

Hormonal Contraception in Postpartum Patients with Gestational Diabetes Mellitus

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Gestational Diabetes Mellitus is a severe complication in every pregnancy at risk, influencing the clinical outcome in postpartum evolution and affecting women predisposition to future diabetic pathologies. Our study goal was to determine which type of hormonal or non-hormonal contraception method nondiabetic women with past GDM used in their first 6 months postpartum. Results showed that Progestogen-only pill (40.0%) and Levonorgestrel-releasing intrauterine device (23.1%) were the most used contraceptives. Around 56% of the patients were not satisfied using the Barrier method, whereas 67% of the patients in the less than 25 kg/m² BMI group reported adverse events. Special consideration must be applied in order to support obese patients and those perpetuating noxious habits.

Keywords: Gestational Diabetes Mellitus, contraception, Progestogen-only pill, Levonorgestrel-releasing intrauterine device

Postnatal contraception is vital in patients diagnosed with Gestational Diabetes Mellitus (GDM). GDM is documented in 3% to 7% pregnancies in USA [1]. The potential effects of hormonal contraception on the risk of developing Diabetes Mellitus (DM) in patients with a recent history of GDM remains uncertain but these women have a 35% to 60% chance of progression towards type 2 diabetes mellitus in 10 years time after birth [1]. Until now, there are no fully-detailed studies in medical literature regarding the optimal contraception solution for woman with past GDM. At the same time few reports have been published on health effects of contraception in women with co-existing medical disorders such as hypertension, obesity, cardiovascular disease or DM [1-3]. In the absence of clear recommendations regarding optimal contraception methods nondiabetic patients but with past history of GDM, medical practitioners need to find a solution that is safe, effective and with few adverse effects on blood glucose, weight gain and lipid metabolism. With respect to breastfeeding, studies examined the use of progestin-only methods of contraception, including progestin-only pills, (POP), depot medroxyprogesterone acetate (DMPA), implants, levonorgestrel-releasing intrauterine device (LNG-IUD) and did not report negative effects on newborn growth up until 6 years old. In this situation Progestin-only injectable contraception is safe, efficient and reversible. DMPA-IM (intramuscular) is an injectable progestin-only contraceptive introduced for medical use in 1960 which consists of a crystalline suspension to be administered intramuscularly in standard dosage 150 mg /1.0mL [2]. An alternative method is based on subcutaneous administration of 104mg/65mL DMPA-SC (subcutaneous) [4]. A efficient threshold for contraception is reached at 24 h after the subcutaneous administration, MPA

maintaining constant serum levels for 91 days. Administration at 3 month interval is valid for both DMA: IM and SC. World Health Organization (WHO) established eligibility criteria for inclusion of DMPA-SC in the Contraceptive use [5].

Even though women breastfeeding will not have another pregnancy earlier than 6 weeks postnatal, many of them who will stop breastfeeding sooner will be at risk of repeating a pregnancy [6]. This is why contraception is very important at this stage in postpartum, methods including progestogen and progestogen implants, progestogen-only pill (POP), progestogen rings, LNG-IUD. These contraceptive options do not display negative effects on breastfeeding performance or on the newborn growth [7,8].

There are no studies regarding metabolic effects of LNG-IUD in women with type 2 DM or addressed to IUD use in patients with GDM in a previous pregnancy, except one which investigated the effect of LNG-IUD on glucose metabolism in postpartum women with GDM [9,10]. There are a few reports in literature conducted on nondiabetic patients with recent history of GDM who underwent hormonal contraception including combined oral contraceptives (COC) underlining their effects on Type 2 DM metabolically induced changes [11, 12]: low-dose COC or nonhormonal contraceptives are safe to use on this study population. Furthermore, the risk of developing Type 2 DM in a future pregnancy is also significantly higher [12]. Diverse medical counseling is vital in this situation and must reach various aspects of a healthy life-style like diet, weight loss, physical exercise, planning of future pregnancies and particularly proper contraceptive methods able to assure both efficiency and minimal adverse effects

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on fat and glucose metabolism as well as on weight and blood pressure.

A peculiar situation is that of obese patients with GDM. Obesity has a powerful impact on maternal and fetal mortality and morbidity. These women are predisposed to multiple pregnancy complications and finding a safe and effective contraception method is still a challenging task; non-contraceptive benefits have been evaluated for obese patients as well [13].

There is few data in literature regarding contraception in obese patients and most information is retrospective concerning self-reported oral contraceptive use and unintended pregnancies associated with contraception being underreported [14]. BMI is a reliable indicator of fat, is easy to perform and inexpensive. The BMI is defined as following: underweight 18.5kg/m^2 , normal $18.5\text{--}24.9\text{kg/m}^2$, overweight $25\text{--}29.9\text{kg/m}^2$, obese $30\text{--}39.9\text{kg/m}^2$ [15].

Because an unbalanced metabolism as additional burden for obese women is difficult to control, there is a general discomfort in counseling patients about hormonal contraception options, this way placing many women at greater risk for unplanned higher risk pregnancy.

Experimental part

The main objective of our observational retrospective study was to identify which type of hormonal or non-hormonal contraception method nondiabetic women with past GDM used in their first 6 months postpartum. We hypothesized that women that are diagnosed with GDM may report different postpartum methods of contraception that non-GDM women.

At the same time we aimed to determine contraceptive satisfaction by the patient and the afferent adverse contraception events.

Inclusion criteria gathers women with GDM within the last pregnancy which desired a contraceptive method, with vaginal or caesarean delivery during the period 1.01.2010-31.12.2016 in two Departments of Obstetrics and Gynecology from St. Pantelimon Clinical Emergency Hospital Bucharest and Dunarea de Jos University Galati. Contraception methods used in this study reunites POP, DMPA, Progestin ring, LNG-IUD and barrier methods. Exclusion criteria based on patients with other comorbidities associated to GDM restricted the research group.

After delivery participants returned for two visits: at 6 weeks and at 6 months. We analyzed the data from medical reports and an informed consent prior to insertion of an LNG-IUD was obtained; as the study was retrospective the ethical committee approval was not necessary, but the informed consent initially signed by the patient at hospital admission contains the acceptance to use their personal data.

At 6 weeks we obtained data concerning physical examination, obstetrical and medical variables, information about different methods of contraception available for GDM as well as IUD placement in patients who preferred this method. At 6 months visit we obtained data concerning the satisfaction of the contraceptive method used and details about possible adverse events.

This research is based on a sample group composed of 65 Caucasian women with different statuses in terms of education, age, marital status, BMI and smoking habits. Data were gathered between 2010 and 2016.

For describing the sample, the following characteristics were documented: gravidity, parity, age (measured as 0 for less than 30 years of age and 1 for 30 years of age or above), BMI (in three categories which stand for less than

25 kg/m^2 [code 1], $25\text{ to }30\text{ kg/m}^2$ [code 2] and more than 30 kg/m^2 [code 3]), marital status (coded as 0 for single women and 1 for married women), education (coded as 0 for women without high school and 1 for women with high school) and smoking status postpartum (measured as 1 for nonsmokers, 2 for non-smokers and 3 for current smokers).

On the other hand, the variables of main interest were measured in the following way: contraceptive method by taking into account Progestogen-only pill (code 1), DMPA injections (code 2), Vaginal ring (code 3), LNG-IUD (code 4) and Barrier method (code 5); contraceptive satisfaction after 6 weeks and after 6 months whether they were not satisfied (code 0) or their level of satisfaction was good (code 1); and adverse events after 6 weeks and after 6 months (coded with 0 for no and 1 for yes).

The current analysis is based on descriptive statistics for the sample characteristics and the variables of main interest and on bivariate associations using contingency tables with percentages, aiming to create a profile for contraceptive methods usage and adverse events. Taking into account that our variables are measured at a nominal level, we report the Goodman and Kruskal tau correlation coefficient to evaluate the strength of the relations between each two set of variables. For evaluating statistical significance, we report the Pearson Chi-square with its computed significance probability.

Results and discussions

Our sample (table 1) is composed of Caucasian women with a mean of 2.43 in terms of gravidity and a mean 1.72 pregnancies (parity). Women under 30 years of age were 33.8%, whereas 66.2% are 30 years of age or above. In terms of BMI, approximately half of the sample is obese ($>30\text{ kg/m}^2$), 42.6% is between 25 and 30 kg/m^2 , and 4.9% is under 25 kg/m^2 . Almost three quarters of the sample is represented by married women and one quarter of single women. Six out of ten finished high school, whereas 4 out of ten did not. Also 73.4% are nonsmokers, 3.1% are ex-smokers and 20.3% are current smokers.

The majority of the sample used Progestogen-only pill (40.0%), 16.9% used DMPA injections, 4.6% used vaginal ring, 23.1% used LNG-IUD and Barrier method used 15.4%. Most of respondents expressed a good level of satisfaction with the contraceptive methods used (72.3% after 6 weeks and 69.2% after 6 months), 69.2% after 6 weeks and 67.7% after 6 months had not adverse events.

Of patients who had adverse events, both after 6 weeks and after 6 months, most of them took progesteron-only pill (about 4 out of 10 patients) and DMPA injections (about a quarter). The differences between percentages are small and the variables are not associated (given the Goodman and Kruskal tau correlation coefficient of .016 and the Pearson Chi-square sig. of .280, which is greater than the theoretical level of .001).

Of patients who were not satisfied with the contraceptive method after 6 weeks, 56% used the Barrier method and 17% the vaginal ring (these two cell level associations are statistically significant). None of those who reported a good level of satisfaction used the barrier method. Of those who reported good levels of satisfaction, 45% used the progestogen-only pill and 30% the LNG-IUD. After 6 months the reported situation is pretty similar with that at 6 weeks. The variables are positively associated in both cases, in the sense that the lower values of the first variable are linked to the lower values of the second variable and the higher values of the first one to the higher values of the second one. According to the Pearson Chi-square

significance probability, the association is statistically significant.

With respect to age, the pattern is the following: the younger group were more likely to use Progestogen-only pill (50% of the younger group) and DMPA injections (25% of the younger group). Of the older group, 35% used Progestogen-only pill, 28% LNG-IUD and 21% Barrier methods. The relation between age and contraceptive methods is not statistically significant though, but there are small differences between categories of age with respect to contraceptive methods (see table 2).

The last but not least relation analyzed is between BMI and adverse events (table 3). At both 6 weeks and 6 months, 67% of the patients in the less than 25 kg/m² had adverse events, whereas the majority over this threshold did not have adverse events. The relation is not statistically significant though.

Contraception counseling is a key factor in good pregnancy outcomes especially in patients with comorbidities who self-reported previous contraception use, since in this situation the American College of Obstetricians and Gynecologists (ACOG) and the US Centers for Disease Control and Prevention (CDC) recommend health optimization prior to conception

[16,17]. Whether it is in antenatal or in postpartum period, medical advice and supervision are imperiously necessary in patient management in order to prevent afferent complications. Women with recent GDM represent a target group to rely on postnatal care regarding contraception, knowing there is a potentially increased risk of Type 2 diabetes with repeat pregnancies [18].

A complete medical planning for these patients must assess patent steps accounting for a balanced metabolism: breastfeeding, diet, weight management and exercise but also planning of future pregnancies and methods of contraception [18].

Although a recent study states that women with pregestational diabetes were less likely to report using postpartum contraception than those without diabetes (OR: 0.4, 95% CI: 0.1–0.9), the same study concluded that women who reported receiving contraceptive counseling were more likely to report using postpartum contraception (OR: 1.6, 95% CI: 1.2–2.0) compared to those who did not [18]. Consequently, promoting postnatal contraception has a documented impact in favourable patient compliance which may lead to a reduced risk of developing further complications.

Contraception industry in its tremendous variety of

	%	Mean	S.D.	Min.	Max
Gravidity		2.43	1.38	1	10
(N)	65				
Parity		1.72	0.69	1	4
(N)	65				
Age					
0. < 30 years	33.8				
1. ≥ 30 years	66.2				
(N)	65				
BMI					
1. <25 kg/m ²	4.9				
2. 25 to 30 kg/m ²	42.6				
3. >30 kg/m ²	52.5				
(N)	61				
Marital status					
0. Single	26.2				
1. Married	73.8				
(N)	65				
Contraceptive method					
1. Progestogen-only pill	40.0				
2. DMPA injections	16.9				
3. Vaginal ring	4.6				
4. LNG IUD	23.1				
5. Barrier method	15.4				
(N)	65				

Table 1
DESCRIPTIVE STATISTICS

	%	Mean	S.D.	Min.	Max.
Contraceptive satisfaction (6 weeks)					
0. Not satisfied	27.7				
1. Good	72.3				
(N)	65				
Contraceptive satisfaction (6 months)					
0. Not satisfied	30.8				
1. Good	69.2				
(N)	65				
Adverse events (6 weeks)					
0. No	69.2				
1. Yes	30.8				
(N)	65				
Adverse events (6 weeks)					
0. No	67.7				
1. Yes	32.3				
(N)	65				
Education					
0. Without high school	38.9				
1. With high school	61.1				
(N)	54				
Smoking status postpartum					
1. Nonsmoker	73.4				
2. Ex-smoker	3.1				
3. Current smoker	20.3				
(N)	64				

Table 1
(continued)

options might induce an elusive patient behaviour in the absence of authorised medical advice. A report based on the evaluation of 170 primiparous women diagnosed with GDM but who had no history of other types of DM concluded that from various hormonal and non-hormonal methods of preventing a pregnancy female sterilization was more frequently adopted (OR=4.99, 95% CI: 1.13–22.17) [18].

However, our results show that the Progesteron-only pill is the most popular contraceptive method independently of adverse events and age in this study group. Hormonal contraception is known to have various effects on serum glucose and Insuline tolerance but with overall small and of uncertain clinical significance [120] as the first study to evaluate metabolic effects of LNG device in patients with recent GDM showed: the LNG-IUD does not impact postpartum glucose tolerance in women with GDM [9]. The safety of POP used during breastfeeding was found not to influence the entire process' performance, including initiation, maintenance, duration of lactation and need for supplementation [21].

Limitations on Progesteron-only pills reside in the medical literature which states that there is a possibility of weight gain related to deleterious effects of DMPA on

glucose regulation in obese women and an unpredictable bleeding pattern of most POP in some patients [22]; thus, physicians must be concerned on establishing therapeutical plans designed to meet each patient's individual requirements.

For patients who experienced GDM using POP, DMPA or LNG-IUD as contraception method during breastfeeding led to no adverse effects on infant growth, health or development through 6 years of age [21].

Patients who are not satisfied with the contraceptive method used are more likely to use the Barrier method. Also, for diabetic women this type of contraception has an unacceptable failure rate [23], submitting them at risk of pregnancy through poor compliance [24].

In our report women who appraised adverse events using contraception were more likely to have a BMI under 25 kg/m² but no statistical evidence was added to this statement. Analyses investigating the extent to which obesity is associated with failure of hormonal contraceptives remain inconclusive. However, a high BMI implies numerous obstetrical complications with severe impact both on delivery method and immediate postpartum health-care, for example high CS rates are

Table 2
CONTRACEPTIVE METHODS BY ADVERSE REACTION: CONTINGENCY TABLES (PERCENTAGES REPORTED; CELL LEVEL POSITIVE ASSOCIATIONS IN BOLD AND NEGATIVE CELL LEVEL ASSOCIATIONS UNDERLINED)

	Progestogen-only pill	DMPA injections	Vaginal ring	LNg IUD	Barrier method	Total
Adverse events (6 weeks)						
0. No	40%	13%	2%	29%	16%	100%
1. Yes	40%	25%	10%	10%	15%	100%
Total	40%	17%	5%	23%	15%	100%
Goodman and Kruskal tau correlation coefficient: .016, Pearson Chi-square: 5.072; Sig.: .280.						
Adverse events (6 weeks)						
0. No	41%	11%	2%	30%	16%	100%
1. Yes	38%	29%	10%	10%	14%	100%
Total	40%	17%	5%	23%	15%	100%
Goodman and Kruskal tau correlation coefficient: .023, Pearson Chi-square: 6.629; Sig.: .157.						
Contraceptive satisfaction (6 weeks)						
0. Not satisfied	22%	0%	17%	6%	56%	100%
1. Good	45%	23%	0%	30%	<u>0%</u>	100%
Total	40%	17%	5%	23%	15%	100%
Goodman and Kruskal tau correlation coefficient: .140, Pearson Chi-square: 43.436; Sig.: .000.						
Contraceptive satisfaction (6 months)						
0. Not satisfied	25%	5%	15%	5%	50%	100%
1. Good	47%	22%	0%	31%	<u>0%</u>	100%
Total	40%	17%	5%	23%	15%	100%
Goodman and Kruskal tau correlation coefficient: .121, Pearson Chi-square: 37.393; Sig.: .000.						
Age						
0. < 30 years	50%	27%	5%	14%	5%	100%
1. ≥30 years	35%	12%	5%	28%	21%	100%
Total	40%	17%	5%	23%	15%	100%
Goodman and Kruskal tau correlation coefficient: .029, Pearson Chi-square: 6.761; Sig.: .149.						

indeed consequence of a prophylactic obstetrical policy [25]. A recent study, underlined that from 169 interviewed patients 42.01% (71/169) were smokers and alcohol consumption was registered in 30.17%(51/169) cases [26]. These noxious habits in pregnant women might require increasing medical awareness about high susceptibility of contraceptive reluctance and future medical monitoring drop-out. Obesity, high cigarette consumption and gestational diabetes are responsible for sudden intrauterine death, so contraception in postpartum period could be challenging in these patients [27].

Study limitations may concern the absence of further serum variables such as glycosylated hemoglobin values, fasting lipid and insulin levels, glucose tolerance on 2-h (OGTT testing), and so on. Taking into account that

exhaustive laboratory screening might objectify a real barrier that is critical in reducing unintended pregnancy, minimal investigations seem to be the cost-efficient path to follow for patients with no comorbidities who wish to pursue contraception planning.

Conclusions

Since gestational diabetes mellitus makes patients prone to develop other types of DM with future pregnancies, active medical counseling is required in immediate postpartum. Synchronous multiple approaches make the best manageable attitude towards a balanced and controlled metabolism. Although breastfeeding enfold both physiological and emotional connections between mother-child dyad, hormonal contraception does not interfere as

Table 3
CONTRACEPTION METHODS by ADVERSE REACTION: CONTINGENCY TABLES (PERCENTAGES REPORTED)

	BMI			Total
	<25 kg/m ²	25 to 30 kg/m ²	>30 kg/m ²	
Adverse events (6 weeks)				
0. No	33%	81%	63%	69%
1. Yes	67%	19%	38%	31%
Total	100%	100%	100%	100%
Goodman and Kruskal tau correlation coefficient: .067, Pearson Chi-square: 4.089; Sig.: .129.				
Adverse events (6 weeks)				
0. No	33%	77%	63%	67%
1. Yes	67%	23%	38%	33%
Total	100%	100%	100%	100%
Goodman and Kruskal tau correlation coefficient: .049, Pearson Chi-square: 2.998; Sig.: .223.				

an issue in the patients' clinical outcome. In our study group Progesterone-only pill was the most used type of contraception, associating at the same time good levels of satisfaction, as well as the LNG-IUD.

Concerning the adverse events of different contraception approaches, most of the documented information aimed towards patients in the less than 25 kg/m² group. There could not be established a statistically significant relation between age and specific contraception option but barrier methods were an alternative for a small number of patients in the older group.

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