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Research article

Evolution of maternal and neonatal outcomes before and after the adoption of the IADPSG/WHO guidelines in Belgium: A descriptive study of 444,228 pregnancies

Philippe Oriot [a,*], Charlotte Leroy [b], Virginie Van Leeuw [b], Jean Christophe Philips [c], Jean François Vanderijst [d], Aline Vuckovic [e], Elena Costa [f], Christian Debauche [g], Frederic Chantraine [h]

[a] Department of Diabetology, Mouscron Hospital Centre, Avenue de Fécamp 49, 7700, Mouscron, Belgium
[b] Centre d'Épidémiologie Périnatale (CEpiP), Clos Chapelle-aux-Champs 30, bte B1.30.04, 1200 Brussels, Belgium
[c] Diabetes, Nutrition and Metabolic Disorders, Liege University, CHU Sart-Tilman, Avenue de L'Hôpital 1, 4000, Liège, Belgium
[d] Department of General Internal Medicine, Clinique Saint-Pierre, Av. Reine Fabiola 9, 1340 Ottignies-Louvain-la-Neuve, Belgium
[e] Neonatal Intensive Care Unit, Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Av. Jean Joseph Crocq 15, 1020, Brussels, Belgium
[f] Department of Obstetrics and Gynecology, Erasme Hospital, Route de Lennik 808, 1070 Brussels, Belgium
[g] Department of Neonatology, Cliniques Universitaires Saint Luc, UCLouvain, Av. Hippocrate 10, 1200 Brussels, Belgium
[h] Department of Obstetrics and Gynecology, Centre Hospitalier Universitaire de Liège, site CHR Citadelle, Boulevard du 12ème de Ligne, 1, 4000 Liège, Belgium

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ABSTRACT

Objectives: To appraise adverse pregnancy outcomes after the adoption of IADPSG/WHO guidelines in Belgium.
Methods: A retrospective study of the Center for Perinatal Epidemiology registry was conducted. Demographic changes and adverse pregnancy outcomes were compared between a pre- and post-guideline period in women with and without hyperglycemia in pregnancy (HIP). Adjusted odds ratios with a 95% confidence interval (CI) were used to compare maternal and neonatal outcomes controlling for potential confounders (maternal age, body mass index (BMI), hypertension, parity, and multiple births).
Results: The prevalence of HIP increased (6.0%–9.2%). In the overall population regardless of glycemic status, gestational weight gain (12.3 ± 5.7 vs 11.9 ± 5.8; $p < 0.001$), hypertension (0.92; 95% CI, 0.89–0.94; $p < 0.001$), and neonatal intensive care unit/special care nursery (0.89; 95% CI, 0.87–0.91; $p < 0.001$) decreased despite increasing maternal age and pre-pregnancy BMI. Emergency cesarean section rates (1.07; 95% CI, 1.05–1.09; $p < 0.001$) increased, but not in the HIP population (1.02; 95% CI, 0.95–1.10; *ns*). The overall incidence of preterm birth (1.09; 95% CI, 1.06–1.12; $p < 0.001$), stillbirth (1.10; 95% CI, 1.01–1.21; $p < 0.05$), and perinatal mortality (1.10; 95% CI, 1.01–1.19; $p < 0.05$) increased, except in the HIP population (1.03; 95% CI, 0.95–1.11; ns), (1.04; 95% CI, 0.74–1.47; ns) and (1.09; 95% CI, 0.80–1.49; ns), respectively. The overall incidence of small-for-gestational-age remained unchanged (0.99; 95%CI, 0.97–1.01; ns) regardless of glycemic status. In the HIP population, large-for-gestational age (0.90; 95% CI, 0.84–0.95; $p < 0.001$) and macrosomia (0.84; 95% CI, 0.78–0.92; $p < 0.001$) decreased.
Conclusion: After the implementation of IADPSG/WHO guidelines, the prevalence of HIP increased by 53.7% and the incidence of major HIP-related pregnancy complications appears to be lower. However, we cannot conclude that the reduction of LGA-macrosomia is due to a better management of diabetes or due to greater recruitment of women with mild HIP associated with a lower risk of obstetrical complications.

* Corresponding author.
E-mail address: p.oriot@chmouscron.be (P. Oriot).

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1. Introduction

Hyperglycemia in pregnancy (HIP) is associated with frequent perinatal complications that affect mothers and newborns [1]. The optimal screening regimen for HIP remains controversial, with varying recommendations for one- or two-step glucose load test, universal or selective according to HIP risk factors, early and late HIP screening during pregnancy, and conflicting glycemic thresholds among different expert groups. Because of the lack of randomized controlled trials on this issue, there is insufficient evidence to determine which better approach should be the gold standard of care during pregnancy. The Carpenter and Coustan (C&C) criteria to diagnose HIP were mainly used in Belgium, prior to the adoption of the International Association of Diabetes and Pregnancy Study Groups/World Health Organization (IADPSG/WHO) criteria in 2012 (Table 1). At the same period, studies designed to evaluate the effectiveness of IADPSG vs. C&C screening conducted shown that the IADPSG criteria reduced adverse pregnancy outcomes such as rates of gestational hypertension, prematurity, cesarean section, large-for-gestational age (LGA), small-for-gestational age (SGA) and neonatal intensive care admission and implied greater cost effectiveness [2, 3]. Therefore, for the Group of Gynecologists and Obstetricians of the French Language of Belgium (GGOLFB) [4], it had become obvious that screening according to IADPSG/WHO criteria was preferable [5]. In Flanders, the Vlaamse Vereniging voor Obstetrie en Gynaecologie (VVOG) has adjusted IADPSG/WHO recommendations by maintaining a two-step load glucose test [6, 7].

We conducted a large-scale national observational study in a French-speaking region of Belgium using data from the Center for Perinatal Epidemiology (CEpiP) database that includes all deliveries.

Obstetrical data from all maternity units were compulsorily recorded by midwives and obstetricians into a computerized database. CEpiP is an interuniversity organization under the aegis of The Brussels Health Observatory and the Walloon Agency for Quality of Life (AViQ) (https://www.cepip.be).

We collected data from the CEpiP database from the Brussels and Wallonia regions, located in the central and southern parts of Belgium, where C&C and IADPSG/WHO criteria screening had been successfully applied. The Flemish data were not retained for the reasons mentioned above.

The objectives of this study were to:

(1) compare adverse pregnancy outcomes in overall population studied after the adoption of the IADPSG/WHO criteria screening and estimate the new prevalence of HIP in pregnant women.
(2) compare changes in adverse pregnancy outcomes by women's HIP or no HIP status after the adoption of the IADPSG/WHO criteria screening.

2. Research design and methods

2.1. Data on population

Data from 604,964 pregnant women in 50 maternity hospitals were collected from 2009 to 2018 in a computerized CEpIP database.

The data provide information on patient demographics, including nationality of origin (ethnicity is not available in the registry), pregnancy-related maternal risk factors such as HIP, overweight, hypertension, medically assisted procedures, delivery method, and perinatal outcomes.

Although the HIP diagnosis was documented for each pregnant woman, the glycemic values were not recorded in the registry. However, the literature indicates that HIP is represented by gestational diabetes mellitus (GDM) in 98.8%–99.5% of cases and overt diabetes with an estimated prevalence from 0.2% to 1.2% [8, 9, 10, 11]. The prevalence of pre-existing diabetes in Europe was low (0.5%, 95 %CI 0.4–0.7), and the pooled prevalence of pre-existing type 1 and type 2 diabetes were 0.3% (95 %CI 0.2–0.4) and 0.2% (95 %CI 0.0–0.9) respectively [12]. Therefore, we can consider that HIP was mainly represented by GDM.

Data from all women with maternal ages <18 and ≥40 years were excluded, as advanced maternal age (defined as ≥ 40 years) has been associated with an increased risk of maternal and fetal complications, which may induce interpretation bias [13].

2.2. Ethical declaration

Access to the anonymized data has been accepted by the CEpiP, after approval by the Direction de la recherche, de la statistique et de la veille des politiques (Agence pour une Vie de Qualité (AViQ)) and the

Table 1. Methods of screening for hyperglycemia in pregnancy.

Two-step screening (Carpenter and Coustan)	One-step screening (IADPSG/WHO)*
2009 to 2012	2015 to 2018
Before 24th week of gestation	
(early screening)	
no GDM** screening	GDM if FPG*** ≥92–125 mg/dl
	Overt diabetes if FPG ≥126 mg/dl
After 24 - 28th weeks of gestation	
50 g OGTT (non-fasting test)	no preload test
if BG	
≥200 mg/dl: diabetes	
or	
1 h later a value of >130 or 140 mg/dL:	
GDM is suspected then 100-g OGTT is indicated	
100-g Oral glucose tolerance test (fasting test)	75-g Oral glucose tolerance test (fasting test)
GDM if 2 abnormal BG values	GDM if at least 1 abnormal BG value
0' ≥ 95 mg/dl	0' ≥ 92 mg/dl
1h ≥ 180 mg/dl	1h ≥ 180 mg/dl
2h ≥ 155 mg/dl	2h ≥ 153 mg/dl
3h ≥ 140 mg/dl	Diabetes if FPG ≥126 mg/dl or ≥200 mg/dl (after 2h)

*IADPSG/WHO: International Association of the Diabetes and Pregnancy Study Groups/World Health Organization.
** GDM: Gestational diabetes mellitus; ***FPG: Fasting plasma glucose; ****BG: Blood glucose.

Observatorium voor Gezondheid en Welzijn in Brussels. Data on births and stillbirths are anonymous and stored in a secure database at CEpiP. The study participants cannot identify the subjects registered in this database. These data allow for retrospective studies. The patient's consent is not requested in this study because the data are collected in a legal and mandatory manner. Therefore, a favorable decision to perform this study was given on June 19, 2020 by the ethics committee n° OM 174 of the Hospital Center of Mouscron.

2.3. Screening exposure periods

Two screening periods were chosen to compare pregnancy outcomes.

The first was from January 1, 2009 to December 31, 2012, when the C&C criteria were fully implemented, and the second from January 1, 2015 to December 31, 2018, when the IADPSG/WHO criteria were fully utilized (Table 1).

The data period from 2013 to 2014 was excluded from the selection because both screening guidelines could still be used. This period is considered a transition period therefore, these data may be confounded.

2.4. Pregnancy outcomes studied

Studied variables associated with HIP studied were:

- Maternal age, parity, pre-pregnancy body mass index (BMI), gestational weight gain (GWG) during pregnancy was calculated by subtracting the weight at the end of pregnancy from the weight at the beginning of pregnancy and hypertension were collected from CEpiP electronic records (excess weight status before pregnancy was defined as a BMI $\geq$25 kg/m^2, and obesity was defined as a BMI $\geq$30 kg/m^2). Hypertension (defined as a systolic blood pressure $\geq$140 mmHg or a diastolic blood pressure $\geq$90 mmHg), including new-onset high blood pressure during gestation and pre-existing hypertension.

The proportion of pregnant women with cumulative high risk factors for HIP, such as age $\geq$30 years and $\geq$35 years and BMI $\geq$25 kg/m^2, was studied [14]. Other risk factors for HIP, such as a family history and previous GDM or macrosomia, were not investigated because these data were not recorded in the CEpiP database.

- Fetal outcomes of interest associated with HIP studied were admission to a neonatal intensive care unit (NICU) or a special care nursery (SCN), large-for-gestational age (LGA, birthweight >90th percentile), macrosomia (birth weight $\geq$4000 g), small-for-gestational age (SGA, birth weight $\leq$10th percentile) according to the Intergrowth-21 curves [15], preterm birth (birth <37 weeks of gestation), stillbirths (fetal deaths in utero from 22 weeks of gestation onward or 500 g for all births; this rate considers spontaneous deaths or medical terminations of pregnancies) and perinatal deaths (including stillbirths and neonatal mortality in the first week of life).

2.5. Statistical analyses

Continuous variables were reported using the mean with standard deviation (SD), and categorical variables were reported as frequencies (%).

To analyze the characteristics of pregnant women and newborn (maternal age, BMI, GWG, gestational age, newborn birth weight) according to the HIP screening period, a comparison of parametric continuous variables was performed using unpaired Student t test.

The normality and equality of the variances (Levene's test) were verified, categorical variables (proportions of risk factors for HIP, nulliparity, multiple pregnancies, prevalence of HIP and obstetrical outcomes) were compared with the chi-squared test, and changes were analysed by chi-squared tests.

To compare pregnancy outcomes between the 2 screening exposure periods, we used also multiple logistic regression models before and after adjustment for confounding risk factors for HIP available in the CEpiP database including maternal age, BMI, hypertension, parity, and multiple pregnancy. The results were expressed for categorical variables as odds ratios (ORs) and adjusted odds ratios (aORs) with their 95% confidence intervals (CIs). Pregnant women screened according to C&C criteria were used as the reference population. Variables with $p < 0.05$ were statistically significant. All statistical analyses were performed by State V.14.0 software.

3. Results

The final analysis was limited to 444,228 pregnant women: 222,011 in the 2009–2012 period and 222,217 in the 2015–2018 period (see flow chart: Figure 1).

For the first endpoint of the study, all maternal characteristics (regardless of pregnant women's glycemic status) are presented in Table 2, and neonatal outcomes are shown in Table 3.

Over time, the maternal age and proportion of pregnant women $\geq$30 years and $\geq$35 years had increased ($p < 0.001$), as did the pre-pregnancy BMI $\geq$25 kg/m^2 and $\geq$30 kg/m^2 ($p < 0.001$). The proportion of nulliparous women decreased ($p < 0.001$). The common nationalities were European (75%), North African (12%), sub-Saharan African (6%) and other (7%).

The prevalence of HIP was 6.0% in the 2009–2012 period and 9.2% in the 2015–2018 period ($p < 0.001$), showing an increase of 53.7% after the implementation of the new guidelines (Table 3). The average GWG during pregnancy decreased (12.3 $\pm$ 5.7 vs 11.9 $\pm$ 5.8; $p < 0.001$), as did hypertension (aOR 0.92; 95% CI, 0.89–0.94; $p < 0.001$), between the 2 periods.

The rates of scheduled cesarean sections remained stable (aOR 1.01; 95% CI, 0.99–1.03; ns).

In contrast, emergency cesarean section (aOR 1.07; 95% CI, 1.05–1.09; $p < 0.001$) and preterm birth (aOR 1.09; 95% CI, 1.06–1.12; $p < 0.001$) rates slightly increased. The rate of NICU/SCN admissions decreased (aOR 0.89; 95% CI, 0.87–0.91; $p < 0.001$). The SGA, LGA rates and macrosomia remained stable. Stillbirth and perinatal death rates increased (aOR 1.10; 95% CI, 1.01–1.21; $p < 0.05$ and aOR 1.10; 95% CI, 1.01–1.19; $p < 0.05$, respectively).

We showed a decrease in GWG independent of maternal glycemic status, HIP (9.9 $\pm$ 6.3 vs. 9.7 $\pm$ 6.3 kg; $p < 0.01$) and no-HIP (12.4 $\pm$ 5.6 vs. 12.1 $\pm$ 5.7 kg; $p < 0.001$) (Table 3).

In Figure 2, comparison of neonatal outcomes is presented between the HIP and non-HIP groups across study periods. The rate of hypertension decreased regardless of maternal glycemic status, HIP (aOR 0.87; 95% CI, 0.80–0.94; $p < 0.01$) and no-HIP (aOR 0.89; 95% CI, 0.86–0.92; $p < 0.001$).

Emergency cesarean section rates increased in the no-HIP group (aOR 1.07; 95% CI, 1.04–1.09; $p < 0.001$) but not in the HIP group (aOR 1.02: 95% CI, 0.95–1.10; ns).

The rates of scheduled cesarean sections decreased in the HIP group (aOR 0.89; 95% CI, 0.83–0.95; $p < 0.01$); in contrast, no change was observed in the no-HIP group (aOR 1.01; 95% CI, 0.99–1.04; ns).

In the HIP/no-HIP groups, the rates of NICU/SCN admission decreased significantly but were even higher in the HIP group (aOR 0.67; 95% CI, 0.63–0.71; $p < 0.001$) than in the no-HIP group (aOR 0.91; 95% CI, 0.89–0.93; $p < 0.001$).

The rates of LGA decreased significantly in the HIP group (aOR 0.90; 95% CI, 0.84–0.95; $p < 0.001$), as did the rates of macrosomia (aOR 0.84; 95% CI, 0.78–0.92; $p < 0.001$); on the other hand, the rates remained stable in the no-HIP [LGA (aOR 0.99; 95% CI, 0.97–1.01; ns) and macrosomia (aOR 0.99; 95% CI, 0.97–1.02; ns)] groups.

In the HIP/no-HIP groups, the rates of SGA remained similar (aOR 1.03; 95% CI, 0.94–1.13; ns and aOR 0.99; 95% CI, 0.97–1.01; ns).

Finally, in the HIP group, the differences between preterm births (aOR 1.03; 95% CI, 0.95–1.11, ns), stillbirths (aOR 1.04; 95% CI, 0.74–1.47; ns) and perinatal deaths (aOR 1.09; 95% CI, 0.80–1.49; ns) were not significant. In contrast, in the no-HIP group, preterm births (aOR 1.09; 95% CI,

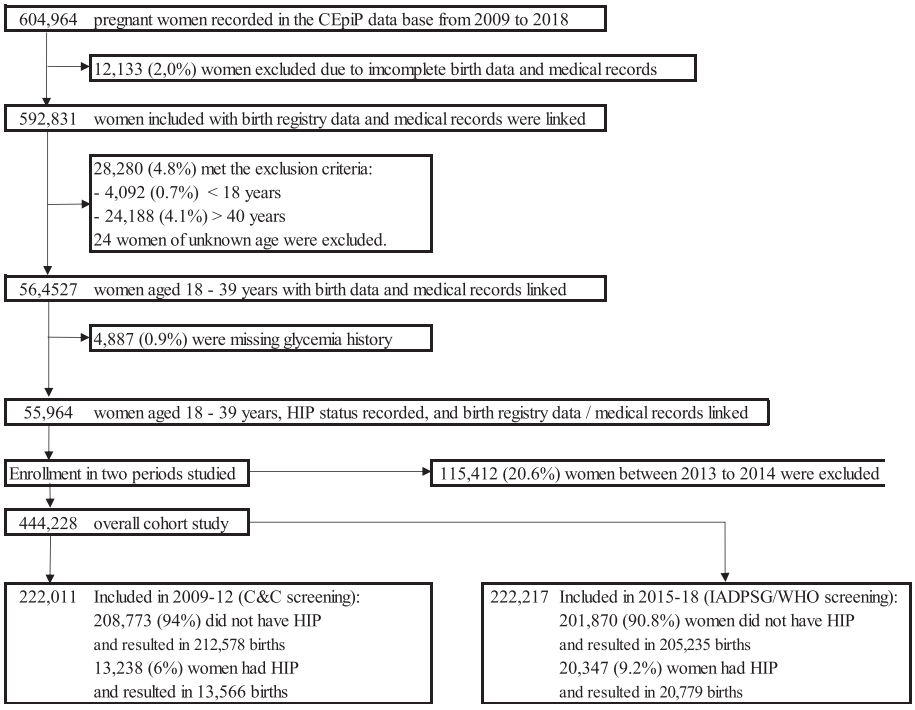

Figure 1. Flowchart of the study population. CEpiP : Centre d'Epidemiologie Perinatale; HIP : Hyperglycemia in pregnancy. C&C : Carpenter & Coustan. IADPSG/ WHO : International Association of Diabetes and Pregnancy Study Groups/ World Health Organization.

1.06–1.11; p < 0.001), stillbirths (aOR 1.11, 95% CI, 1.10–1.22; p < 0.05) and perinatal deaths (aOR 1.10; 95% CI, 1.01–1.20; p < 0.05) increased.

4. Discussion

To improve adverse diabetes-related outcomes in pregnancy, the GGOFLB recommended the adoption of the IADPSG/WHO guidelines rather than the C&C screening criteria based on the conclusions of the Hyperglycemia and Adverse Pregnancy Outcome study (HAPO) [16]. To date, no large-scale Belgian population study has been carried out to confirm the effectiveness of these guidelines. Indeed, international studies show conflicting results on the effects of screening and treatment of HIP by comparing the one-step approach with the two-step approach. Some studies have reported better pregnancy outcomes [3, 17, 18, 19], while others have not [20, 21, 22, 23, 24].

In the present study, we show an increase in the HIP prevalence from 6.0 to 9.2% after the implementation of IADPSG/WHO guidelines. Our findings are in line with previous studies that observed an increase in the prevalence of HIP based on IADPSG/WHO screening [25]. However, the Belgian prevalence appears to be lower than in some previous studies in other countries (18.9–35.5%) [3, 26, 27]. Previous studies in Belgium have shown that the prevalence of HIP before and after application of the IADPSG/WHO criteria increased from 3.3% to 5.7% at the University Hospital of Gasthuisberg (UZ Leuven) [21], from 3.4% to 16.2% at the Erasme Hospital Brussels [22], and from 8.0% to 23.0% at the Mouscron Hospital Centre in Western Hainaut [23]. The reasons for these discrepancies are unclear but may be related to universal screening for HIP and the high or low proportion of diabetes risk factors in the pregnant populations studied (age, excess weight, different ethnicities, or social demographic statuses) [21, 23, 28, 29]. The observed increase in prevalence is also related to the IADPSG/-WHO guidelines that call for universal screening for HIP, which is diagnosed when a single blood glucose value is above the threshold defined by the one-step loading test.

Table 2. Comparison of socio-demographic characteristics and obstetrical conditions between the two study periods.

Periods	2009–2012 (C&C screening)	2015–2018 (IADPSG/WHO screening)	*p*-value
Number of pregnant woman	222011	222217	
Pregnant woman age (years)	27.7 ± 4.9	30.4 ± 4.7	*<0.001*
Pregnant woman age ≥30 years	107582 (48.5)	119172 (53.6)	*<0.001*
Pregnant woman age ≥35 years	35737 (16.1)	41014 (18.5)	*<0.001*
Pre-pregnancy BMI (kg/m^2)	24.2 ± 5.0	24.6 ± 5.1	*<0.001*
Pre-pregnancy BMI ≥25 kg/m^2	65182 (34.1)	77714 (37.7)	*<0.001*
Pre-pregnancy BMI ≥30 kg/m^2	23835 (12.5)	29443 (14.3)	*<0.001*
Proportion ≥30 years and/or BMI ≥25 kg/m^2	125416 (65.6)	146050 (70.8)	*<0.001*
Proportion ≥35 years and/or BMI ≥25 kg/m^2	84068 (44.0)	99923 (48.5)	*<0.001*
Nulliparity (%)	98617 (44.6)	93956 (42.3)	*<0.001*
Multiple pregnancy (%)	4065 (1.8)	3732 (1.7)	*<0.001*

C&C: Carpenter & Coustan. IADPSG/WHO: International Association of Diabetes and Pregnancy Study Groups/World Health Organization.
Reference group: 2009–2012. The results are expressed as means ± SD, or n or n (%).

Table 3. Comparison of overall neonatal outcomes for women and newborns according to HIP screening period.

Periods	2009–2012 (C&C screening)	2015–2018 (IADPSG/WHO screening)	OR* (95% CI)	*p*-value	aOR** (95% CI)	*p*-value
Number of pregnant women	222011	222217				
Prevalence of HIP	13238 (6.0)	20347 (9.2)				*< 0.001*
Gestational weight gain (kg)	12.3 ± 5.7	11.9 ± 5.8				*< 0.001*
- HIP group:	9.9 ± 6.3	9.7 ± 6.3				*< 0.01*
- no-HIP group	12.4 ± 5.6	12.1 ± 5.7				*< 0.001*
Gestational age at delivery (weeks)	38.7 ± 1.9	38.7 ± 2.0				*< 0.001*
Hypertension	9988 (4.5)	9520 (4.3)	0.95 (0.92–0.98)	*< 0.001*	0.92 (0.89–0.94)	*< 0.001*
Scheduled cesarean sections	21060 (9.5)	21805 (9.8)	1.04 (1.02–1.06)	*< 0.001*	1.01 (0.99–1.03)	*ns*
Emergency cesareans sections	22724 (10.3)	23399 (10.5)	1.03 (1.01–1.05)	*< 0.01*	1.07 (1.05–1.09)	*< 0.001*
Number of newborn	226144	226014				
Newborn birth weight (g)	3.245 ± 571	3.252 ± 573				*< 0.001*
Preterm birth <37 weeks	19275 (8.5)	19468 (8.6)	1.01 (0.99–1.03)	*ns*	1.09 (1.06–1.12)	*< 0.001*
NICU† or SCN‡ admissions	24701 (11.2)	22416 (9.9)	0.87 (0.86–0.89)	*<0.001*	0.89 (0.87–0.91)	*<0.001*
SGA$^{\beta}$ (birth weight <10th)	19681 (8.7)	18691 (8.3)	0.94 (0.93–0.96)	*<0.001*	0.99 (0.97–1.01)	*ns*
LGA^{++} (birth weight >90th)	26047 (11.6)	26862 (11.9)	1.04 (1.02–1.05)	*<0.001*	0.99 (0.98–1.01)	*ns*
Macrosomia (birth weight ≥4000 g)	15242 (6.8)	15558 (6.9)	1.02 (0.99–1.05)	*ns*	0.99 (0.96–1.01)	*ns*
Stillbirth	1456 (0.6)	1530 (0.7)	1.05 (0.98–1.13)	*ns*	1.10 (1.01–1.21)	*<0.05*
Perinatal death	1787 (0.8)	1875 (0.8)	1.05 (0.98–1.12)	*ns*	1.10 (1.01–1.19)	*<0.05*

Reference: 2009–2012 period.
The results are expressed as means ± SD, or n or n (%) or *OR: Odds ratio, and **aOR: adjusted Odds Ratio, adjusted for maternal age, pre-pregnancy BMI, hypertension, parity, and multiple pregnancy.
95% CI: confidence interval. C&C: Carpenter & Coustan. IADPSG/WHO: International Association of Diabetes and Pregnancy Study Groups/World Health Organization.
†NICU: neonatal intensive care unit. ‡SCN: special Care Nursery. $^{++}$LGA: larg-for-gestational age, $^{\beta}$SGA: small-for-gestational age.

Some studies have shown that women with "mild HIP" (women who met the IADPSG criteria but would not have been diagnosed with HIP based on the Carpenter and Coustan 2-step diagnostic strategy) had higher rates of adverse outcomes than those without HIP [30]. Therefore, the increase in prevalence could also be related to the fact that more pregnant women were diagnosed with mild HIP. However, the prevalence could also be higher because risk factors for HIP in pregnant women changed significantly over the 9-year period analyzed, as evidenced by advanced pregnancy age, overweight and obesity.

We showed for overall maternal and fetal outcomes a decrease in the rate of GWG, hypertension and NICU/SCN admissions with a significant trend in women with HIP.

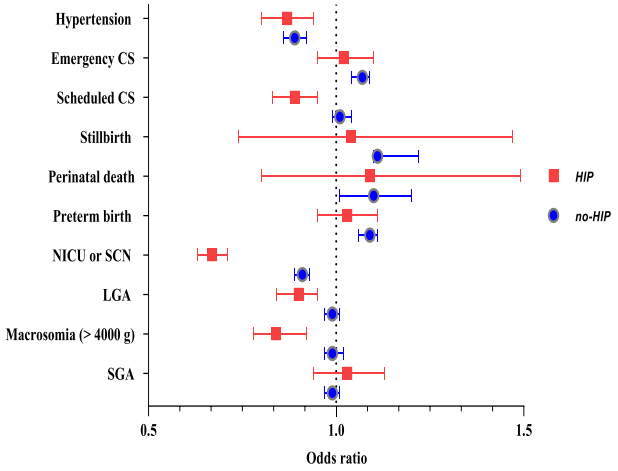

Figure 2. Comparisons of maternal-fetal outcomes in hyperglycemia in pregnancy (HIP) group and no-HIP group in the periods 2009-2012 and 2015-2018. Odds ratios and 95% confidence intervals are shown. Odds ratios were adjusted for maternal age, body mass index, hypertension, parity,and multiple pregnancy.Abbreviations : CS : Cesarean section; LGA: large-for-gestional age; SGA : small-for-gestational age; NICU: neonatal intensive care unit; SCN : special care nursery.

The overall rates of emergency cesarean sections (no scheduled cesarean sections) continued to increase even after implementing the new guidelines. However, this trend was observed in women no-HIP.

Our current data are in contradiction with some literature that showed that the increase in the prevalence of HIP could lead to an increase in the rates of cesarean sections in the HIP population [31, 32].

SGA rates did not change significantly in the total population, including women with HIP. These results do not support the assumption proposed by some authors that IADPSG/WHO guidelines could lead to an increased risk for SGA newborns due to overtreatment in HIP pregnant women [33, 34].

The rates of LGA and macrosomia did not change significantly in the overall population. On the other hand, women with HIP had less hypertension, cesarean sections, NICU admissions, LGA and macrosomia than women without HIP. Rates of SGA, preterm births, stillbirth, and perinatal mortality remained stable in women with HIP. In contrast, a previous Belgian study by Benhalima et al [21] showed no significant differences in the rates of hypertension, LGA, and caesarean delivery between women screened by the IADPSG/WHO criteria and the two-step approach in a population with a lower prevalence of GDM. However, in this study, the early screening of GDM was not considered. However, our study does not allow us to confirm that early screening and early health care management of HIP explain this difference in outcomes.

The limitations and bias are described below, including the following:

- The retrospective nature of the analysis performed across clinical sites.
- Pregnancies were followed over a long period of time (2009–2018), so differences in practice and management of medical care could be present. However, diabetes health care for pregnant HIP women did not change during these periods.
- Some historical risk factors, such as a history of GDM, macrosomia and a history of familial diabetes, could not be included as potential confounders.
- Because we do not have data on blood glucose levels, we cannot conclude that the difference in obstetric outcomes between the two

periods is solely due to glycemic management. The analysis of these data would be interesting to help us to understand whether the observed improvement in neonatal outcomes was due to better detection and care management of women with mild HIP. Therefore, it is not possible to conclude that the improvement in LGA/macrosomia outcomes observed over the last period was simply the result of treating more women with HIP or recruiting more "mild-HIP" individuals with a lower risk of adverse outcomes.

The major strength of this study is the large cohort of pregnant women and their newborns with clinical data from the CEpiP database with the ability to study a wide variety of outcomes and to adjust for several confounding factors. Analysis of this large cohort supports the study of outcomes such as cesarean sections, NICU admission, LGA, SGA, preterm birth, stillbirth and neonatal death. Therefore, the present study provided information on all pregnant women with and without HIP after the introduction of the IADPSG/WHO criteria in this part of Belgium.

5. Conclusion

In the overall population, there was less GWG, hypertension, and NICU/SCN in pregnant women. There was no increase in SGA or LGA. Emergency cesarean sections, preterm births, stillbirths, and perinatal deaths increased slightly. The prevalence of HIP increased by 53.7%, but this was associated in HIP women by a decrease in LGA, macrosomia, and NICU/SCN admission rates, with no increase in SGA and scheduled cesarean section rates. Rates of preterm birth, stillbirth, and perinatal mortality remained stable. The decrease in LGA and macrosomia rates observed in pregnant HIP women may be related to glycemic management but also to a greater recruitment of women with mild diabetes and therefore at low risk of obstetric complications.

Declarations

Author contribution statement

Philippe Oriot: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Charlotte Leroy: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Virginie Van Leeuw, Jean Christophe Philips, Jean François Vanderijst, Aline Vuckovic, Elena Costa, Christian Debauche and Frederic Chantraine: Conceived and designed the experiments; Analyzed and interpreted the data.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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References

[1] E.M. Wendland, M.R. Torloni, M. Falavigna, J. Trujillo, M.A. Dode, M.A. Campos, et al., Gestational diabetes and pregnancy outcomes - a systematic review of the World Health Organization (WHO) and the International Association of Diabetes in pregnancy study groups (IADPSG) diagnostic criteria, BMC Pregnancy Childbirth 12 (1) (2012) 23.

[2] A. Duran, S. Saenz, M.J. Torrejon, E. Bordiú, L. Del Valle, M. Galindo, et al., Introduction of IADPSG criteria for the screening and diagnosis of gestational diabetes mellitus results in improved pregnancy outcomes at a lower cost in a large cohort of pregnant women: the St. Carlos Gestational Diabetes Study, Diabetes Care 37 (9) (2014) 2442–2450.

[3] L.K. Weile, J.G. Kahn, E. Marseille, D.M. Jensen, P. Damm, N. Lohse, Global cost-effectiveness of GDM screening and management: current knowledge and future needs, Best. Pract. Res. Clin. Obstet. Gynaecol. 29 (2) (2015 Feb) 206–224. Epub 2014 Aug 21. PMID: 25225056.

[4] J.F. Vanderijst, F. Debieve, F. Doucet, P. Emonts, S. Haumont, C. Hubinont, et al., Groupement des Gynécologues Obstétriciens; Langue Française de Belgique. Stratégie de dépistage et critères diagnostiques du diabète gestationnel. Propositions du GGOLFB [Screening strategy and diagnostic criteria for gestational diabetes. Proposals of the GGOLFB], Rev. Med. Liege 67 (4) (2012 Apr) 179–185 (French). PMID: 22670444.

[5] B.E. Metzger, S.G. Gabbe, B. Persson, T.A. Buchanan, P.A. Catalano, P. Damm, et al., International association of diabetes and pregnancy study group consensus panel: recommendations on the diagnostic and classification of hyperglycemia in pregnancy, Diabetes Care 33 (3) (2010) 676–682.

[6] K. Benhalima, P. Van Crombrugge, C. Moyson, J. Verhaeghe, S. Vandeginste, H. Verlaenen, et al., A modified two-step screening strategy for gestational diabetes mellitus based on the 2013 WHO criteria by combining the glucose challenge test and clinical risk factors, J. Clin. Med. 7 (10) (2018) 351.

[7] K. Benhalima, C. Minschart, P. Van Crombrugge, P. Calewaert, J. Verhaeghe, S. Vandamme, et al., The 2019 Flemish consensus on screening for overt diabetes in early pregnancy and screening for gestational diabetes mellitus, Acta Clin. Belg. 75 (5) (2020) 340–347.

[8] E. Cosson, E. Vicaut, D. Sandre-Banon, F. Gary, I. Pharisien, J.-J. Portal, et al., Performance of a selective screening strategy for diagnosis of hyperglycaemia in pregnancy as defined by IADPSG/WHO criteria, Diabetes Metab. 46 (4) (2020) 311–318.

[9] Y. Wei, Q. Xu, H. Yang, Y. Yang, L. Wang, H. Chen, et al., Preconception diabetes mellitus and adverse pregnancy outcomes in over 6.4 million women: a population-based cohort study in China, PLoS Med. 16 (10) (2019), e1002926.

[10] H. Razzaghi, J. Marcinkevage, C. Peterson, Prevalence of undiagnosed diabetes among nonpregnant women of reproductive age in the United States. 1999-2010, Prim. Care Diabetes 9 (1) (2015) 71–73.

[11] A.S. Alexopoulos, R. Blair, A. Peters, Management of preexisting diabetes in pregnancy: a Review, JAMA 321 (18) (2019) 1811–1819.

[12] T. Chivese, C.A. Hoegfeldt, M. Werfalli, L. Yuen, H. Sun, S. Karuranga, N. Li, A. Gupta, J. Immanuel, H. Divakar, C.E. Powe, N.S. Levitt, X. Yang, D. Simmons, IDF Diabetes Atlas: the prevalence of pre-existing diabetes in pregnancy - a systematic review and meta-analysis of studies published during 2010-2020, Diabetes Res. Clin. Pract. (2021 Sep 14) 109049. Epub ahead of print. PMID: 34883190.

[13] A. Khalil, A. Syngelaki, N. Maiz, Y. Zinevich, K.H. Nicolaides, Maternal age and adverse pregnancy outcome: a cohort study, Ultrasound Obstet. Gynecol. 42 (6) (2013 Dec) 634–643. PMID: 23630102.

[14] D. Farrar, M. Simmonds, M. Bryant, A.D. Lawlor, F. Dunne, D. Tuffnell, et al., Risk factor screening to identify women requiring oral glucose tolerance testing to diagnose gestational diabetes: a systematic review and meta-analysis and analysis of two pregnancy cohorts, PLoS One 12 (4) (2017), e0175288.

[15] J. Villar, L. Cheikh Ismail, C.G. Victora, E.O. Ohuma, E. Bertino, D.G. Altman, et al., International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project, Lancet 384 (9946) (2014) 857–868.

[16] B.E. Metzger, L.P. Lowe, A.R. Dyer, E.R. Trimble, U. Chaovarindr, D.R. Coustan, et al., Hyperglycemia and adverse pregnancy outcomes, N. Engl. J. Med. 358 (19) (2008) 1991–2002.

[17] E. Clarke, J.T. Cade, S. Brennecke, Early Pregnancy Screening for Women at High-Risk of GDM Results in reduced neonatal morbidity and similar maternal outcomes to routine screening, J. Pregnancy 2020 (2020 Jan 29) 9083264.

[18] E.-T. Wu, F.-J. Nien, C.-H. Kuo, S.-C. Chen, K.-Y. Chen, L.M. Chuang, et al., Diagnosis of more gestational diabetes lead to better pregnancy outcomes: comparing the international association of the diabetes and pregnancy study group

criteria, and the carpenter and coustan criteria, J. Diabetes Investig. 7 (1) (2016) 121–126.
[19] M. Lucovnik, L. Steblovnik, I. Verdenik, T. Premru-Srsen, M. Tomazic, N. Tul, Changes in perinatal outcomes after implementation of IADPSG criteria for screening and diagnosis of gestational diabetes mellitus: a national survey, Int. J. Gynaecol. Obstet. 149 (1) (2020 Apr) 88–92. Epub 2020 Jan 27. PMID: 31925788.
[20] R.K. Feldman, R.S. Tieu, L. Yasumura, Gestational diabetes screening: the international association of the diabetes and pregnancy study groups compared with carpenter-coustan screening, Obstet. Gynecol. 127 (1) (2016) 10–17.
[21] K. Benhalima, M. Hanssens, R. Devlieger, J. Verhaeghe, C. Mathieu, Analysis of pregnancy outcomes using the new IADPSG recommendation compared with the carpenter and coustan criteria in an area with a low prevalence of gestational diabetes, Internet J. Endocrinol. 2013 (2013) 248121.
[22] E. Costa, C. Kirckpartick, C. Gerday, A. De Kempeneer, S. Derisbourg, A. Vercoutere, et al., Change in prevalence of gestational diabetes and obstetric complications when applying IADPSG screening criteria in a Belgian French speaking University Hospital. A retrospective cohort study, BMC Pregnancy Childbirth 19 (1) (2019) 249.
[23] P. Oriot, J. Radikov, U. Gilleman, R. Loumaye, V. Ryckoort, E. Debue, et al., Gestational diabetes mellitus screening according to carpenter-coustan and IADPSG criteria: a 7-year follow-up of prevalence, treatment, and neonatal complications at a Belgian general hospital, Diabetes Metab. 44 (3) (2018) 309–312.
[24] T.A. Hillier, K.L. Pedula, K.K. Ogasawara, K.K. Vesco, C.E.S. Oshiro, S.L. Lubarsky, J. Van Marter, A pragmatic, randomized clinical trial of gestational diabetes screening, N. Engl. J. Med. 384 (10) (2021 Mar 11) 895–904. PMID: 33704936.
[25] E.P. O'Sullivan, G. Avalos, M. O'Reilly, M.C. Dennedy, G. Graffney, F. Dunne, On behalf of the Atlantic DIP collaborators. Atlantic Diabetes in Pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using the new criteria, Diabetologia 54 (7) (2011) 1670–1675.
[26] A. Ellenberg, N. Sarvilinna, M. Gissler, V.M. Ulander, New guidelines for screening, diagnosing, and treating gestational diabetes - evaluation of maternal and neonatal outcomes in Finland from 2006 to 2012, Acta Obstet. Gynecol. Scand. 96 (3) (2017) 372–381.
[27] R.K. Feldman, R.S. Tieu, L. Yasumura, Gestational diabetes screening: the international association of the diabetes and pregnancy study groups compared with carpenter-coustan screening, Obstet. Gynecol. 127 (1) (2016) 10–17.
[28] Ch Leroy, V. Van Leeuw, Y. Englert, Données périnatales en Wallonie – Année 2013, Centre d'Épidémiologie Périnatale, 2015. https://www.cepip.be.
[29] Ch Leroy, V. Van Leeuw, Y. Englert, W.H. Zhang, Santé périnatale en Wallonie – Année 2015, Centre d'Épidémiologie Périnatale, 2017. https://www.cepip.be.
[30] C. Caissutti, A. Khalifeh, G. Saccone, V. Berghella, Are women positive for the One Step but negative for the Two Step screening tests for gestational diabetes at higher risk for adverse outcomes? Acta Obstet. Gynecol. Scand. 97 (2) (2018 Feb) 122–134. Epub 2017 Dec 12. PMID: 29091257.
[31] H. Long, T. Cundy, Establishing consensus in the diagnosis of gestational diabetes following HAPO: where do we stand? Curr. Diabetes Rep. 13 (2013) 43–50.
[32] E.A. Ryan, Diagnosing gestational diabetes, Diabetologia 54 (2011) 480–486.
[33] O. Langer, J. Levy, L. Brustman, A. Anyaegbunam, R. Merkatz, M. Divon, Glycemic control in gestational diabetes mellitus–how tight is tight enough: small for gestational age versus large for gestational age? Am. J. Obstet. Gynecol. 161 (3) (1989 Sep) 646–653. PMID: 2782347.
[34] P.M. Catalano, L. Mele, M.B. Landon, S.M. Ramin, U.M. Reddy, B. Casey, et al., Shriver national institute of child health and human development maternal-fetal medicine units network. Inadequate weight gain in overweight and obese pregnant women: what is the effect on fetal growth? Am. J. Obstet. Gynecol. 211 (2) (2014 Aug) 137.e1–137.e7. Epub 2014 Feb 11. PMID: 24530820; PMCID: PMC4117705.