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ORIGINAL

Pregnancy outcomes of gestational diabetes mellitus according to pre-gestational BMI in a retrospective multi-institutional study in Japan

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Abstract. The aim of this study was to determine the effects of pre-gestational body mass index on pregnancy outcomes of women with gestational diabetes in Japan. A multi-institutional retrospective study was performed. We examined pregnant women who met the former criteria for gestational diabetes in Japan, receiving dietary intervention with self-monitoring of blood glucose with or without insulin therapy. Women with gestational diabetes were divided into three groups according to pre-gestational body mass index: body mass index <25 (control group), 25 ≤ body mass index <30 (overweight group), body mass index ≥30 (obese group). Data from a total of 1,758 eligible women were collected from 40 institutions. Participants included 960 controls, 426 overweight women, and 372 obese women with gestational diabetes. Gestational weight gain was highest in the control and lowest in the obese group. The prevalences of chronic hypertension and pregnancy induced hypertension were higher in the overweight and obese groups than in the control group. Multiple logistic regression analysis revealed pre-gestational body mass index, gestational weight gain, chronic hypertension, and nulliparity to be associated with the onset of pregnancy induced hypertension, while the 75-g OGTT results were unrelated to pregnancy induced hypertension. The prevalence of large-for-gestational age was lower in infants born to obese women than in those born to overweight or control women. The present results suggest that medical interventions for obese women with gestational diabetes may contribute to reducing the prevalence of large-for-gestational age but would not achieve marked reductions in maternal complications.

Key words: Gestational diabetes mellitus, Pregnancy outcome, Body mass index

GESTATIONAL DIABETES MELLITUS (GDM) is defined as glucose intolerance that first occurs or is first identified during pregnancy [1]. GDM has been recognized as being associated with not only maternal complications including pregnancy induced hypertension (PIH) and cesarean section, but also neonatal complications such as macrosomia, hypoglycemia, jaundice, and respiratory distress syndrome (RDS) [2-3]. Most notably, large-for-gestational age (LGA) infants are well known to be a significant obstetrical compli-

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cation of GDM [4-5] and mean glucose concentration is strongly associated with neonatal birth weight in women with GDM [6].

The Hyperglycemia Adverse Pregnancy Outcome (HAPO) study showed the maternal hyperglycemia level to definitely correlate with adverse maternal, fetal, and/or neonatal outcomes [2]. On the other hand, sub-analyses of HAPO study showed that the combination of GDM and obesity showed substantially higher odds ratio compared with those for either GDM or obesity alone, suggesting that both maternal overweight and obesity are independently associated with adverse pregnancy outcomes [7]. Also, Blanc *et al.* reported that prepregnancy overweight and obesity account for a high proportion of LGA, even in the absence of GDM [8].

We hypothesized that overweight or obese GDM women should be at high risk of adverse pregnancy outcomes, however, appropriate pregnancy management of these women is anticipated to decrease somewhat the degrees of maternal and/or neonatal morbidity. Therefore, a multi-institutional retrospective review was performed by the Japan Diabetes and Pregnancy Study (JDPS) Group to assess whether the maternal pre-gestational body mass index (BMI) affects pregnancy outcomes of Japanese women with GDM.

Materials and Methods

Study design

The present retrospective study was conducted using data from 40 general hospitals in Japan for the period from 2003 through 2009. The protocol was approved by the ethics committee at each of the 40 collaborating centers. All women with a singleton pregnancy and no prior diagnosis of diabetes mellitus were included. Women with multi-fetal gestations, pre-gestational diabetes, previously treated for gestational diabetes or active chronic systemic disease other than chronic hypertension, and those with the second of two pregnancies in the same year were excluded. Each woman underwent a universal two-step screening process for GDM: a casual glucose test or 50-g glucose challenge test (GCT) between 24 and 30 weeks of gestation. Then, women who had random plasma glucose measurements ≥100 mg/dL or plasma glucose of GCT ≥140 mg/dL were scheduled for a diagnostic, 75 g, 2-h oral glucose tolerance test (OGTT) after an overnight fast. JSOG criteria were applied (fasting, 100 mg/dL: 1 h, 180 mg/dL; 2 h, 150 mg/dL) [9]. GDM was defined as present when at least two plasma glucose measurements were the same as or higher than the cut-off points. Overweight or obese women are recommended to undergo a 75-g OGTT at any time in gestation. Underweight, overweight, and obese were defined as a BMI of less than 18.5 kg/m^2, between 25 and 29 kg/m^2, and 30 kg/m^2 or more, respectively. Underweight women were categorized as normal weight for the purposes of these analyses.

Data collected included maternal age, parity, pre-pregnancy BMI, chronic hypertension, PIH including pre-eclampsia, gestational age at delivery, delivery characteristics including spontaneous or induced delivery, vaginal delivery or cesarean section, and newborn characteristics such as birth weight, sex, Apgar score, perinatal mortality and major congenital malformations. Pre-gestational weight was self-reported at the first prenatal visit. Gestational age was defined as the number of weeks since the last menstrual period or the ultrasound assessment of crown-rump length if discordancy was recognized. Chronic hypertension was defined as hypertension treated with medication before pregnancy or arterial blood pressure ≥140/90 mm Hg before 20 weeks of pregnancy. Macrosomia was defined as a birth weight at or above 4,000 g. LGA was defined as sex- and parity-specific birth weight for gestational age being above the 90th percentile of Japanese fetal growth curves [10]. Also, small-for-gestational age (SGA) was defined as sex- and parity -specific birth weight for gestational age being below the 10th percentile of Japanese fetal growth curves [10]. Major congenital malformations were defined as those causing significant functional impairment, requiring surgery or being life-threatening.

In all institutes, women with GDM received dietary management with self-monitoring of blood glucose (SMBG) and, if needed, insulin therapy. Dietary therapy was based on a woman's pre-pregnancy BMI, and dietary intake and gestational weight gain guidance were provided as necessary. The JSOG recommends that 250 kcal is added as an additional energy intake during pregnancy to 30 kcal/kg for ideal body weight at non-pregnancy in non-obese subjects [11]. Ideal body weight is defined by the data of the Japan Ministry of Health, Labour, and Welfare's [12]. In the case of obese GDM women, an additional calorie intake during pregnancy was not prescribed. Also, these women received guidance on how to determine SMBG levels 4 to 6 times a day. In this study, if targeted glucose lev-

els (i.e., preprandial glucose levels of less than 100 mg/dL and levels 2 hours postprandially that were less than 120 mg/dL) were not achieved, insulin therapy was initiated.

Study outcomes

The composite study outcome included perinatal mortality (stillbirth or neonatal death) and complications associated with maternal hyperglycemia: congenital malformation, LGA, macrosomia, hypoglycemia, hyperbilirubinemia, shoulder dystocia, RDS, and admission to the neonatal intensive care unit.

Neonatal blood for glucose measurement was collected 1 or 2 hours after birth and before feeding; hypoglycemia was defined as a glucose value of less than 35 mg/dL. Hyperbilirubinemia was defined as a requirement for phototherapy.

Maternal outcomes included weight gain from the time of enrollment until delivery, PIH including gestational hypertension and preeclampsia, cesarean delivery, and labor induction. Gestational hypertension was defined as a systolic pressure of 140 mm Hg or more and/or a diastolic pressure of 90 mm Hg or more on two occasions at least 4 hours apart. Preeclampsia was defined as blood pressure elevation (according to the definition of gestational hypertension) together with proteinuria (300 mg of protein or more in a 24-h urine collection or a result of 2+ or greater on a dipstick test when a 24-h collection was not available). Shoulder dystocia was defined clinically, and the providers were required to document the specific maneuvers used to release the fetal shoulders.

HbA1c values were defined by the National Glycohemoglobin Standardization Program (NGSP) standards [13].

Statistical analyses

Baseline characteristics and laboratory measurements are presented as means ± SD, as either medians or percentages. Univariate tests for differences in values between any two groups were performed employing the chi-square test. Also, Tukey-Kramer test was used to compare continuous variables. Multiple logistic regression analysis (MLRA) was performed to explore variables contributing to differentiation of any two groups. All reported P values are two-tailed and $P < 0.05$ was taken to indicate a statistically significant difference. All statistical analyses were performed using general-purpose statistical software, StatFlex version 6.0 (Artech Inc., Osaka, Japan).

Results

From 2003 through 2009, we retrospectively collected 1,806 GDM subjects from 40 institutions in Japan. One thousand, seven hundred and fifty eight women with GDM were studied. These women were divided into three groups based on their BMI: the normal group (< 25, n = 960), the overweight group (25-30, n = 426), and the obese group (≥ 30, n = 372).

The 1,758 women received diet therapy and SMBG with or without insulin therapy after the diagnosis of GDM. The baseline characteristics of women with GDM in this retrospective study are shown in Table 1. Maternal age in the obese group was younger than that in the normal and overweight groups. Gestational weight gain was highest in the control, followed by the overweight group and lowest in the obese group.

Table 1 Baseline characteristics

	Body mass index		
	< 25 (n = 960)	25-30 (n = 426)	≥ 30 (n = 372)
Age (yrs)	33.5±4.9	33.9±5.0	32.9±4.9*†
Nulliparity – n (%)	471 (49.1)	190 (44.6)	179 (48.2)
Pre-gestational body mass index (kg/m^2)	21.1±2.2	27.3±1.4*	34.4±3.7*†
Gestational weight gain (kg)	7.9±4.3	5.6±5.4*	2.8±6.3*†
Gestational age at diagnosis (wks)	24.3±8.0	22.5±8.3*	20.6±8.8*†
Glucose levels on 75-g OGTT (mg/dL)			
Fasting	91.5±18.7	98.3±21.4*	104.5±21.9*†
1-h	200.8±32.1	209.9±37.4*	212.6±33.7*
2-h	177.7±34.2	182.2±41.1	176.0±35.9†

Data are mean ± SD or n. *, $P < 0.05$ *vs.* BMI <25; †, $P < 0.05$ *vs.* BMI 25-30

Table 2 Maternal complications

	Body mass index		
	< 25 (n = 960)	25-30 (n = 426)	≥ 30 (n = 372)
Chronic hypertension – n (%)	15 (1.6)	34 (8.0)*	43 (11.6)*
Pregnancy induced hypertension - n (%)	14 (1.5)	46 (10.8)*	55 (14.8)*
Cesarean section – n (%)	269 (28.1)	167 (39.2)*	172 (46.2)*†
Primary cesarean section – n (%)	95 (9.9)	93 (21.8)*	109 (29.3)*†
Induction of labor – n (%)	210 (21.9)	103 (24.2)	113 (30.4)*†

*, $P < 0.05$ *vs.* BMI <25; †, $P < 0.05$ *vs.* BMI 25-30

Table 3 Risk factors for pregnancy induced hypertension

Variables	β	SE (β)	z	*P*	Odds Ratio	95% CI
Pre-gestational BMI	0.11	0.02	6.39	< 0.001	1.12	1.08-1.15
Gestational weight gain	0.08	0.02	4.21	< 0.001	1.08	1.04-1.12
75-g OGTT 1-h	0.93	0.60	1.56	0.118		
Chronic hypertension	1.65	0.29	5.76	< 0.001	5.20	3.00-9.10
Nulliparity	0.72	0.21	3.39	< 0.001	2.06	1.36-3.12
Age at delivery	0.03	0.02	1.4	0.146	1.03	0.90-1.07

AIC = 742.22176, AUC = 0.76648

Table 4 Risk factors for primary cesarean section

Variables	β	SE (β)	z	*P*	Odds Ratio	95% CI
Age at delivery	0.06	0.01	5.63	<0.001	1.06	1.04-1.09
Pre-gestational BMI	0.06	0.01	6.36	< 0.001	1.06	1.04-1.09
Gestational weight gain	0.03	0.20	4.20	0.001	1.03	1.01-1.06
PIH	0.82	0.20	4.20	<0.001	2.28	1.56-3.34
Chronic hypertension	0.51	0.23	2.19	0.029	1.67	1.06-2.65

AIC = 2155.56897, AUC = 0.65143

Gestational age at diagnosis of GDM was slightly earlier in the obese group than in the overweight group and was latest in the control group. Fasting plasma glucose levels on 75-g OGTT were lowest in the control, somewhat higher in the overweight and highest in the obese group. Glucose levels 1 hour after 75-g OGTT were higher in the overweight and obese groups than in the control group. Glucose levels 2 hours after 75-g OGTT were higher in the obese group than in the control and overweight groups.

Maternal complications are shown in Table 2. The prevalences of chronic hypertension were higher in the overweight and obese groups than in the control group. Similarly, the prevalences of PIH were significantly higher in the overweight and obese groups than in the control group. The primary cesarean section rate was highest in the obese women. Induction of labor was very common in the obese group. Table 3 shows the risk factors for PIH identified by MLRA. Pre-gestational BMI, gestational weight gain, chronic hypertension, and nulliparity were found to be associated with the onset of PIH. Also, Pre-gestational BMI, gestational weight gain, PIH, and chronic hypertension were found to be associated with primary cesarean section (Table 4).

Neonatal complications in the present study are shown in Table 5. Gestational ages at delivery and birth weights did not differ significantly among the three groups. The prevalence of SGA did not differ among the three groups. The prevalence of LGA was significantly lower in infants born to obese women than to overweight or normal weight women. Other neonatal

Table 5 Neonatal complications

	Body mass index		
	< 25 (n = 960)	25-30 (n = 426)	≥ 30 (n = 372)
Gestational age at delivery (wks)	38.1±2.0	37.9±2.4	37.8±2.6
Birth weight (g)	2988.9 ±637.9	2975.2±603.2	2909.1±597.6
Small-for gestational age – n (%)	160 (16.7)	73 (17.1)	58 (16.0)
Large-for-gestational age – n (%)	216 (22.5)	101 (23.7)	57 (15.3)*†
Macrosomia – n (%)	31(3.2)	10 (2.3)	5 (1.3)
Shoulder dystocia – n (%)	68 (7.1)	24 (5.6)	31 (8.3)
Congenital malformations – n (%)	59 (6.1)	17 (4.1)	20 (5.3)
Respiratory distress syndrome – n (%)	119 (12.4)	38 (9.0)	39 (10.4)
Hypoglycemia – n (%)	121 (12.6)	61 (14.4)	45 (12.2)
Jaundice – n (%)	151 (15.7)	58 (13.6)	49 (13.3)
Neonatal intensive care unit – n (%)	357 (37.2)	150 (35.2)	120 (32.3)

*, $P < 0.05$ *vs.* BMI <25; †, $P < 0.05$ *vs.* BMI 25-30

complications such as congenital malformations, RDS, hypoglycemia, and jaundice showed no significant differences among the three groups.

Discussion

This is the first large-scale study of pregnancy outcomes of women with GDM according to pre-gestational BMI in Japan. Our results revealed the prevalences of baseline features of GDM according to pre-gestational BMI, as well as maternal and neonatal complications. Thus, we focus mainly on these points in the following discussion.

Characteristics of women with GDM

In the present study, plasma glucose levels on 75-g OGTT showed a gradual increase according to pre-gestational BMI. This trend is consistent with observations in previous reports. For instance, Black *et al.* reported that glucose levels on 75-g OGTT gradually increased according to pre-gestational BMI [8].

In this study, gestational age at diagnosis was earlier in overweight and obese women. This result is likely attributable to the recommendation that 75-g OGTT is performed at any time a pregnant woman is found to be overweight or obese in Japan [14]. On the other hand, gestational weight gain was decreased according to pre-gestational BMI, suggesting that diet therapy intervention ameliorated excessive weight gain during pregnancy. As the strategies for managing women with GDM were similar among the institutes participating in this study, the present results suggest diet therapy to effectively reduce maternal weight gain during pregnancy. Langer *et al.* also showed that gestational weight gain was decreased according to pre-gestational BMI [15]. There are no available data for ideal body weight gain in women with GDM. The Japan Ministry of Health, Labour, and Welfare's recommended nutritional requirements do not list restrictions dependent on a pregnant woman's physique. In the nutritional guidelines for pregnancy in the "Healthy Family 21" of the Ministry of Health, Labour, and Welfare, weight gain is basically about 5 kg in women with a BMI of 25 of higher, with individual consideration to be given [16]. The Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), a randomized trial of treatment for GDM, concluded that treatment reduces serious perinatal complications with significant reduction of maternal weight gain during pregnancy [17]. In that trial, intervention included individualized dietary advice from a registered dietitian. Researchers considered a woman's pre-gestational body weight, dietary intake, activity level, and weight gain. In another randomized controlled trial in the United States, the National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network (NCHD) trial [18], nutritional counseling and diet therapy were provided based on nutritional recommendations made by the American Diabetes Association (ADA). Although the content of dietary counseling in the ACHOIS trial [17] is not clear, another trial by the NCHD trial [18] used the ADA guidelines in their protocol. Briefly, the ADA recommends nutritional counseling, if possible by a registered dietician, with indi-

vidualization of a nutrition plan based on height and weight [19].

Therefore, the protocol of diet therapy for women with GDM in Japan is not so different from the protocol of other countries.

Maternal and neonatal complications

Maternal complications including the prevalences of chronic hypertension, PIH, primary cesarean section, and induction of labor were higher in overweight or obese women with GDM than in normal weight women with GDM. The MLRA revealed pre-gestational BMI, gestational weight gain, chronic hypertension, and nulliparity to be associated with the onset of PIH, while the 75-g OGTT results were unrelated to PIH. Also, the MLRA revealed that pre-gestational BMI, gestational weight gain, PIH, and chronic hypertension were associated with primary cesarean section. These results suggest maternal complications to be more closely associated with maternal pre-gestational BMI than with blood glucose levels. Catalano *et al.* also showed both maternal GDM and obesity to be independently associated with adverse pregnancy outcomes [7].

On the other hand, it is noteworthy that the only significant difference identified was in the prevalence of LGA, a neonatal complication. The prevalence of LGA in the obese group was the lowest among the three groups and the prevalences of LGA were similar in the normal weight and overweight groups, suggesting intervention for women with GDM to be effective. Langer *et al.* also reported that obese and overweight GDM patients achieving targeted levels of glucose control with insulin therapy showed no increased risk for LGA and macrosomia [15]. As the prevalences of SGA were similar among the three groups in the present study, glycemic control was apparently not excessively strict. Because mean glucose levels less than 87 mg/dL indicate strict control, the prevalence of SGA is reported to be increased [5]. Ben-Haroush *et al.* reported that both the severity of GDM and maternal weight are independent predictors of infant birth weight [20]. Most *et al.* reported that different thresholds used for different maternal BMI categories in addition to the achievement of glycemic control and pharmacological therapy will enhance pregnancy outcomes [21]. As the MLRA showed that gestational weight gain was not associated with LGA in the present study (data not shown), improvement of maternal lipid metabolism through reduction of excessive gestational weight gain during pregnancy might reduce excessive fetal growth. Taken together from these findings, glycemic control under control of gestational weight gain by diet therapy may be effective for obese women with GDM.

The present study has limitations that must be taken into account when interpreting the data. First, as there are no data from women with normal glucose tolerance in this study, we cannot compare real pregnancy outcomes between women with normal glucose tolerance and those with GDM. Second, we cannot ascertain whether glycemic control for GDM in each group was appropriate or whether glycemic control was similar in the third trimester of gestation. Also, the subjects were recruited based on the previous JSOG criteria for GDM, such that we cannot compare our GDM groups with subjects studied using the IADPSG criteria. Furthermore, as gestational age at diagnosis of GDM is earlier in the obese group compared with the overweight group, duration of treatments were longer in the obese group than those in the overweight group. Therefore, we should consider the possibility that the intervention could vary by obesity status.

In summary, in the current study we found that medical interventions such as diet therapy and SMBG with or without insulin therapy for obese GDM women may contribute to reducing the prevalence of LGA but do not markedly reduce maternal complications. Prevention of LGA is important because these infants are at risk for metabolic syndrome in later life [22-23]. Therefore, the essential strategy for preventing GDM and LGA should include an appropriate diet prior to conception. Further study focusing on such a pre-conception program for overweight and obese women is required. Also, further study on the effects of ketone body by diet therapy for obese women with GDM on offspring in later life.

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Conflict of Interests

None of the authors have any potential conflicts of interest associated with this study.

Appendix

The contributors of the Japan Diabetes and Pregnancy Study Group are follows:

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ORIGINAL

Pregnancy outcomes in women with type 1 and type 2 diabetes mellitus in a retrospective multi-institutional study in Japan

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Abstract. The present study was performed to evaluate pregnancy outcomes in women with type 1 and type 2 diabetes mellitus (DM) in Japan. This multi-institutional retrospective study was conducted in 40 general hospitals in Japan during 2003-2009. We evaluated 369 and 579 pregnant women with type 1 and type 2 DM, respectively, and compared pregnancy outcomes between the two groups. Glycosylated hemoglobin levels in the first trimester did not differ significantly between the studied groups. Gestational weight gain was lower in type 2 DM than in type 1 DM. Although there were no significant differences in perinatal outcomes between the groups, the primary cesarean section rate was higher in type 2 DM than in type 1 DM. Multiple logistic regression analysis revealed that primigravida status, pre-gestational body mass index (BMI), gestational weight gain, chronic hypertension, and microvascular disease including diabetic retinopathy or nephropathy were associated with onset of pregnancy-induced hypertension. Further, pre-gestational BMI was associated with the need for primary cesarean section. This study demonstrated that no differences were observed in the rates of perinatal mortality and congenital malformation between pregnant women with type 1 DM and type 2 DM; however, women with type 2 DM displayed a higher risk of primary cesarean section.

Key words: Diabetes mellitus, Type 1 diabetes mellitus, Type 2 diabetes mellitus, Pregnancy outcome

IN RECENT years, the prevalence of type 2 diabetes mellitus (DM) has increased worldwide, and the number of pregnant women with this disease has increased similarly [1, 2]. In many areas of the world, the number of women with type 2 DM in pregnancy exceeds that of women with type 1 DM [3]; for example, a study in Japan reported that 67% of pregnant diabetic women had type 2 DM [4]. Glycemic disturbances are usually less severe in pregnant women with type 2 DM than in those with type 1 diabetes; therefore, type 2 DM is often perceived as a less serious condition. However, it has been reported that women with type 2 DM tend to have worse pregnancy outcomes than those in the general pregnant population [5-9]. In addition, increasing attention has recently been paid to pregnancies com-

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plicated by type 2 DM; for example, their increasing prevalence has been examined [3].

Taken together with previous investigations, there is no agreement regarding comparative obstetric and perinatal outcomes in women with type 1 and type 2 DM. Some studies have shown similar results for both types of patients [10, 11], while others have noted higher rates of maternal morbidity, perinatal morbidity and mortality, and congenital malformations in pregnancies complicated by type 2 DM than in those with type 1 DM [12]. Therefore, further studies are required to compare pregnancy outcomes between women with type 1 and type 2 DM. Moreover, it is not known whether the factors related to obstetric and perinatal outcomes are similar for both types of DM in Japan. Understanding these factors may help in preventing complications in pregnancy and in improving pregnancy outcomes in women with DM.

In Japan, few studies have compared pregnancy outcomes between women with type 1 and type 2 DM. The present study therefore aimed to compare both maternal and neonatal complications between women with type 1 and type 2 DM and to identify and analyze factors related to adverse pregnancy outcomes.

Methods

The present retrospective study was conducted in 40 general hospitals in Japan during 2003-2009. The study protocol was approved by the ethics committee at each of the 40 collaborating centers. All patients had been diagnosed with DM before the pregnancy and had received anti-diabetic therapy. After pregnancy was detected, all the patients received dietary management with self-monitoring of blood glucose along with insulin therapy, if necessary.

Data were collected on maternal age, parity, the age at which diabetes was diagnosed, the duration of diabetes, pre-pregnancy BMI, weight gain, glycosylated hemoglobin (HbA1c) levels, diabetic retinopathy, diabetic nephropathy, chronic hypertension, gestational week of delivery, maternal complications, and neonatal complications. Maternal complications were pregnancy-induced hypertension (PIH) including preeclampsia, induced labor, and primary cesarean section. Neonatal complications were preterm birth, small-for-gestational age (SGA), large-for-gestational age (LGA), macrosomia, fetal congenital malformation, hypoglycemia, jaundice, polycythemia, hypocalcemia, respiratory disorder (RDS), plexus paralysis, neonatal intensive care unit (NICU) hospitalization, intrauterine fetal death, and neonatal mortality.

A primary cesarean section was defined as a cesarean section performed on a patient who had previously never undergone a cesarean section. Pre-gestational weight was self-reported at the first prenatal visit. Gestational age was defined by the number of weeks since the last menstrual period or the ultrasound assessment of crown-rump length if a discrepancy was recognized. Chronic hypertension was defined as hypertension treated with medication before pregnancy or arterial blood pressure 140/90 mmHg before 20 weeks of pregnancy. SGA and LGA were defined as sex- and delivery-specific birth weight for gestational age being below or above the 90th percentile of Japanese fetal growth curves, respectively [13]. Macrosomia was defined as birth weight at or above 4,000 g. Major congenital malformations were defined as those causing significant functional impairment, requiring surgery, or being life-threatening. The composite study outcome included perinatal mortality (stillbirth or neonatal death) and complications associated with maternal hyperglycemia, including congenital malformation, LGA, macrosomia, hypoglycemia, hyperbilirubinemia, shoulder dystocia, respiratory distress syndrome, and admission to the neonatal intensive care unit. Neonatal blood samples for measuring glucose were collected at 1 or 2 h after birth and before feeding; hypoglycemia was defined as a glucose value of less than 35 mg/dL. Hyperbilirubinemia was defined as a requirement for phototherapy. Maternal outcomes included weight gain from the time of enrollment to delivery, PIH including gestational hypertension and preeclampsia, cesarean delivery, labor induction, and shoulder dystocia. Gestational hypertension was defined as systolic pressure of 140 mm Hg or more or diastolic pressure of 90 mm Hg or more on two occasions at least 4 h apart. Preeclampsia was defined as blood pressure elevation (according to the definition of gestational hypertension) together with proteinuria (300 mg of protein or more in 24-h urine collection or a result of 2+ or greater on a dipstick test when 24-h collection was not available). Shoulder dystocia was defined clinically, and the providers were required to document the specific maneuvers used to release the fetal shoulders. HbA1c values were defined according to the National Glycohemoglobin Standardization Program (NGSP) standards [14].

Baseline characteristics and laboratory measurements are presented as mean ± SD, median values, or percentages. Univariate tests for differences in values between the two groups were performed using the chi-square test and Fisher's exact test. The mean values were compared using Student's *t*-test. Multiple logistic regression analysis (MLRA) was performed to identify variables contributing to some outcome. All reported P values are two-tailed, and $P < 0.05$ was considered to indicate a statistically significant difference. All statistical analyses were performed using a general-purpose statistical software, JMP version 10.0 (SAS Institute Inc., Tokyo, Japan).

Results

From 2003 through 2009, we retrospectively analyzed 369 women with pre-gestational type 1 DM and 579 women with type 2 DM from 40 institutions in Japan.

The baseline characteristics of the women included in this retrospective study are shown in Table 1. Women with type 2 DM were significantly older than those with type 1 DM (30.9 ± 4.8 *vs.* 32.9 ± 5.0, respectively). The percentage of nulliparous women was significantly higher in type 1 DM patients (64.0% *vs.* 51.3%, respectively). The age at the time of diagnosis of diabetes was lower in type 1 DM patients than in type 2 DM patients (18.2 ± 8.0 *vs.* 28.0 ± 6.9 years old, respectively). The duration of diabetes was greater in women with type 1 DM than in those with type 2 DM (12.9 ± 7.6 years *vs.* 5.0 ± 5.2 years, respectively). Pre-gestational BMI was significantly higher in women with type 2 DM than in those with type 1 DM (22.3 ± 8.9 *vs.* 27.6 ± 5.8, respectively). In contrast, gestational weight gain was lower in women with type 2 DM than in those with type 1 DM (10.3 ± 4.6 *vs.* 7.3 ± 5.8, respectively). No significant differences were observed in the HbA1c levels at the first trimester between the two groups (6.8 ± 1.3 *vs.* 6.9 ± 1.7, respectively). The frequency of diabetic microangiopathy, such as retinopathy and nephropathy, was significantly higher in women with type 1 DM than in those with type 2 DM. The prevalence of chronic hypertension was significantly higher in women with type 2 DM than in those with type 1 DM (8.6% *vs.* 3.3%, respectively). Maternal complications are shown in Table 2. The prevalence of PIH including preeclampsia was higher in women with type 2 DM than in those with type 1 DM; however, the difference was not significant. Induction of labor was performed more frequently in women with type 1 DM (41.5% *vs.* 33.3%, respectively). In contrast, the rate of primary cesarean section was significantly higher in type 2 DM patients than in type 1 DM patients (28.4% *vs.* 21.6%, respectively).

MLRA for detecting factors associated with PIH showed that primigravida status, pre-gestational BMI, gestational weight gain, chronic hypertension, and diabetic nephropathy and retinopathy were associated with the frequency of PIH (Table 3). Further, MLRA showed that the pre-gestational BMI was associated with primary cesarean section (Table 4).

Neonatal complications observed in the present study

Table 1 Basal characteristics

	Type 1 DM n=369	Type 2 DM n=579
Age (year)	30.9 ± 6.9	32.9 ± 5.0[a]
Primigravida, n (%)	236 (64.0)	297 (51.3)[a]
Age at diagnosis (year)	18.2 ± 8.0	28.0 ± 6.9[a]
Duration of diabetes (years)	12.9 ± 7.6	5.0 ± 5.2[a]
Pregestational BMI (kg/m^2)	22.3 ± 8.9	27.6 ± 5.8[a]
Overweight, n (%)	48 (13.0)	187 (32.3)[a]
Obesity, n (%)	10 (2.7)	184 (31.8)[a]
Gestational weight gain (kg)	10.3±4.6	7.3 ± 5.8[a]
HbA1c levels in the first trimester (%)	6.8 ± 1.3	6.9 ± 1.7
Retinopathy, n (%)	75 (20.3)	52 (9.0)[a]
Nephropathy, n (%)	34 (9.2)	28 (4.8)[a]
Chronic hypertension, n (%)	12 (3.3)	50 (8.6)[a]

mean±SD; [a]$p<0.05$ *vs.* type 1 DM; DM, diabetes mellitus

Table 2 Maternal complications

	Type 1 DM n=369	Type 2 D Mn=579
Pregnancy-induced hypertension, n (%)	41 (11.1)	77 (13.3)
Preeclampsia, n (%)	32 (8.7)	70 (12.1)
Induced labor, n (%)	153 (41.5)	193 (33.3)[a]
Primary cesarean section, n (%)	80 (21.6)	165 (28.4)[a]

[a]$p<0.05$ *vs.* type 1 DM; DM, diabetes mellitus

Table 3 Risk factors for pregnancy-induced hypertension

Variable	Odds Ratio	95%CI	*P*
Age	1.009	0.969-1.052	0.6549
Primigravida	1.865	1.213-2.914	0.0052
Type 2 diabetes mellitus	1.047	0.636-1.733	0.8565
Pregestational BMI	1.072	1.031-1.114	0.0005
Gestational weight gain	1.065	1.027-1.105	0.0007
Retinopathy/Nephropathy	1.767	1.052-2.908	0.0276
Chronic hypertension	3.695	1.98-6.769	0.0001

Table 4 Risk factors for primary cesarean section

Variable	Odds Ratio	95%CI	*P*
Pregnancy-induced hypertension	1.385	0.917-2.080	0.1187
Age	1.023	0.994-1.053	0.1175
Pregestational BMI	1.046	1.018-1.076	0.0015
Weight gain	1.015	0.989-1.041	0.2736
Large-for-gestational age	1.381	1.030-1.850	0.0304
Primigravida	0.763	0.576-1.010	0.0587
Type 2 diabetes mellitus	0.823	0.593-1.139	0.2406

Table 5 Neonatal complications

	Type 1 DM n=369	Type 2 DM n=579
Gestational week of delivery (weeks)	37.6 ± 2.3	37.7 ± 2.4
Birth weight (kg)	3045.8 ± 562	2997 ± 660.1
Preterm birth, n (%)	55 (14.9)	102 (17.6)
Small-for-gestational age, n (%)	43 (11.7)	91 (15.7)
Large-for-gestational age, n (%)	112 (30.2)	190 (32.8)
Macrosomia, n (%)	17 (4.6)	29 (5.0)
Congenital malformation, n (%)	17 (4.6)	24 (4.1)
Hypoglycemia, n (%)	45 (12.2)	78 (13.5)
Jaundice, n (%)	56 (15.2)	89 (15.4)
Polycythemia, n (%)	7 (1.9)	12 (2.1)
Hypocalcemia, n (%)	3 (0.8)	13 (2.2)
Respiratory disorder, n (%)	34 (9.2)	62 (10.7)
Plexus paralysis, n (%)	1 (0.3)	2 (0.3)
NICU hospitalization, n (%)	123 (33.3)	229 (39.6)
Intrauterine death, n (%)	2 (0.54)	2 (0.34)
Neonatal death, n (%)	2 (0.54)	3 (0.52)

are shown in Table 5. Gestational age at delivery and birth weight showed no significant differences between the two groups; moreover, the prevalence of SGA and LGA showed no significant differences. Other neonatal complications, such as congenital malformations, hypoglycemia, polycythemia, hypocalcemia, jaundice, RDS, plexus paralysis, NICU hospitalization, and neonatal mortality, did not differ significantly between the two groups.

Discussion

The present study has demonstrated a recent large-scale comparison of pregnancy outcomes between women with type 1 DM and type 2 DM in Japan for the first time. This study showed that there were no differences in the rates of perinatal mortality and congenital malformation between pregnant women with type 1 DM and type 2 DM; however, women with type 2 DM displayed a higher risk of primary cesarean section.

Women with type 2 DM were older than those with type 1 DM; therefore, the rate of nulliparity appeared to be lower in type 2 DM than in type 1 DM. Women with type 1 DM were diagnosed at a younger age than were those with type 2 DM. Subsequently, as the duration of diabetes was longer in type 1 DM as compared with that in type 2 DM, the frequency of diabetic microangiopathies, such as retinopathy and nephropathy, was higher in women with type 1 DM than in those with type 2 DM. Moreover, the pregestational BMI was higher in women with type 2 DM than in those with type 1 DM; thus, the obesity rate was higher in women with type 2 DM than in women with type 1 DM. These results showed trends similar to those observed in a previous small-scale study in Japan [15]. Gestational weight gain was lower in women with type 2 DM than in those with type 1 DM. In the case of gestational diabetes mellitus (GDM), gestational weight gain has been reported be less in women with higher pregestational BMI than in women with lower pregestational BMI [16].

Maternal obesity or overweight status has been shown to be associated with adverse maternal pregnancy outcomes such as PIH, preeclampsia, and cesarean section [17]. The present study demonstrated that no significant differences occurred in the PIH rate between women with type 1 and type 2 DM. Even in normal glucose-tolerant women and those with gestational diabetes, maternal BMI is an independent risk factor for PIH [18, 19]. Moreover, along with maternal pregestational BMI, the presence of diabetic microangiopathy, including retinopathy or nephropathy, in type 1 DM has also been previously reported as a risk factor for PIH [20]. In the present study, MLRA revealed that maternal BMI, gestational weight gain, and the presence of microangiopathy were associated with PIH. The prevalence of obesity was much higher in women with type 2 DM; therefore, we consider that obesity in type 2 DM and microangiopathy in type 1 DM may be strong risk factors for PIH. Preconceptional diet therapy, with reduction in gestational body weight, may be effective in reducing the risk of PIH in women with DM. The rate of primary cesarean section was higher in women with type 2 DM than in those with type 1 DM. In the subanalysis of hyperglycemia and adverse pregnancy outcome (HAPO) study, maternal BMI was independently associated with cesarean section [21]. In the present study, MLRA also revealed that pregestational BMI was a risk factor for primary

cesarean section. Pregestational BMI and gestational weight gain in nulliparous women with type 1 DM has been reported to be associated with an increased rate of cesarean section [22]; therefore, diet therapy may play an important role in the management of pregnant women with DM.

A meta-analysis by Basells *et al.* showed that HbA1c levels at booking were higher in type 1 DM patients, with similar congenital malformation rates in women with type 1 and type 2 DM, and lower rates of diabetic ketoacidosis and cesarean section in type 2 DM patients than in type 1 DM patients [23]. This meta-analysis summarized pregnancy outcomes in women with type 1 and type 2 DM worldwide over 20 years; however, the progress and improvement in the management for diabetes was not evaluated by this study. Further, since the exact prevalence of primary cesarean section was not evaluated in the meta-analysis, we could not compare the results of the meta-analysis with those of the present study in terms of the primary cesarean section rate.

Approximately 20 years previously, Omori *et al.* reported that Japanese pregnancy outcomes in type 2 DM were poorer than those in type 1 DM. However, their subjects were evaluated from 1964 to 1992, and their results were therefore considered to reflect the poor clinical management of type 2 DM. In fact, the prevalence of congenital malformation and neonatal death has been shown to be higher in women with type 2 DM than in those with type 1 DM [4]. Presumably, improvements in HbA1c levels at the first trimester in pregnancy resulted from improved management for women with DM. In particular, the preconceptional management for women with type 2 DM may have improved as compared that in previously studied subjects.

The present study has certain limitations that must be taken into account when interpreting the data. First, since there are no data from women with normal glucose tolerance or gestational diabetes mellitus in this study, we could not compare incidence of pregnancy outcomes between women with these subjects and those with DM. Second, we could not ascertain whether glycemic control for DM in each group was appropriate throughout the pregnancy or whether glycemic control was similar for the two groups in the third trimester. Further, the prevalence of preconceptional care and the progression of retinopathy or nephropathy during pregnancy were not examined in women with DM.

In conclusion, the present study suggests that the rate of primary cesarean section is higher in women with type 2 DM than in those with type 1 DM, with the pregestational BMI being associated with cesarean section. Although the prevalence of PIH did not differ between women with type 1 and type 2 DM, the presence of microangiopathy, pregestational BMI, and gestational weight gain were associated with PIH, suggesting that diet therapy before and throughout the gestation period would improve pregnancy outcomes.

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Conflict of Interest

The authors indicate no potential conflict of interest.

Appendix

The contributors of the Japan Diabetes and Pregnancy Study Group are shown as follows: Hirosaki University Graduate School of Medicine; Nishisaitama-Chuo National Hospital; Asahi Hospital; NTT East Hospital; Keio University School of Medicine; Tokyo Medical and Dental University; Tokyo Women's University School of Medicine; Tokyo Medical School of Medicine Hachioji Medical Center; National Center for Child Health and Development; Saiseikai Yokohamashi Tobu Hospital; St. Marianna University School of Medicine; Yokohama City University Medical Center; Toyama University Graduate School of Medicine; Shinshu University Graduate School of Medicine; Fukui University Graduate School of Medicine; Fukui Prefectural Hospital; Mie University Graduate School of Medicine; Ise Red Cross Hospital; Shiga University of Medical Science; Kyoto University School of Medicine, Kyoto Prefectural University of Medicine; Osaka University School of Medicine; Osaka Medical Center and Research Institute for Maternal and Children Health; Nara Medical University, Kobe University School of Medicine; Hyogo Prefectural Kobe Children's Hospital; Himeji Red Cross Hospital; Okayama Medical Center; Hiroshima University Graduate School of Medicine; Tottori University Graduate School of Medicine; Ehime University School of Medicine; Ehime Prefectural Central Hospital; Kurume University

School of Medicine; Oita University Graduate School of Medicine; Nagasaki University Graduate School of Medicine; National Hospital Organization Nagasaki Medical Center; Nagasaki City Hospital Organization Nagasaki Municipal Hospital; Kumamoto City Hospital; Miyazaki University Graduate School of Medicine; Okinawa Chubu Hospital

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Present status of clinical care for postpartum patients with hypertensive disorders of pregnancy in Japan: findings from a nationwide questionnaire survey

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Objective: To assess the present status of clinical care for postpartum patients with hypertensive disorders of pregnancy (HDP) in Japan. *Methods*: We conducted a nationwide questionnaire survey of obstetricians, internists and hypertension specialists and analyzed 686 valid responses. *Results*: Though HDP is widely known as a risk factor for subsequent hypertension and cardiovascular disease, over one-third of obstetricians terminated their postpartum follow-up of HDP patients without referring them to other departments. *Conclusion*: It is important to establish an effective referral system, whereby patients with HDP can be smoothly transferred to primary care or a specialist physician after childbirth for long-term monitoring and management of blood pressure.

Keywords Antihypertensive agent, Breast feeding, Hypertensive disorders of pregnancy, Hypertension in pregnancy, Postpartum hypertension

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INTRODUCTION

The incidence of new-onset postpartum hypertension has been reported in the range 0.3–28%, depending on the period of observation (1). The mechanism of its development is not well established, although studies have suggested the involvement of atrial natriuretic peptide (ANP) (2) and the renin–angiotensin system (3). Blood pressure progressively increases over the first five postnatal days, peaking on days 3–6 after delivery (4). It has been reported that approximately 10% of maternal deaths are associated with hypertension in the postpartum period, suggesting the need for its careful management (5). However, approaches to the treatment and care of postpartum hypertension vary among physicians (6).

Hypertensive disorders of pregnancy (HDP) affect 3 to 10% of all pregnancies (7,8), and are associated with significant maternal, fetal, and neonatal morbidity and mortality (7,9,10). Patients with HDP are likely to have hypertension in the postpartum period (5). Practicing obstetricians sometimes see patients with persistent postpartum hypertension. A recent study showed that hypertension did not resolve in 18% of women at two years of post-delivery, drawing attention to postpartum hypertension in HDP patients (11). In addition, women with a history of HDP had higher incidences of hypertension and cardiovascular events even though their blood pressures had normalized in the postpartum period (12–20). These findings underscore the importance of long-term management of HDP patients after delivery. Given these circumstances, we conducted a nationwide questionnaire survey on obstetricians and internists in Japan, aimed at assessing the current status of treatment and care for postpartum hypertension in patients with HDP.

METHODS

A questionnaire was prepared to investigate clinical care for postpartum hypertension in patients with HDP. Specifically, the questionnaire included three items related to awareness of long-term risks of HDP and identification of the department that took care of postpartum patients with hypertension. Additionally, the questionnaire included four questions on drug therapy protocols for postpartum hypertension.

A cover letter and a paper copy of the questionnaire were mailed to chief obstetricians and chief internists at the 650 medical institutions recognized by the Japan Society of Perinatal and Neonatal Medicine. Questionnaires were also mailed to 539 hypertension specialists certified by the Japanese Society of Hypertension. The respondents were asked to fill out the survey anonymously and to return it by either post or fax. The period of investigation was between September and October 2012.

RESULTS

Of the questionnaire packages sent to 650 chief obstetricians, 650 chief internists and 539 hypertension specialists, six, three and eight packages, respectively, were returned to the sender. Completed forms were received from 355 chief obstetricians (questionnaire recovery rate, 55.1%), 141 chief

internists (21.8%) and 197 hypertension specialists (37.1%). Seven chief obstetricians provided completely blank responses and were removed from further analysis. Altogether, valid responses were obtained from 686 respondents, consisting of 348 chief obstetricians, 141 chief internists and 197 hypertension specialists. The ensuing paragraphs summarize the questions and responses.

Awareness of Long-term Risks and Clinical Care for Patients with HDP

(1) Question: In your routine clinical care, do you handle HDP as a risk factor for future development of cerebral-cardiovascular diseases and chronic hypertension?

A total of 82.8% (288/348) of chief obstetricians, 78.7% (111/141) of chief internists and 91.4% (180/197) of hypertension specialists recognized HDP as a risk factor for cerebral-cardiovascular diseases and chronic hypertension. By contrast, 15.5% (54/348), 20.6% (29/141) and 8.6% (17/197), respectively, responded that they did not (Figure 1).

(2) Question: Do you tell patients diagnosed with HDP that they are prone to developing cerebral-cardiovascular diseases and chronic hypertension?

A total of 79.3% (276/348) of chief obstetricians, 63.8% (90/141) of chief internists and 80.2% (158/197) of hypertension specialists provided explanation on long-term prognosis for patients diagnosed with HDP. However, 17.5% (61/348), 32.6% (46/141) and 17.3% (34/197), respectively, responded that they did not (Figure 2).

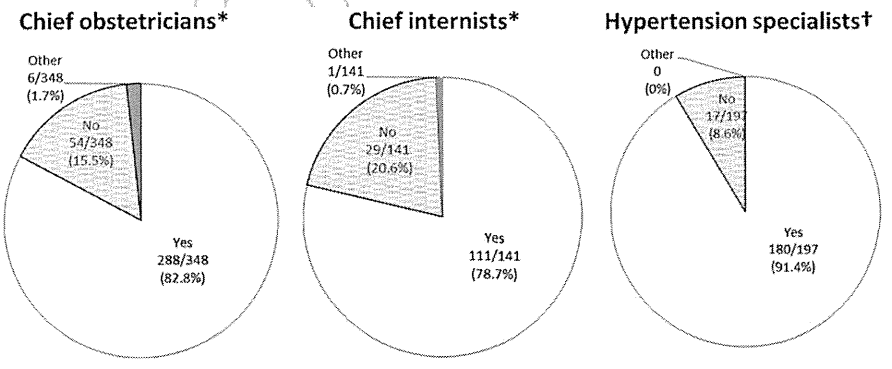

Figure 1. Awareness of long-term risks of HDP. A total of 82.8% (288/348) of chief obstetricians, 78.7% (111/141) of chief internists and 91.4% (180/197) of hypertension specialists recognized HDP as a risk factor for cerebral-cardiovascular diseases and chronic hypertension. By contrast, 15.5% (54/348), 20.6% (29/141) and 8.6% (17/197), respectively, responded that they did not. Figures not enclosed in parentheses represent the numbers of respondents, and the percentages in parentheses, their proportions. *Chief obstetricians and chief internists represented the medical institutions recognized by the Japan Society of Perinatal and Neonatal Medicine. †Hypertension specialists were certified by the Japanese Society of Hypertension.

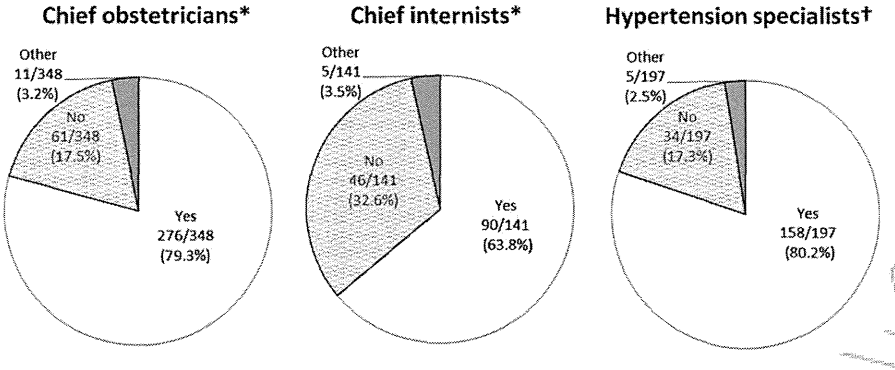

Figure 2. Informing about the prognosis of HDP. A total of 79.3% (276/348) of chief obstetricians, 63.8% (90/141) of chief internists and 80.2% (158/197) of hypertension specialists provided explanation on long-term prognosis for patients diagnosed with HDP. However, 17.5% (61/348), 32.6% (46/141) and 17.3% (34/197), respectively, responded that they did not. Figures not enclosed in parentheses represent the numbers of respondents, and the percentages in parentheses, their proportions. *For an explanation of chief obstetricians, chief internists and hypertension specialists, see the footnotes to Figure 1.

Table 1. Clinical care for patients with HDP.

Continue treatment	Refer to internist	No such case experienced	Other	Total
Panel a: Distribution of chief obstetricians by the type of follow-up treatment for patients with HDP who did not become normotensive after delivery[a]				
122 (35.1%)	215 (61.8%)	1 (0.3%)	10 (2.9%)	348 (100%)
	Yes	No	Other	Total
Panel b: Physicians routinely seeing patients with HDP within 12 weeks postpartum[a]				
Chief internists[b]	58 (41.1%)	77 (54.6%)	6 (4.3%)	141 (100%)
Hypertension specialists[b]	71 (36.0%)	126 (64.0%)	0 (0%)	197 (100%)

[a]Figures not enclosed in parentheses represent the numbers of respondents, and the percentages in parentheses, their proportions.
[b]For an explanation of chief internists and hypertension specialists, see footnotes to Figure 1.

(3a) Question specific to chief obstetricians: If a patient diagnosed with HDP does not become normotensive after delivery, what department is responsible for her?

A total of 35.1% (122/348) of chief obstetricians indicated that the department of obstetrics would be responsible, and 61.8% (215/348) responded that they would refer the patient to the department of internal medicine after providing care for a certain period of time (Table 1, panel a).

(3b) Question for chief internists and hypertension specialists only: Do you routinely see HDP patients in the postpartum period (i.e. within 12 weeks of delivery)?

Positive answers were given by 41.1% (58/141) of chief internists and 36.0% (71/197) of hypertension specialists, while negative answers were provided by 54.6% (77/141) and 64.0% (126/197), respectively (Table 1, panel b).

Drug Therapy for Postpartum Hypertension

(4) Question: Do you prescribe antihypertensive medications for patients with postpartum hypertension (i.e. within 12 weeks of delivery)?

Among the physicians who responded that they routinely provided medical care to patients with postpartum hypertension (Question No. 3), 73.6% (256/348) of chief obstetricians, 94.8% (55/58) of chief internists and 85.9% (61/71) of hypertension specialists answered that they prescribed antihypertensives, while 22.4% (78/348), 3.4% (2/58) and 14.1% (10/71), respectively, did not (Table 2).

(5) Question: Please describe the threshold blood pressure required to start drug interventions. (This question was applicable only to the physicians who responded positively to Question No. 4.)

For systolic blood pressure, 40.2% (103/256), 31.6% (81/256) and 17.6% (45/256) of chief obstetricians indicated 160–169, 140–149 and 150–159 mmHg, respectively. Of chief internists, 47.3% (26/55), 30.9% (17/55) and 20.0% (11/55) indicated 140–149, 160–169 and 150–159 mmHg, respectively. Of hypertension specialists, 36.1% (22/61), 27.9% (17/61) and 23.0% (14/61) indicated 140–149, 160–169 and 150–159 mmHg, respectively.

For diastolic blood pressure, 35.2% (90/256), 32.4% (83/256) and 24.6% (63/256) of chief obstetricians indicated 90–99, 100–109 and 110–119 mmHg, respectively. Of chief internists, 65.4% (36/55) and 25.5% (14/55) responded with 90–99 and 100–109 mmHg, respectively. Of hypertension specialists, 60.7% (37/61) and 26.2% (16/61) responded with 90–99 and 100–109 mmHg, respectively (Figure 3).

Table 2. Physicians prescribing antihypertensives to patients within 12 weeks of delivery.

	Yes	No	Other	Total
Chief obstetricians[a]	256 (73.6%)	78 (22.4%)	14 (4.0%)	348 (100%)
Chief internists[a]	55 (94.8%)	2 (3.4%)	1 (1.7%)	58 (100%)
Hypertension specialists[a]	61 (85.9%)	10 (14.1%)	0 (0%)	71 (100%)

Among the physicians who responded that they routinely provided medical care to patients with postpartum hypertension (Question No. 3), 73.6% (256/348) of chief obstetricians, 94.8% (55/58) of chief internists and 85.9% (61/71) of hypertension specialists answered that they prescribed antihypertensives, while 22.4% (78/348), 3.4% (2/58) and 14.1% (10/71), respectively, did not.

Figures not enclosed in parentheses represent the numbers of respondents, and the percentages in parentheses, their proportions.

The respondents to this item were limited to those who routinely provided medical care for patients with postpartum hypertension.

[a]For an explanation of chief obstetricians, chief internists and hypertension specialists, see footnotes to Figure 1.