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### ► To cite this version:

E. Cosson, E. Vicaut, N. Berkane, T.L. Cianganu, C. Baudry, et al.. Prognosis associated with initial care of increased fasting glucose in early pregnancy: A retrospective study. *Diabetes & Metabolism*, 2021, 47 (3), pp.101197. 10.1016/j.diabet.2020.08.007. hal-04042680

**HAL Id: hal-04042680**

**<https://cnam.hal.science/hal-04042680>**

Submitted on 22 Jul 2024

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**Prognosis associated with initial care of increased fasting glucose in early pregnancy: A retrospective study**

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**Short running title:** Increased fasting glucose in early pregnancy

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**Declarations of interest:** none.

Lilly France partially funded this study, but did not interfere with any part of the study (collection, analysis, interpretation of data; writing the report; decision to submit for publication).

Received 8 June 2020; Accepted 20 September 2020

## **Abstract**

*Aim.* – To evaluate whether the initial care of women with fasting plasma glucose (FPG) levels at 5.1–6.9 mmol/L before 22 weeks of gestation (WG), termed ‘early fasting hyperglycaemia’, is associated with fewer adverse outcomes than no initial care.

*Methods.* – A total of 523 women with early fasting hyperglycaemia were retrospectively selected in our department (2012–2016) and separated into two groups: (i) those who received immediate care (n = 255); and (ii) those who did not (n = 268), but had an oral glucose tolerance test (OGTT) at or after 22 WG, with subsequent standard care if hyperglycaemia (by WHO criteria) was present. The number of cases of large-for-gestational age (LGA) infants, shoulder dystocia and preeclampsia with initial care of early fasting hyperglycaemia were compared after propensity score modelling and accounting for covariates.

*Results.* – Of the 268 women with no initial care, 134 had hyperglycaemia after 22 WG and then received care. Women who received initial care vs those who did not were more likely to be insulin-treated during pregnancy (58.0% vs 20.9%, respectively;  $P < 0.00001$ ), gained less gestational weight ( $8.6 \pm 5.4$  kg vs  $10.8 \pm 6.1$  kg, respectively;  $P < 0.00001$ ), had a lower rate of preeclampsia [1.2% vs 2.6%, respectively; adjusted odds ratio (aOR): 0.247 (0.082–0.759),  $P = 0.01$ ], and similar rates of LGA infants (12.2% vs 11.9%, respectively) and shoulder dystocia (1.6% vs 1.5%, respectively). When initial FPG levels were  $\geq 5.5$  mmol/L (prespecified group, n = 137), there was a lower rate of LGA infants [6.7% vs 16.1%, respectively; aOR: 0.332 (0.122–0.898);  $P = 0.03$ ].

*Conclusion.* – Treating women with early fasting hyperglycaemia, especially when FPG is  $\geq 5.5$  mmol/L, may improve pregnancy outcomes, although this now needs to be confirmed by randomized clinical trials.

**Keywords:** Early screening; Gestational diabetes mellitus; Prognosis

**Abbreviations:**

BMI: body mass index

GDM: gestational diabetes mellitus

FIGO: International Federation of Gynecology and Obstetrics

FPG: fasting plasma glucose

IADPSG: International Association of the Diabetes and Pregnancy Study Group

IPTW: inverse probability of treatment weighting

LGA: large-for-gestational age

OGTT: oral glucose tolerance test

RCT: randomized clinical trial

WG: weeks of gestation

WHO: World Health Organization

**Acknowledgements**

We wish to thank: (i) Lilly France, for partly funding this study; (ii) Dr Sylvie Picard, Dijon, France, for her help in the preparation of the English manuscript; (iii) Ms Françoise Gary, AP-HP, Unité de Recherche Clinique, Fernand Widal Hospital, Paris, and Ms Isabelle Pharisien, AP-HP, Gynecology-Obstetrics, Jean Verdier Hospital, Bondy, for data collection; (iv) Mr Abdourahmane Diallo, AP-HP, Unité de Recherche Clinique Fernand Widal, for his help in propensity score weighting; and (v) Mr Didier André, AP-HP, Unité de Recherche Clinique GHU-SSPD, for data management.

## **Introduction**

Hyperglycaemia in pregnancy excludes known diabetes before pregnancy and refers to (i) diabetes in pregnancy, defined as unknown type 2 diabetes mellitus before pregnancy; and (ii) gestational diabetes mellitus (GDM), usually diagnosed after 24 weeks of gestation (WG) [1–4]. Diabetes in pregnancy is diagnosed using the same glucose threshold values [fasting plasma glucose (FPG)  $\geq 7$  mmol/L] and/or HbA1c [ $\geq 6.5\%$  (48 mmol/mol)] as used to define diabetes in non-pregnant individuals. Diabetes in pregnancy is associated with an especially poor prognosis [5–7], and its identification in early pregnancy is considered important as it leads to earlier treatment [1–4,8].

Treating GDM after 24 WG reduces adverse events during pregnancy [9,10] and is considered the standard of care. However, whether this guideline can be applied to women with early fasting hyperglycaemia (defined in this study as FPG levels between 5.1 and 6.9 mmol/L in early pregnancy) is still uncertain [11–13]. In fact, at least half of all untreated women with early fasting hyperglycaemia do not develop GDM later in pregnancy [14–17]. Therefore, immediate care may not be mandatory for some women with early fasting hyperglycaemia. Moreover, there is no rationale for choosing 5.1 mmol/L as the threshold for an elevated FPG level in early pregnancy, as this was extrapolated from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study performed in pregnant women between 24 and 32 WG [1,18]. In fact, a threshold of 5.5 mmol/L may be more appropriate. Indeed, it has recently been reported that women with an early FPG of 5.5–6.9 mmol/L had a threefold greater risk of GDM after 22 WG compared with women with early FPG levels at 5.1–5.4 mmol/L [17].

Our large retrospective cohort of women [17,19,20] provided an opportunity to differentiate, among women with early fasting hyperglycaemia, those who received initial care and those who did not, but who instead underwent routine screening after 22 WG, followed by subsequent care if necessary. Our hypothesis was that the pregnancy prognosis would be

improved if women with early fasting hyperglycaemia were initially treated compared with women who were not. In addition, there was also a specific plan to assess whether or not there was any potential benefit of initial care in the subgroup of women with FPG levels  $\geq 5.5$  mmol/L in early pregnancy.

## **Material and methods**

### ***Participants***

The present observational study was conducted at the Jean Verdier University Hospital in a suburban area of Paris (Bondy), France. It was based on the electronic medical records of women who delivered between 2012 and 2016, as obstetric data are prospectively routinely and systematically collected at birth in the hospital by the midwife assisting with delivery. In addition, data were also collected on hyperglycaemia screening [17,19,20]. Women were informed that their medical records could be used for research unless they were opposed to such use [17,19,20]. None were opposed and their data were analyzed anonymously. Our database was registered with the French National Commission on Information Technology and Civil Liberties (CNIL; *Commission Nationale de l'Informatique et des Libertés*, no. 1704392v0) [17,19,20]. Inclusion criteria were age 18–50 years, singleton pregnancy, and no personal history of either diabetes outside of pregnancy or previous bariatric surgery (Fig. 1). Women with early fasting hyperglycaemia were specifically selected.

### ***Glycaemic status during pregnancy and management of hyperglycaemia***

Our policy was to universally screen women at both the beginning of pregnancy and after 24 WG if previous screening had been either normal or not done. Early screening was based on FPG measurement, whereas late screening was based on a 75-g oral glucose tolerance test (OGTT) with measurement of fasting, 1-h and 2-h plasma glucose levels [4]. Hyperglycaemia

in pregnancy was defined according to International Association of the Diabetes and Pregnancy Study Group (IADPSG)/World Health Organization (WHO) recommendations [1,2], as these guidelines have been endorsed in France [4].

In our study, early fasting hyperglycaemia was defined as an FPG of 5.1–6.9 mmol/L before 22 WG [17,19,20] rather than 24 WG because OGTTs are often used for screening at 22–24 WG [19] even though they are intended for screening after 24 WG. Our study also did not include women with diabetes diagnosed early in pregnancy (FPG levels  $\geq 7$  mmol/L before 22 WG), as immediate care is clearly considered to improve pregnancy outcomes [1–4,8]. In France [4], women with early fasting hyperglycaemia are usually treated as if they have GDM. Accordingly, our study assumed that women initially received care for early fasting hyperglycaemia if they were referred to a hospital multidisciplinary team, comprising a diabetologist, an obstetrician, a midwife, a dietitian and a nurse educator, within 12 weeks of diagnosis. A maximum delay of 12 weeks was chosen to ensure that care was not initiated too late. According to French recommendations [4], these women would have received personalized dietary advice and instructions on how to perform self-monitoring of blood glucose six times a day, and would have seen the diabetologist every 2–4 weeks. Insulin therapy was also prescribed when preprandial and/or 2-h postprandial glucose levels were  $> 5.0$  mmol/L and/or 6.7 mmol/L, respectively, as per French guidelines [4]. Obstetric care was likewise given according to French recommendations [4].

As with a previous study [17], women with early fasting hyperglycaemia who had not been considered for initial treatment at our hospital or elsewhere were specifically selected. In addition, this subset of women included only those who were screened again for hyperglycaemia after 22 WG (Fig. 1), as this is the standard of care [9,10]. At this step, diabetes in pregnancy was defined as FPG  $\geq 7.0$  mmol/L and/or 2-h plasma glucose  $\geq 11.1$  mmol/L, while GDM was defined as FPG at 5.1–6.9 mmol/L and/or 1-h plasma glucose  $\geq$

10.0 mmol/L and/or 2-h plasma glucose at 8.4–11.0 mmol/L during an OGTT [4]. Women with early fasting hyperglycaemia who received no initial care, but who had GDM or diabetes in pregnancy after 22 WG, were referred to our multidisciplinary team, after which they then received the same treatment as the women who received initial care for early fasting hyperglycaemia. Those without hyperglycaemia after 22 WG received no specific care. It should also be mentioned that smoking cessation was promoted in all women.

### ***Pregnancy outcomes***

Our study also examined rates of the following adverse outcomes: (i) large-for-gestational age (LGA) infants (birth weight > 90<sup>th</sup> percentile for the standard French population); (ii) small-for-gestational age infants (birth weight < 10<sup>th</sup> percentile); (iii) shoulder dystocia, considered to have happened if, after delivery of the fetal head, an obstetric manoeuvre was required to release the infant's shoulders (McRoberts manoeuvre and suprapubic pressure, posterior arm delivery by rotation to an oblique angle or rotation of the infant by 180°) after gentle downward traction had failed; (iv) preeclampsia (systolic/diastolic blood pressure  $\geq$  140/90 mmHg on two recordings taken 4 h apart and proteinuria  $\geq$  300 mg/24 h or  $\geq$  2+ on dipstick testing of a random urine sample); and (v) caesarean section [17,19,20]. The need for insulin at the time of delivery and gestational weight gain during pregnancy (body weight before delivery minus preconception weight) were also noted [21].

### ***Statistical analysis***

Baseline continuous variables were expressed as means  $\pm$  standard deviation (SD), and categorical variables as frequencies and percentages [n (%)]. The two study groups [women receiving initial care for early fasting hyperglycaemia and those who did not (reference group)] were compared using Student's *t* or Mann–Whitney tests for Gaussian or non-



Gaussian continuous variables, respectively, with chi-squared ( $\chi^2$ ) or Fisher's exact tests for categorical variables.

As already described in the introduction, there was a specific plan to assess whether or not there was any potential benefit with immediate care in women with FPG levels  $\geq 5.5$  mmol/L in early pregnancy (sensitivity analysis). A propensity score model was developed using logistic regression because the women receiving initial care or not for early fasting hyperglycaemia were not balanced in our observational study. Thus, two weighted propensity score models were designed to estimate the causal effect of exposure on an outcome, and the one that best balanced the covariates between the two groups was chosen. The selected method is termed an 'estimator of the inverse probability of treatment weighting' (IPTW) [22]. The IPTW logistic-regression model included both known confounding factors and unbalanced covariates between our two groups. For the total study population, unbalanced covariates were: FPG level; gestational age at initial screening; age; body mass index (BMI); familial history of diabetes; parity; personal history of GDM; and year of delivery (which remained unbalanced between the two groups after propensity score weighting); the results were therefore further adjusted for year of delivery ([Table S1; see supplementary materials associated with this article online](#)).

In women with initial FPG levels at 5.5–6.9 mmol/L, the model included gestational age at initial screening, parity, personal history of GDM and year of delivery as unbalanced covariates, with age and BMI as known confounding factors. The characteristics of these women after propensity score weighting were balanced ([Table S2; see supplementary materials associated with this article online](#)).

All tests were two-sided and used a *P* value of 0.05 to define significance. Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R-2.8 ([www.r-project.org](http://www.r-project.org)) software.

## Results

### *Population characteristics*

As presented in Fig. 1, 523 women were ultimately included in our observational study; their baseline characteristics are presented in [Table S3 \(see supplementary materials associated with this article online\)](#). A total of 137 of these 523 women had an initial FPG  $\geq 5.5$  mmol/L, and their characteristics are also shown in Table S3.

Women who received initial care for early fasting hyperglycaemia (n = 255) had higher preconception BMI and FPG values on initial screening; they were also older than those who had not received initial care (n = 268), and were more likely to have a family history of diabetes or a personal history of GDM ([Table I](#)). Of the 268 women not receiving initial care for early fasting hyperglycaemia who underwent OGTT after 22 WG, GDM was diagnosed in 123 of them and diabetes in pregnancy in 11 cases, whereas 132 had a normal OGTT ([Table II](#)); treatment began later in these women than in those who received initial care. Table II also shows that women receiving initial care for early fasting hyperglycaemia were more likely to be insulin-treated, with the insulin initiated earlier during pregnancy. Women with initial care also gained less weight during pregnancy. Early care was given more frequently in recent years.

On considering only the 137 women with initial FPG  $\geq 5.5$  mmol/L, those who had received initial care for early fasting hyperglycaemia (n = 75) had higher baseline FPG, higher gestational age at diagnosis and higher frequency of previous GDM than those who had not (n = 62; [Table I](#)). Of the 62 women not given immediate care for early fasting hyperglycaemia, GDM was diagnosed in 34 cases and diabetes in pregnancy in 11 cases when OGTT was performed after 22 WG ([Table II](#)). Care was initiated later in these women than in those who received initial care for early fasting hyperglycaemia. Table II also shows that women

receiving initial care were more likely to be insulin-treated and that insulin was initiated earlier. Early treatment was also performed more frequently in recent years.

### ***Outcomes according to initial care of early fasting hyperglycaemia***

Table III shows that receiving initial care for early fasting hyperglycaemia was not associated with differences in rates of adverse outcomes except for preeclampsia. In fact, preeclampsia rates were lower in women with vs without initial care for early fasting hyperglycaemia [1.2% vs 2.6%, respectively; adjusted odds ratio (aOR): 0.247 (0.082–0.759), adjusted  $P = 0.01$ ]. On considering only the 137 women with early FPG  $\geq 5.5$  mmol/L, the rate of LGA infants was lower in those receiving initial care for early fasting hyperglycaemia vs those who did not [6.7% vs 16.1%, respectively; aOR: 0.332 (0.122–0.898), adjusted  $P = 0.03$ ].

### **Discussion**

Higher FPG levels during the first trimester of pregnancy have reportedly been associated with an increased risk of adverse pregnancy outcomes, including macrosomia [23,24] and caesarean section [23]. Therefore, our hypothesis was that the initial care of women with early fasting hyperglycaemia would be associated with fewer adverse pregnancy outcomes compared with later care in women with confirmed hyperglycaemia after 22 WG. This hypothesis was verified for preeclampsia, although the rate was low. However, the rate of LGA infants was significantly lower in women with early FPG levels at 5.5–6.9 mmol/L receiving initial care for the condition, suggesting that such treatment should be immediately initiated in such cases.

In retrospective studies, women with early fasting hyperglycaemia are generally more likely to be given pharmacological treatment [19,25–28] and to gain less weight during pregnancy [19,26,27,29,30] than those with a later diagnosis of GDM. Nevertheless, after adjusting for

risk factors, early fasting hyperglycaemia is often associated with a less favourable prognosis than GDM diagnosed later in pregnancy, including more preterm deliveries [25–28], LGA infants [25–28], caesarean sections [25] and pregnancy-related hypertensive disorders [25,29]. Other studies have reported similar prognoses for both situations, with comparable rates of preterm deliveries [26], LGA infants [28,30], caesarean sections [28], pregnancy-related hypertensive disorders [26,28] and neonatal morbidity [26]. Two studies have even found lower rates of LGA infants [27,29] and neonatal hypoglycaemia [27] in women with early fasting hyperglycaemia. A similar or even better prognosis for early fasting hyperglycaemia compared with GDM is generally consistent with early treatment of early fasting hyperglycaemia as: (i) women with early fasting hyperglycaemia are consistently reported to have more risk factors than women with GDM (for a review, see Cosson et al. [12]); and (ii) risk factors *per se* come with a poor prognosis [20]. However, overall, the results of these retrospective studies have been equivocal; one systematic review and meta-analysis [13] reported that perinatal mortality and neonatal hypoglycaemia were greater among women with early fasting hyperglycaemia—usually called ‘early-diagnosed GDM’—compared with women with GDM, despite treatment including more frequent use of insulin.

In a previous evaluation carried out in our hospital (covering the 2012–2016 period) of the incidence of a composite outcome, women were screened either after 22 WG (‘late screening only’, n = 5190) or before 22 WG and treated for early fasting hyperglycaemia or, if present, for diabetes diagnosed early in pregnancy, with repeat screening after 22 WG if absent (‘early ± late screening’, n = 4605). Our finding was that, while a strategy including early measurement of FPG during pregnancy increased the incidence and treatment of hyperglycaemia in pregnancy, this was not associated with better pregnancy outcomes after propensity scoring [19]. However, in that study, the potential benefit of early screening and subsequent treatment of women with early fasting hyperglycaemia was probably diluted.

Thus, our present results are complementary and, at least in part, address the frequently asked question: Should immediate treatment be given to women with FPG levels at 5.1–6.9 mmol/L in early pregnancy? Our results suggest that women with early FPG values of 5.5–6.9 mmol/L should be immediately managed with dietary counselling, self-monitoring of blood glucose and pharmacological treatment if glucose targets have not been reached, as such care is associated with fewer LGA infants, the usual outcome in cases of hyperglycaemia in pregnancy. Considering that preeclampsia is unusual, our results also suggest that women with early FPG at 5.1–5.5 mmol/L should only be tested again at 24–28 WG and treated for hyperglycaemia if diagnosed at that time, which is the standard of care [9,10]. The 5.5 mmol/L threshold is in line with several guidelines. In the International Federation of Gynecology and Obstetrics (FIGO) report [3], as well as in Belgium [31], China, Latin America and the UK (<https://pathways.nice.org.uk/pathways/diabetes-in-pregnancy>), FPG values between 5.5 and 6.9 mmol/L are considered early fasting hyperglycaemia. In our present study, none of the untreated women who developed diabetes in pregnancy had FPG levels < 5.5 mmol/L. Thus, FPG values > 5.5 mmol/L are associated with more GDM after 24 WG [14,15,23,32–34].

The results of randomized clinical trials (RCTs) are invaluable for definitively supporting guidelines advocating the immediate care of women with FPG levels  $\geq 5.5$  mmol/L in early pregnancy. A recent post-hoc analysis of an RCT (Lifestyle in Pregnancy, LiP) suggested that lifestyle interventions in 90 obese women (BMI 34.5 kg/m<sup>2</sup>) with early fasting hyperglycaemia were not effective in improving obstetric outcomes. However, self-monitoring of blood glucose was not part of the intervention, and women receiving insulin treatment during pregnancy were excluded [35]. More recently, another RCT [36] found that early screening of hyperglycaemia in pregnancy failed to reduce incidence of the adverse perinatal composite outcome. The trial included only obese women, and screening for

hyperglycaemia was performed using the two-step method. Treating only women with FPG levels  $\geq 5.5$  mmol/L at the initial screening would be of interest in future studies.

Our study has both strengths and limitations. Recruiting at a public hospital included a large proportion of women with vulnerable conditions and multiple ethnicities, precluding generalization of our findings. However, the data are the result of a single institution with a comprehensive and consistent programme of perinatal care. The care of women with hyperglycaemia in pregnancy was similar in both study groups, although insulin therapy (when required) was begun 10 weeks later in women not receiving initial care for early fasting hyperglycaemia who then presented with hyperglycaemia after 22 WG, in which case, only the IADPSG/WHO criteria for hyperglycaemia were considered. In addition, our study was not randomized and, therefore, women with and without initial care for early fasting hyperglycaemia were unmatched.

On the other hand, a wide range of potential confounders was taken into account. For example, as women not receiving initial care for early fasting hyperglycaemia were more frequently found during the early years of the study probably because the French recommendations had only just recently been published and were not always widespread knowledge, our present results were nonetheless adjusted for that factor. However, despite all our efforts, unmeasured differences between groups may have influenced the results. Finally, our focus was on pregnancy outcomes, including some unusual ones, and the consequences of selective screening on intergenerational transmission of metabolic disorders, which can be partially prevented through interventions during pregnancy, cannot be excluded [37].

In conclusion, our present results point to no immediate treatment when women have FPG levels  $< 5.5$  mmol/L in early pregnancy, even though a few cases of preeclampsia might be avoided with immediate care. However, such women do require repeat screening with OGTTs later in pregnancy and the usual management of hyperglycaemia after diagnosis [9,10]. Our

findings also suggest that the immediate care of women with FPG levels  $\geq 5.5$  mmol/L may reduce rates of LGA infants, and should include dietary counselling, self-monitoring of blood glucose and insulin treatment when necessary.

### **Appendix supplementary material**

Supplementary materials (Tables S1–S3) associated with this article can be found at <http://www.sciencedirect.com> at doi . . .

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## Figure legend

Fig. 1. Flow chart of study recruitment.

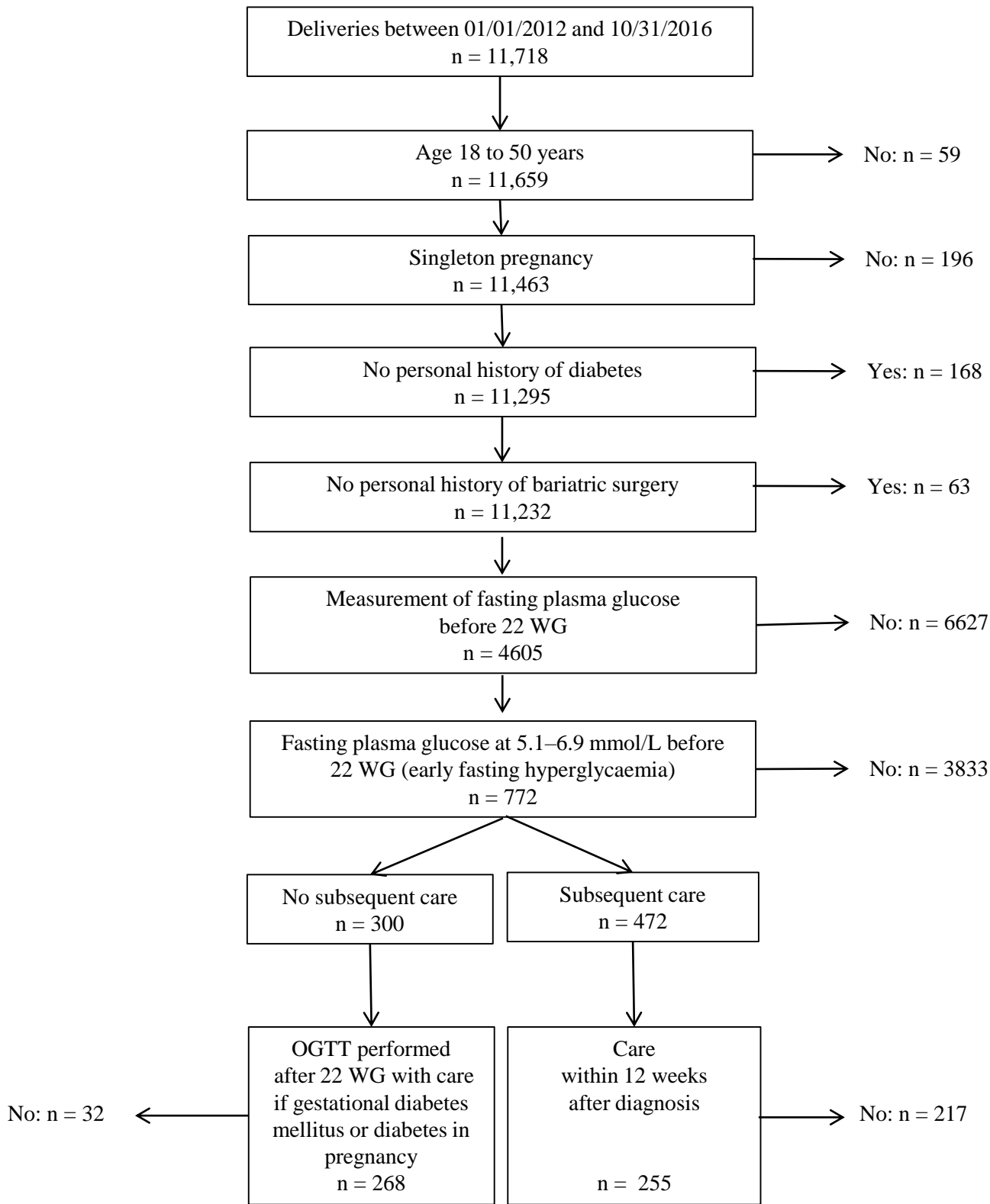


Table I

Characteristics of women receiving immediate care or not for early fasting hyperglycaemia during pregnancy

	Fasting plasma glucose 5.1–6.9 mmol/L			Fasting plasma glucose 5.5–6.9 mmol/L		
	No initial care	Initial care	Diff. [95% CI]	No initial care	Initial care	Diff. [95% CI]
	n = 268	n = 255		n = 62	n = 75	
<i>Early screening</i>						
Fasting plasma glucose (mmol/L)	5.3 ± 0.3	5.4 ± 0.3	<b>-0.10 [-0.15; -0.05]</b>	5.7 ± 0.2	5.8 ± 0.3	<b>-0.12 [-0.22; -0.02]</b>
Gestational age at screening (WG)	10.2 ± 4.2	13.2 ± 4.0	<b>-3.1 [-3.8; -2.4]</b>	10.1 ± 4.4	12.4 ± 4.0	<b>-2.3 [-3.8; -0.9]</b>
<i>Screening after 22 WG</i>						
Fasting plasma glucose (mmol/L)	4.9 ± 0.7	–	–	5.1 ± 0.7	–	–
1-h plasma glucose (mmol/L)	8.45 ± 2.2	–	–	9.4 ± 2.3	–	–
2-h plasma glucose (mmol/L)	7.1 ± 1.9	–	–	7.8 ± 2.1	–	–
Gestational age at screening (WG)	27.2 ± 3.3	–	–	27.4 ± 3.5	–	–
<i>Characteristics</i>						
Age (years)	31.8 ± 5.4	33.3 ± 5.4	<b>-1.5 [-2.4; -0.5]</b>	32.7 ± 5.9	33.3 ± 4.9	-0.6 [-2.4; 1.2]
Preconception body mass index (kg/m <sup>2</sup> )	26.9 ± 5.3	28.3 ± 5.9	<b>-1.4 [-2.4; -0.5]</b>	28.2 ± 6.1	29.5 ± 5.6	-1.3 [-3.3; 0.7]
Body mass index ≥ 30 kg/m <sup>2</sup>	72 (27.9)	95 (38.3)	<b>-10.4% [-18.6; -2.2]</b>	22 (36.7)	33 (45.8)	-9.2 [-25.9; 7.6]
Preconception hypertension	6 (2.2)	5 (2.0)	0.3% [-2.2; 2.7]	2 (3.2)	1 (1.3)	1.9 [-3.2; 7.0]
Family history of diabetes	70 (26.1)	103 (40.4)	<b>-14.3% [-22.3; -6.3]</b>	20 (32.3)	34 (45.3)	-13.1 [-29.3; 3.1]
Employment	103 (38.6)	90 (35.4)	3.1% [-5.1; 11.4]	19 (30.6)	26 (34.7)	-4.0 [-19.8; 11.7]
Smoking before pregnancy	20 (7.5)	15 (5.9)	1.6% [-2.7; 5.9]	3 (4.8)	3 (4.0)	0.8 [-6.1; 7.8]
Parity	2.30 ± 1.22	2.34 ± 1.18	<b>-0.04 [-0.25; 0.17]</b>	2.44 ± 1.22	2.47 ± 1.21	<b>-0.03 [-0.44; 0.38]</b>
<i>Previous pregnancy(ies)</i>						
History of gestational diabetes mellitus						
First child*	85 (31.7)	64 (25.1)		16 (25.8)	15 (20.0)	
No	157 (85.8)	132 (69.1)		42 (91.3)	37 (61.7)	
Yes	26 (14.2)	59 (30.9)	<b>-16.7 [-25.0; -8.4]</b>	4 (8.7)	23 (38.3)	<b>-29.6 [-44.4; -14.9]</b>
History of macrosomia						
First child*	85 (31.7)	64 (25.1)		16 (25.8)	15 (20.0)	
No	174 (95.1)	171 (89.5)		45 (97.8)	55 (91.7)	
Yes	9 (4.9)	20 (10.5)	-5.6 [-10.9; -0.2]	1 (2.2)	5 (8.3)	-6.2 [-14.3; 2.0]
History of hypertensive disorders						
First child*	58 (21.6)	35 (13.7)		9 (14.5)	9 (12.0)	
No	202 (96.2)	208 (94.5)		52 (98.1)	63 (95.5)	
Yes	8 (3.8)	12 (5.5)	-1.6 [-5.6; 2.3]	1 (1.9)	3 (4.5)	-2.7 [-8.9; 3.6]
History of fetal death						
First child*	58 (21.6)	35 (13.7)		9 (14.5)	9 (12.0)	

No	200 (95.2)	209 (95.0)		49 (92.5)	63 (95.5)	
Yes	10 (4.8)	11 (5.0)	-0.2 [-4.3; 3.8]	4 (7.5)	3 (4.5)	3.0 [-5.7; 11.7]
<i>Ethnicity</i>						
North African	85 (31.8)	94 (37.0)	-5.2 [-13.3; 3.0]	19 (30.6)	31 (41.3)	-10.7 [-26.7; 5.3]
European	66 (24.7)	47 (18.5)	6.2 [-0.8; 13.3]	13 (21.0)	10 (13.3)	7.6 [-5.1; 20.4]
Sub-Saharan African	54 (20.2)	38 (15.0)	5.3 [-1.3; 11.8]	12 (19.4)	14 (18.7)	0.7 [-12.5; 13.9]
Indian/Pakistani/Sri Lankan	42 (15.7)	49 (19.3)	-3.6 [-10.1; 3.0]	13 (21.0)	15 (20.0)	1.0 [-12.6; 14.6]
Caribbean	7 (2.6)	12 (4.7)	-2.1 [-5.3; 1.1]	1 (1.6)	4 (5.3)	-3.7 [-9.7; 2.3]
Other	13 (4.9)	14 (5.5)	-0.6 [-4.5; 3.2]	4 (6.5)	1 (1.3)	5.1 [-1.5; 11.8]

Data are means  $\pm$  standard deviation or n (%); \* calculated based on overall population;  
Diff. [95% CI], difference in % [95% confidence interval]; WG: weeks of gestation

	Fasting plasma glucose 5.1–6.9 mmol/L			Fasting plasma glucose 5.5–6.9 mmol/L		
	No initial care	Initial care	Diff. [95% CI]	No initial care	Initial care	Diff. [95% CI]
	n = 268	n = 255		n = 62	n = 75	
Glycaemic status after 22 WG						
Normal oral glucose tolerance test	134 (50.0)	Unknown		17 (27.4)	Unknown	
Gestational diabetes mellitus	123 (45.9)	Unknown		34 (54.8)	Unknown	
Diabetes in pregnancy	11 (4.1)	Unknown		11 (17.7)	Unknown	
Gestational age when care initiated (WG)	<b>31 ± 4*</b>	<b>19 ± 5</b>	<b>12 [11; 13]</b>	<b>31 ± 4*</b>	<b>11 ± 5</b>	<b>13 [11; 14]</b>
Insulin therapy	56 (20.9)	148 (58.0)	<b>-37.1 [-44.9; -29.4]</b>	18 (29.0)	53 (70.7)	<b>-41.6 [-56.9; -26.3]</b>
Gestational age when insulin initiated (WG)	30.1 ± 3.6	20.4 ± 6.4	<b>9.65 [7.83; 11.47]</b>	30.2 ± 3.6	19.2 ± 6.5	<b>11.03 [7.79; 14.27]</b>
Gestational weight gain (kg)	10.8 ± 6.1	8.6 ± 5.4	<b>2.2 [1.2; 3.2]</b>	8.9 ± 5.4	8.6 ± 6.3	<b>0.3 [-1.8; 2.4]</b>
Year of delivery						
2012	77 (28.7)	26 (10.2)	<b>18.5 [12.0; 25.1]</b>	21 (33.9)	11 (14.7)	<b>19.2 [5.0; 33.4]</b>
2013	66 (24.6)	40 (15.7)	<b>8.9 [2.1; 15.8]</b>	16 (25.8)	10 (13.3)	12.5 [-0.9; 25.8]
2014	48 (17.9)	49 (19.2)	-1.3 [-8.0; 5.4]	10 (16.1)	17 (22.7)	-6.5 [-19.7; 6.6]
2015	29 (10.8)	78 (30.6)	<b>-19.8 [-26.5; -13.0]</b>	7 (11.3)	17 (22.7)	-11.4 [-23.7; 0.9]
2016	48 (17.9)	62 (24.3)	-6.4 [-13.4; 0.6]	8 (12.9)	20 (26.7)	<b>-13.8 [-26.8; -0.7]</b>
Maternal smoking during pregnancy	9 (3.4)	11 (4.3)	-1.0 [-4.3; 2.3]	2 (3.2)	2 (2.7)	0.6 [-5.2; 6.3]

Table II

Follow-up of women receiving initial care or not for early fasting hyperglycaemia during pregnancy

Data are means ± standard deviation or n (%); \* no initial care for early fasting hyperglycaemia, with care only if diagnosed with gestational diabetes mellitus or diabetes in pregnancy on oral glucose tolerance testing after 22 WG;

Diff. [95% CI], difference in % [95% confidence interval]; WG, weeks of gestation

Table III

Outcomes in women receiving initial care or not for early fasting hyperglycaemia during pregnancy

	Fasting plasma glucose 5.1–6.9 mmol/L					Fasting plasma glucose 5.5–6.9 mmol/L				
	No initial care	Initial care	<i>P</i>	Adjusted OR [95% CI]	Adjusted <i>P</i> *	No initial care	Initial care	<i>P</i>	Adjusted OR [95% CI]	Adjusted <i>P</i> **
	n = 268	n = 255				n = 62	n = 75			
<i>Neonatal events</i>										
Large-for-gestational age	32 (11.9)	32 (12.5)	0.8318	1.338 [0.90; -1.982]	0.1467	10 (16.1)	5 (6.7)	0.0775	<b>0.332 [0.122; 0.898]</b>	<b>0.0299</b>
Shoulder dystocia	4 (1.5)	4 (1.6)	1.0000	0.519 [0.201; 1.341]	0.1758	0	0	–		–
Neonatal hypoglycaemia	2 (0.8)	0 (0.0)	0.2455	0.604 [0.294; 1.239]	0.9320	0	0	–		–
Small-for-gestational age	28 (10.4)	21 (8.2)	0.3854	0.820 [0.524; 1.285]	0.3872	6 (9.7)	6 (8.0)	0.7296	1.155 [0.422; 3.161]	0.7789
<i>Maternal events</i>										
Preeclampsia	7 (2.6)	3 (1.2)	0.3405	<b>0.247 [0.080; 0.759]</b>	<b>0.0146</b>	1 (1.6)	1 (1.3)	1.0000	0.539 [0.050; 5.778]	0.6096
Caesarean section	61 (22.8)	70 (27.5)	0.2160	1.199 [0.901; 1.597]	0.2137	13 (21.0)	20 (26.7)	0.4375	1.625 [0.878; 3.006]	0.1222

Data are means ± standard deviation or n (%); \* for propensity score including fasting plasma glucose level and gestational age at initial screening, age, body mass index (BMI), parity, familial history of diabetes, personal history of gestational diabetes mellitus (GDM) and year of delivery; \*\* for propensity score including gestational age at initial screening, parity, personal history of GDM and year of delivery, with age and BMI forced into the model;

OR, odds ratio; CI, confidence interval