormality 16.7% the first year postpartum, during which time 10.5% of women with GDM history manifested prediabetes, 5.2% T2DM and 1% T1DM. Furthermore, we demonstrated that routine glycaemic parameters (FPG, 1-h and 2-h post 75 g load glucose) examined in all pregnant women as a part of their standard antenatal care can reliably predict early postpartum glucose intolerance and thus improve health outcomes and perspectives in this group of young women at high risk for diabetes (10) and cardiovascular diseases (18). Finally, optimal cut-off values for maternal risk of postpartum diabetes ascertained in our sample are in general very close to the IADPSG criteria that are evidence-based for the perinatal outcomes.

As mentioned earlier, early postpartum screening has a great chance to detect glucose abnormality in large proportion of women who can then be efficiently intervened. For this reason we studied population of GDM cases who have been re-tested within the first 12 months postpartum since – according to our view – positive attitude towards lifestyle changes lasting for some time after pregnancy might still span the early postpartum period and repeated oGTT is thus attended by a realistic maximum of cases. In spite of the currently practiced recommendations – to repeat testing for diabetes or prediabetes roughly 3-6 months after delivery and then every 3 years (19), considerable proportion of women with GDM history fail to turn up (11,12). This is quite unfortunate considering diabetes development is largely preventable by lifestyle and pharmacologic interventions (20).

This unsatisfactorily low compliance in postpartum screening can either be changed by various strategies to increase motivation of GDM patients to seek the postpartum test or by timely antepartum stratification of GDM cases according to their post-gestational metabolic risk. The latter strategy – selective postpartum follow-up of high risk subgroup is according to our view more effective and prompted us to undertake the current study.

Although it is physiologically highly plausible that the degree of impairment of glucose homeostasis in pregnancy is continually reflected in the postpartum glucose (in)tolerance, studies relating antepartum glycaemic indices to postpartum status with the attempt to quantitatively estimate the risk and to predict postpartum diabetes are still limited. Previous studies have shown post-load glucose levels (1-hr, 2-hr or 3-hr of antepartum oGTT) (21) or FPG (22) or all of these (23) associated with postpartum glucose abnormality. Retnakaran *et al*. reported prevalence of postpartum glucose intolerance progressively increased across the continuous spectrum of women with metabolically distinct glucose tolerance (including NGT) assessed by the combination of glucose challenge test and oGTT at mid-pregnancy (24). Ekelund *et*

*al*. showed that FPG and HbA1c were significant predictors of postpartum diabetes (25). Finally, antepartum disposition index was shown to be predictive for postpartum glucose intolerance (26). However, majority of these studies employed either (i) medical practice distinct from the one currently provided in our country (and most of the Europe) such as two-step screening algorithm, higher glucose load in diagnostic oGTT (100 g), more frequent sampling (including 30 min and/or 3-hr), later testing spanning the third trimester, (ii) longer postpartum follow-up or (iii) measurements done solely for the research purposes not covered by a standard medical care such as insulin measurement to assess insulin sensitivity (HOMA insulin resistance index, insulin sensitivity index) and beta cell function (HOMA beta cell index, insulinogenic and oral disposition index).

In the current study we found significantly higher mid-gestation FPG, 1-hr and 2-hr post-75g load glucose, $AUC_{oGTT}$ and HbA1c in GDM women with persistent postpartum glucose metabolism abnormality compared to those with NGT postpartum. Relative risk of post-partum persistence of glucose intolerance gradually increased with the number of above threshold values whereas all three glycaemic indices above threshold (i.e. FPG, 1-hr and 2-hr post 75 g load glucose) conferred independent predictive potential for postpartum glucose intolerance. Inclusion of HbA1c among the standard screening/diagnostic parameters for GDM might be profitable due to limited reproducibility of oGTT (27), however further studies are required to assess the cost-benefit relationship.

Possibility to reliably predict postpartum diabetes using routine and financially covered parameters assessed in mid-gestation is a desirable scenario; however, former non-evidence-based WHO diagnostic criteria did not seem to reflect both relevant medical outcomes – i.e. short-term neonatal and obstetrical risks nor long-term maternal metabolic risk – to the same extent as shown by several studies (28,29). Although the initial diagnostic criteria of GDM proposed by Carpenter and Coustan (30) were based primarily on the risk of subsequent maternal diabetes, further modifications incl. IADPSG criteria favoured predominantly the perinatal risks. It becomes increasingly apparent that a dual set of diagnostic criteria might be necessary if we should capture all adverse outcomes of GDM including postpartum maternal glucose abnormality. Due to this reason we applied ROC analysis to find optimal discriminating cut-offs (yielding the highest $AUC_{ROC}$) for mid-gestation FPG, 1-hr and 2-hr post 75 g load glucose and HbA1c. The actual suggested cut-offs are more stringent for FPG (≥ 5.1 mmol/L) than those currently practiced according to WHO criteria (≥ 5.6 mmol/L) and are in fact identical with consensus criteria derived from the HAPO study recommended by IADPSG (≥ 5.1 mmol/L). Furthermore, our analysis justifies the relevance of 1-h post 75 g load glucose measurement since the suggested 2-h cut-off value equals to the current WHO GDM diagnostic value. Postpartum glucose abnormality risk-based 1-h post 75 g load cut-off (≥ 10.7 mmol/L) is less inclusive than the current GDM criteria by IADPSG (≥ 10 mmol/L). We can therefore speculate that substantially elevated 1-h post 75 g load glucose (possibly in combination with HbA1c > 36 mmol/mol) is the most sensitive and discriminative parameter distinguishing subset of DM cases with increased risk of postpartum glucose abnormality.

We are of course aware of several limitations such as that our study cohort does not represent the entire GDM population and model constructed from a retrospective data of single cohort study with possible selection bias needs to be replicated and validated. Furthermore, direct comparison of former and new (IADPSG) WHO criteria in terms of sensitivity and specificity is unfortunately not possible in the same study sample since it was recruited by former national modification of WHO criteria and is therefore distorted by different cut-offs (esp. higher upper limit for FPG). Nevertheless, as a proof of principle this study provides incentive to explore the predictive potential of routine diagnostic criteria in larger scale studies.

The major message of the current study is principally conveyed by the finding that prevalence of early postpartum glucose abnormality is not negligible and reaches 16.7% during the first year postdelivery. Furthermore, by annotation of current GDM diagnostic criteria it appears possible to yield

extra information not only on obstetrical and neonatal but also maternal metabolic risks. Apparently, currently practiced simple dichotomization of the mid-trimester oGTT into physiological and pathological reduces information gained from a standard routine well accessible test. Modification of the criteria with the complex view (e.g. dual set of cut-offs) of both obstetrical/neonatal and future metabolic risk could help to identify high risk population to be followed immediately postpartum at no additional cost on top of routine antenatal care. The documented efficiency of early diagnosis and lifestyle or pharmacological intervention on prevention or postponing diabetes development is a powerful argument for further development of risk-based model. Subsequent long-term health care economic benefits represent significant added value of the proposed approach.

In conclusion, parameters of glucose metabolism measured during 24-28$^{th}$ week of pregnancy fulfilling criteria of GDM diagnosis exhibited highly statistically significant differences between women with and without persistent postpartum glucose metabolism abnormality and conferred significant predictive potential for early postpartum glucose abnormality. Considering generally low-compliance of GDM women in postpartum screening, risk-based stratification of GDM population could improve efficiency of the screening for diabetes after the delivery and decrease the burden of its metabolic and cardiovascular consequences in this high-risk population. IADPSG criteria recommended by Czech Diabetes Society (and in many other countries in Europe) seem to optimally capture both perinatal and maternal metabolic risks and are therefore medically and economically justified.

**Acknowledgement**

The authors thank the management of the University Hospital Brno for consent to use their electronic health record system. The authors also thank Tomáš Barták and Zdeněk Kratochvíl for a technical assistance with data mining and quality control. This study was supported by grant NT/11405 from Ministry of Health of Czech Republic.

**Potential conflict of interest**

None declared.

**References**

1. *American Diabetes Association Clinical Practice Recommendations 2001. Diabetes Care 2001;24 Suppl 1:S1-133. http://dx.doi.org/10.2337/diacare.24.1.1.*
2. *Newbern D, Freemark M. Placental hormones and the control of maternal metabolism and fetal growth. Curr Opin Endocrinol Diabetes Obes 2011;18:409-16. http://dx.doi.org/10.1097/MED.0b013e32834c800d.*
3. *Reece EA, Leguizamón G, Wiznitzer A. Gestational diabetes: the need for a common ground. Lancet 2009;373:1789-97. http://dx.doi.org/10.1016/S0140-6736(09)60515-8.*
4. *Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991-2002. http://dx.doi.org/10.1056/NEJMoa0707943.*
5. *Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676-82. http://dx.doi.org/10.2337/dc10-0719.*
6. *Weinert LS. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy: comment to the International Association of Diabetes and Pregnancy Study Groups Consensus Panel. Diabetes Care 2010;33:e97; author reply e98. http://dx.doi.org/10.2337/dc10-0544.*
7. *Lovrencić MV, Honović L, Kralik S, Matica J, Prasek M, Pape-Medvidović E, et al. Redefinition of gestational diabetes mellitus: implications for laboratory practice in Croatia. Biochem Med (Zagreb) 2013;23:7-11. http://dx.doi.org/10.11613/BM.2013.002.*
8. *Krejci H, Anderlova K. [Why do we still hesitate to accept the new international criteria for the diagnosis of gestational diabetes mellitus? The current screening is non-uniform and does not correspond with evidence-based medicine]. Ceska Gynekol 2014;79:206-12. (in Czech)*
9. *Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 2002;25:1862-68. http://dx.doi.org/10.2337/diacare.25.10.1862.*

10. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009;373:1773-79. http://dx.doi.org/10.1016/S0140-6736(09)60731-5.
11. Hunt KJ, Logan SL, Conway DL, Korte JE. Postpartum screening following GDM: how well are we doing? Curr Diab Rep 2010;10:235-41. http://dx.doi.org/10.1007/s11892-010-0110-x.
12. Keely E. An opportunity not to be missed--how do we improve postpartum screening rates for women with gestational diabetes? Diabetes Metab Res Rev 2012;28:312-16. http://dx.doi.org/10.1002/dmrr.2274.
13. Friedecký B, Zima T, Kratochvíla J, Springer D. [Diabetes mellitus - laboratorní diagnostika a sledování stavu pacientů]. 2005. Available at: http://www.cskb.cz/res/file/doporuceni/DM_verze%202012.pdf. Accessed June 20, 2015. (in Czech)
14. Reinauer H, Home P, Kanabasagapathy A, Heuck C-C. Laboratory diagnosis and monitoring of diabetes mellitus. In: World Health Organization 2002.
15. Matthews JN, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. BMJ 1990;300:230-35. http://dx.doi.org/10.1136/bmj.300.6719.230.
16. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837-45. http://dx.doi.org/10.2307/2531595.
17. Youden WJ. Index for rating diagnostic tests. Cancer 1950;3:32-35. http://dx.doi.org/10.1002/1097-0142(1950)3:1<32::AID-CNCR2820030106>3.0.CO;2-3.
18. Retnakaran R. Glucose tolerance status in pregnancy: a window to the future risk of diabetes and cardiovascular disease in young women. Curr Diabetes Rev 2009;5:239-44. http://dx.doi.org/10.2174/157339909789804378.
19. Kim C, Herman WH, Vijan S. Efficacy and cost of postpartum screening strategies for diabetes among women with histories of gestational diabetes mellitus. Diabetes Care 2007;30:1102-06. http://dx.doi.org/10.2337/dc06-2237.
20. Saaristo T, Moilanen L, Korpi-Hyövälti E, Vanhala M, Saltevo J, Niskanen L, et al. Lifestyle intervention for prevention of type 2 diabetes in primary health care: one-year follow-up of the Finnish National Diabetes Prevention Program (FIN-D2D). Diabetes Care 2010;33:2146-51. http://dx.doi.org/10.2337/dc10-0410.
21. Wein P, Beischer NA, Sheedy MT. Studies of postnatal diabetes mellitus in women who had gestational diabetes. Part 2. Prevalence and predictors of diabetes mellitus after delivery. Aust N Z J Obstet Gynaecol 1997;37:420-23. http://dx.doi.org/10.1111/j.1479-828X.1997.tb02450.x.
22. Schaefer-Graf UM, Buchanan TA, Xiang AH, Peters RK, Kjos SL. Clinical predictors for a high risk for the development of diabetes mellitus in the early puerperium in women with recent gestational diabetes mellitus. Am J Obstet Gynecol 2002;186:751-56. http://dx.doi.org/10.1067/mob.2002.121895.
23. Akinci B, Celtik A, Genc S, Yener S, Demir T, Secil M, et al. Evaluation of postpartum carbohydrate intolerance and cardiovascular risk factors in women with gestational diabetes. Gynecol Endocrinol 2011;27:361-67. http://dx.doi.org/10.3109/09513590.2010.492885.
24. Retnakaran R, Qi Y, Sermer M, Connelly PW, Hanley AJ, Zinman B. Glucose intolerance in pregnancy and future risk of pre-diabetes or diabetes. Diabetes Care 2008;31:2026-31. http://dx.doi.org/10.2337/dc08-0972.
25. Ekelund M, Shaat N, Almgren P, Groop L, Berntorp K. Prediction of postpartum diabetes in women with gestational diabetes mellitus. Diabetologia 2010;53:452-57. http://dx.doi.org/10.1007/s00125-009-1621-3.
26. Saisho Y, Miyakoshi K, Tanaka M, Matsumoto T, Minegishi K, Yoshimura Y, et al. Antepartum oral disposition index as a predictor of glucose intolerance postpartum. Diabetes Care 2012;35:e32. http://dx.doi.org/10.2337/dc11-2549.
27. Rasmussen SS, Glümer C, Sandbaek A, Lauritzen T, Carstensen B, Borch-Johnsen K. Short-term reproducibility of impaired fasting glycaemia, impaired glucose tolerance and diabetes The ADDITION study, DK. Diabetes Res Clin Pract 2008;80:146-52. http://dx.doi.org/10.1016/j.diabres.2007.11.003.
28. Retnakaran R, Qi Y, Sermer M, Connelly PW, Zinman B, Hanley AJ. Comparison of National Diabetes Data Group and American Diabetes Association diagnostic criteria for gestational diabetes in their identification of postpartum risk of glucose intolerance. Diabetes Res Clin Pract 2009;85:40-46. http://dx.doi.org/10.1016/j.diabres.2009.04.008.
29. Retnakaran R, Qi Y, Sermer M, Connelly PW, Hanley AJ, Zinman B. The antepartum glucose values that predict neonatal macrosomia differ from those that predict postpartum prediabetes or diabetes: implications for the diagnostic criteria for gestational diabetes. J Clin Endocrinol Metab 2009;94:840-45. http://dx.doi.org/10.1210/jc.2008-2434.
30. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol 1982;144:768-73.