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PREVALENCE, RISK FACTORS AND PREGNANCY OUTCOMES OF WOMEN WITH GESTATIONAL DIABETES IN CROATIA – A NATIONAL STUDY

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SUMMARY. *Introduction.* Gestational diabetes is a very important obstetrical issue and one of the most frequent metabolic disorders with differing prevalence among various populations. *Aim.* To determine the prevalence of gestational diabetes in Croatia and to detect main risk factors and adverse pregnancy outcomes associated with gestational diabetes. *Methods.* This is a cross sectional study performed using data from medical birth certificates collected in 2014 in Croatia. All pregnant women who gave birth in year 2014 were included in the study, excluding those with known diabetes mellitus type I or type II. *Results.* Among 39.132 deliveries in 2014 incidence of gestational diabetes was 4.67%. Women with gestational diabetes were older, more overweight before pregnancy but gained less weight during pregnancy (all P's < 0.001). Onset of labour among women with gestational diabetes was less often spontaneous and more often induced. Also, women with gestational diabetes had a significantly lower incidence of vaginal delivery and concomitantly a higher incidence of delivery by caesarean section. Women with gestational diabetes gave birth to infants with higher birth weight, but other neonatal complications were not more often present among neonates of women with gestational diabetes compared to neonates of women without gestational diabetes. *Conclusion.* Prevalence of gestational diabetes in Croatia based on medical birth certificates is 4.67% and gestational diabetes in Croatia is associated with important risk factors and adverse perinatal outcomes.

Introduction

Gestational diabetes (GD) is a very important obstetrical issue and one of the most frequent metabolic disorders affecting up to one in seven births (14.2%) worldwide.[1] It is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy that is not clearly overt diabetes.[2] Specifically, according to recent guidelines by World Health Organisation, GD is diagnosed if one or more of the following criteria are met: fasting plasma glucose 5.1–6.9 mmol/l, 1-hour plasma glucose $\geq$ 10.0 mmol/l or 2-hour plasma glucose 8.5–11.0 mmol/l following a 75g oral glucose load, while higher values of hyperglycaemia are considered diagnostic for overt diabetes in pregnancy.[3]

Prevalence of GD differs among various populations according to ethnicity, race, age, screening polices and diagnostic criteria used,[1,4] and is reflective of prevalence of type 2 diabetes in that population. Therefore, an individual from a population with high prevalence of type 2 diabetes is at higher risk of developing GD.[5] It is difficult to compare GD prevalence rates across populations, mainly because of different screening policies and diagnostic criteria used in different countries, as well as particular occurrence of various risk factors associated with GD. An additional cause of wide variations in estimated GD prevalence among populations is the diversity of criteria used for its screening and diagnosis. Prevalence of gestational diabetes is reported to be as high as 9.2% in the USA[6] compared to Europe where it is lower and most often reported in 2–6% of pregnancies.[7] In Croatia, awareness regarding GD has

been continuously rising over recent years, however reporting and accurate epidemiological data on gestational diabetes prevalence and complications are still scarce.

A lot of factors seem to contribute to the development of gestational diabetes among which maternal age, obesity and excessive weight gain during pregnancy are the most important.[8–10] Changes in incidence of these factors in recent years lead to an increasing number of pregnant women being burdened by GD in their pregnancy.[11–13] Also, high parity, history of diabetes mellitus in first degree relatives, short stature, polycystic ovary syndrome (PCOS), past history of GD or poor pregnancy outcomes, pre-eclampsia, and multifetal pregnancy are known risk factors for development of GD, even though their exact impact on raising the risk for developing GD is not known.[14–16] Adverse perinatal outcomes associated with GD reported in literature are excessive fetal growth leading to macrosomia, infants large for gestational age and consequently obstructed labour, increased rate of caesarean deliveries[17] shoulder dystocia and other birth injuries.[9] GD is also related to the risk of neonatal hypoglycaemia, hyperbilirubinemia, hypocalcaemia, polycythaemia and respiratory distress.[15]

The aim of this study was to determine the prevalence of GD in Croatia and to detect main risk factors and adverse pregnancy outcomes associated with GD in our population.

Materials and methods

This cross sectional study was performed using data from medical birth certificates (MBC) collected in Cro-

atia as a part of perinatal statistics data reported to the Croatian Institute of Public Health (CIPH). It is mandatory to complete the medical birth certificate by the doctor attending each birth for mother and her new-born child. The doctor derives data from medical charts, which are assigned to each mother during her hospital stay where everything that occurs during her stay is noted. Completed medical birth certificates are then regularly sent to and collected at CIPH.

Data from medical birth certificates used in this study consists of maternal data (age, height, weight before and at the end of pregnancy), antenatal and obstetric issues (presence of GD, onset of delivery, mode of delivery, adverse delivery outcomes) as well as perinatal outcomes and neonatal data (birth weight, five minute Apgar score, early neonatal complications and congenital malformations).

All pregnant women who gave birth in year 2014 were included, excluding those with known diabetes mellitus type I or type II.

Present national guidelines for diagnosis of GD by the Croatian Society for Gynaecology and Obstetrics are based on the findings of the HAPO study and the International Association of Diabetes and Pregnancy Study Group (IADPSG)[18] and recommend performing a one step 75-g OGTT test at 24–28 weeks of pregnancy in women not previously diagnosed with overt diabetes. GD is diagnosed if plasma glucose values meet or exceed: fasting value 5.1mmol/L, 1-hour value 10.0 mmol/L and 2-hours value 8.5 mmol/L.[19]

All statistical analyses were performed using STATISTICA ver. 12.0. Normality of distribution was tested using Shapiro-Wilks test, while homogeneity of variance was tested using Levene's test. Differences between groups of independent continuous variables were analysed using student t-test for two independent samples (groups) while differences in the occurrence of individual conditions (categorical variables) were compared using the chi^2 test. Statistical significance was defined as P<0.05.

Results

A total of 39.132 deliveries with 39.788 born children between 1st of January 2014 and 31st of December 2014 had been reported through medical birth certificates to CIPH and analysed in this study. Among all women who gave birth, 1.869 had GD as per predefined criteria,[19] revealing an incidence of GD of 4.67%. Women with GD were older and more overweight before pregnancy, but gained less weight during pregnancy compared to the rest of the Croatian pregnant population in the studied period. All of these findings were statistically significant (p < 0.001, student t test) and are presented in *table 1*.

Some differences in labour characteristics and complications as well as early neonatal complications between women with and without GD are presented in *table 2*. In occasional cases some data were missing in medical birth certificates resulting in different numbers listed in tables compared to the total number of participants included in the study.

Table 1. Maternal and new-born characteristics of women with GD in Croatia in 2014

	Without GD* Mean ± SD	With GD* Mean ± SD	p value
Maternal characteristic	*n=37263*	*n=1829*	
Age (years)	29.49 ± 5.33	31.34 ± 5.19	<0.001
BMI (kg/m^2)	23.37 ± 4.11	26.03 ± 5.64	<0.001
Weight gain (kg)	14.17 ± 5.71	12.49 ± 5.81	<0.001
Newborn characteristic	*n=37770*	*n=1869*	
Infant birth weight (g)	3386 ± 564.42	3458 ± 613.52	<0.001

* GD: gestational diabetes

Table 2. Characteristics and outcomes of pregnancies with and without GD

Pregnancy outcome	Without GD* n (%)	With GD* n (%)	p values
Newborn weight	*37770 (100)*	*1869 (100)*	
BW<2500g	2013 (5.33)	96 (5.14)	
BW 2500–4000g	31534 (83.49)	1459 (78.06)	p<0.001
BW>4000g	4223 (11.18)	314 (16.80)	
Newborn 5 min Apgar score	*34629 (100)*	*1729 (100)*	
Apgar score <3	168 (0.49)	15 (0.87)	
Apgar score 4-5-6	183 (0.53)	8 (0.46)	p=0.085
Apgar score ≥7	34278 (98.99)	1706 (98.67)	
Onset of labour	*37737 (100)*	*1868 (100)*	
Spontaneous onset	30368 (80.47)	1256 (67.24)	
Induction of labour	4165 (11.04)	354 (18.95)	p<0.001
Elective C.S.	3204 (8.49)	258 (13.81)	
Labour complications			
PROM	838 (2.22)	52 (2.78)	p=0.109
Genital lacerations	4324 (11.45)	283 (15.14)	p<0.001
Retained placenta	692 (1.83)	30 (1.61)	p=0.472
Postpartum hemorrhage	62 (0.16)	2 (0.11)	p=0.759
Shoulder dystocia	72 (0.19)	2 (0.11)	p=0.587
Episiotomy	25531 (30.64)	11276 (30.71)	p=0.950
Mode of delivery	*37655 (100)*	*1865 (100)*	
Vaginal delivery	29657 (78.76)	1271 (68.15)	
Operative vaginal delivery	455 (1.21)	19 (1.02)	p<0.001
Caesarean section	7543 (20.03)	575 (30.83)	
Neonatal complications			
RDS	237 (0.63)	12 (0.64)	p=0.938
Other respiratory complications	437 (1.16)	13 (0.70)	p=0.661
Hyperbilirubinemia	5565 (14.73)	304 (16.27)	p=0.069
Sepsis	196 (0.52)	11 (0.59)	p=0.684
Intracranial hemorrhage	316 (0.84)	11 (0.59)	p=0.247
Birth trauma	472 (1.25)	45 (2.41)	p<0.001
Congenital malformations	930 (2.46)	59 (3.16)	p=0.060

* BW – birth weight, GD – Gestational diabetes, PROM – Premature rupture of membranes

Statistically significant difference between women with and without GD was present in pregnancy outcomes (all p's <0.001). Onset of labour among women with GD was less often spontaneous and more often induced. Also, women with GD had a significantly lower incidence of vaginal delivery and concomitantly a higher incidence of delivery by caesarean section, while rates of operative vaginal deliveries and episiotomy were similar. Concerning labour complications, no difference was found between women with or without GD in prevalence of premature rupture of membranes, retained placenta, postpartum haemorrhage, and shoulder dystocia while statistically significant difference was found concerning prevalence of vaginal and perineal lacerations.

Women with GD gave birth to infants with higher birth weight and more often to infants who weighed above 4000g. Apgar scores after 5 minutes of infants of women with GD were more often critically low (0,1,2 or 3) but the difference was not statistically significant. Neonatal complications including RDS, other respiratory complications, hyperbilirubinemia, sepsis, intracranial haemorrhage and congenital malformations were not more often present among neonates of women with GD (all P's >0.05) compared to neonates of women without GD. The only exception was neonatal birth trauma, which was more often present among women with GD compared to those without. Birth trauma refers to intracranial haemorrhage and injuries to central or peripheral nervous system, scalp or skeleton.

Discussion

According to medical birth certificates, prevalence of GD in Croatia is 4.67% which is consistent with GD prevalence in other European countries reported by Buckley et al.[7] Still, since Croatian national guidelines recommend usage of IADPSG criteria for diagnosis of GD with a lower threshold for diagnosis of GD and since recent studies suggest IADPSG criteria result in a diagnosis of GD in about 18% of pregnancies,[20,21] a considerably higher GD prevalence would be presumed. This discrepancy can be interpreted in two ways. Primarily, it can be presumed that a mixture of two diagnostic criteria was used in different Clinics and by different medical doctors during the study period- the current one and the former criteria from 1999 which include a higher glucose thresholds.[22] Secondly, it can be hypothesised that GD was not accurately reported in medical birth certificates and consequently underestimated among women in Croatia. This is also one of the possible limitations of this study. Either way, GD prevalence of 4.67% is a valuable starting point for managing GD in Croatia. It is essential to have accurate national data on GD prevalence since differences in diagnostic criteria and population specificity make it difficult to compare frequencies of GD among various populations.[23] Also, epidemiological data on GD are the main prerequisite for prevention, diagnosis and management of this metabolic disorder.

Concerning associated risk factors for GD, the Croatian population does not differ significantly compared to neighbouring European countries since it has been shown that age and obesity prior to pregnancy play a key role in development of GD.[8–10] Therefore, older and more obese women planning to conceive or those already pregnant should be additionally counselled and educated before pregnancy and early in pregnancy in order to prevent development of GD. A systematic review and meta-analysis by Oteng-Ntim el al. confirms lifestyle interventions for overweight and obese pregnant women are associated with a trend towards a reduced prevalence of gestational diabetes.[24] The fact that women burdened with GD in this study group gained less weight during pregnancy can be interpreted as good perinatal management as appropriate diet, weight control and regular exercise are the first steps in management of GD.

Concerning pregnancy outcome, higher birth weights of infants, especially above 4000g, are expected since in GD maternal hyperglycaemia results in more blood glucose transferred through the placenta into fetal circulation. Consequently, more glucose in the fetus is stored as body fat causing macrosomia and excessive fetal insulin levels generate accelerated fetal growth.[25] Higher rates of fetal macrosomia among women burdened with GD is in concordance with previously published studies.[25,26]

Higher rates of induction of labour among women with GD are expected as clinical guidelines recommend that pregnant women with GD and with estimated fetal weight between 3800 and 4000g or poor glycaemic control should be induced between 38 and 39 weeks, while those with infants estimated above 4000g are offered elective caesarean section.[15] Still, this is only a presumption since no national guidelines on management of GD exist in Croatia. Higher rates of caesarean section can be interpreted by a mixture of these two outcomes, since estimated fetal weight above 4000g among women with GD and unsuccessful labour induction lead performing a caesarean section. A potential limitation of this study is the fact that validation of the acquired data at CIPH is not performed, nor has the accuracy of the medical births certificates been assessed. However, as an educated medical professional (doctor) completes the medical birth certificate we have full reason to assume that the data are representative and correct, with possible errors potentially occurring.

Conclusion

Prevalence of GD in Croatia based on MBC is 4.67%. We believe this result still does not represent the complete picture of GD prevalence in Croatia due to underreporting and/or underdiagnosis. Medical birth certificates are a useful tool in estimating GD prevalence among women in Croatia but further research is needed to determine if and to what extent medical birth certificates are underestimating GD prevalence in Croatia due to low reporting.

GD is a significant public health concern because of its long-term implications for maternal and child health, primarily increased risk of developing diabetes mellitus later in life. This study provides fundamental information about prevalence of GD in Croatia, population based risk factors and adverse pregnancy outcome, which is the first step for appropriate screening, management and treatment of this condition. Further research for proceeding years is needed to evaluate the trend of GD prevalence, which is key for improvement of perinatal care related to gestational diabetes among Croatia population.

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UČESTALOST, RIZIČNI ČIMBENICI I ISHODI TRUDNOĆA KOMPLICIRANIH GESTACIJSKIM DIJABETESOM U HRVATSKOJ – NACIONALNA STUDIJA

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Izvorni znanstveni članak

Ključne riječi: gestacijski dijabetes, prevalencija, trudnoća, rizični čimbenici, epidemiologija, pretilost

SAŽETAK. Gestacijski dijabetes važan je izazov u suvremenom porodništvu i najčešći metabolički poremećaj u trudnoći koji zahvaća jednu od sedam trudnoća diljem svijeta. Prevalencija ove bolesti se značajno razlikuje između promatranih populacija jer ovisi o brojnim čimbenicima poput dobi i prehrambenih navika trudnica, rase te vrsti metoda probira i dijagnostičkih kriterija koji se koriste za dijagnozu same bolesti. Prema suvremenim smjernicama Svjetske zdravstvene organizacije i Hrvatskog društva za ginekologiju i porodništvo dijagnoza gestacijskog dijabetesa postavlja se ako vrijednost glukoze u krvi bilo kad u trudnoći iznosi: natašte 5,1–6,9 mmol/L ili kod testa opterećenja 75g glukozom (OGTT test): natašte 5,1–6,9 mmol/L, nakon 1 sat ≥10.0 mmol/L ili nakon 2 sata 8,5–11,0 mmol/L.

Cilj. Ovim istraživanjem željeli smo utvrditi učestalost gestacijskog dijabetesa u Hrvatskoj, glavne rizične čimbenike i ishode trudnoća povezanih s gestacijskim dijabetesom u Hrvatskoj.

Metode. Provedeno je presječno istraživanje pomoću podataka iz prijava porođaja sakupljenih u 2014. godini u Hrvatskoj. Prijava porođaja je propisano zdravstveno-statističko istraživanje kojeg ispunjava zdravstveno osoblje pri porođaju svakog djeteta, provodi ga Hrvatski zavod za javno zdravstvo te služi za nadzor i praćenje perinatalne skrbi i perinatalnog zdravlja u Republici Hrvatskoj. U istraživanje su bile uključene sve trudnice koje su rodile u 2014. godini u Hrvatskoj, isključivši one koje boluju od šećerne bolesti tipa 1 ili 2. Za statističku analizu korišten je program Statistica ver. 12.0 te je statistički značajnom smatrana vrijednost empirijske razine značajnosti p<0,05.

Rezultati. Od 39132 žene koje su rodile u 2014. godini 1869 je imalo gestacijski dijabetes, što čini prevalenciju gestacijskog dijabetesa 4,67%. Žene s gestacijskim dijabetesom bile su starije naspram žena koje nisu imale gestacijski dijabetes, bile su češće pretile prije trudnoće, ali su dobile manje kilograma tijekom trudnoće (svi p < 0,001). Početak porođaja kod žena s gestacijskim dijabetesom bio je rjeđe spontan i češće induciran. Također, žene s gestacijskim dijabetesom imale su značajno manju incidenciju dovršetka porođaja vaginalnim putem i popratno veću incidenciju dovršetka porođaja carskim rezom naspram žena koje nisu imale gestacijski dijabetes (svi p <0,001). Žene s gestacijskim dijabetesom rađale su djecu veće tjelesne težine, dok druge neonatalne komplikacije nisu bile učestalije kod novorođenčadi žena s gestacijskim dijabetesom u usporedbi s novorođenčadi žena koje nisu imale gestacijski dijabetes.

Zaključak. Prevalencija gestacijskog dijabetesa u Hrvatskoj temeljem prijava poroda je 4,67% te je gestacijski dijabetes u trudnoći povezan s važnim rizičnim čimbenicima i nepoželjnim perinatalnim ishodima. Smatramo da su ovi podatci temelj i prvi korak za primjereni probir, praćenje i liječenje trudnoća kompliciranih gestacijskim dijabetesom. Zbog kratkoročnih i dugoročnih posljedica koje ovo stanje ima na zdravlje djeteta i majke (prvenstveno povećan rizik razvoj dijabetesa kasnije tijekom života), važno je osvjestiti javnozdravstveni značaj gestacijskog dijabetesa te u rješavanje i razgovor oko ovog problema uključiti širu medicinsku javnost.