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Pregnancy Outcome in Women with Gestational Diabetes Mellitus: Age and Pre-pregnancy BMI-Matched Prospective Cohort Study in Ulaanbaatar of Mongolia

Nomin-Erdene Minjuurdorj[1,2], Altaisaikhan Khasag[1], Chuluunbileg Batbold[3], Enkhtsetseg Jamsranjav[4]

[1]Department of Endocrinology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia;
[2]Center of Nephrology, Dialysis and Endocrinology, Third State Central Hospital, Ulaanbaatar, Mongolia;
[3]Department of Internal Medicine, Third State Central Hospital, Ulaanbaatar, Mongolia;
[4]Department of Obstetrics and Gynecology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia.

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Corresponding Author:
Enkhtsetseg Jamsranjav (M.D., Ph.D., Prof.)
Department of Obstetrics and Gynecology, School of Medicine, Mongolian National University of
Medical Sciences, S. Zorig's street, Ulaanbaatar-14210, Mongolia
E-mail: enkhtsetseg@mnums.edu.mn
ORCID: https://orcid.org/0000-0001-6343-8200

Running title: Pregnancy Outcome in Women with Gestational Diabetes Mellitus

Objective: This study aimed to assess maternal outcomes in women with Gestational Diabetes Mellitus. **Method:** A multicenter, age, and pre-pregnancy body mass index-matched prospective cohort study was conducted in five maternity hospitals across Ulaanbaatar, Mongolia, between February and April 2022. All participants (24-28 weeks pregnant) underwent an oral glucose tolerance test (OGTT; 75 g, oral glucose, capillary), and the results were considered as GDM (ADA, 2022). The GDM and non-GDM groups were followed from pregnancy to delivery. Maternal and neonatal delivery outcome data were extracted from the clinical records of five maternity hospitals. **Results:** The mean age and pre-pregnancy BMI were 35.05±3.8 years and 26.21±3.7 kg/m2, respectively. According to the univariate analysis, women with gestational diabetes had higher rates of pregnancy-induced hypertension, cesarean delivery, and labor induction than the non-GDM group. On the multivariate analysis, the risk of undergoing cesarean delivery and developing pregnancy-induced hypertension were 2.8 (aOR=2.83 CI=1.07-7.47) and 6.9 (aOR=6.91 CI=1.35-35.23) times higher, respectively, in the case group compared to the non-GDM group. **Conclusion:** Women with GDM had more complications during pregnancy and delivery than those without.

Keywords: Diabetes, Gestational, Cesarean Section, Pregnancy Outcome, Glucose Tolerance Test

Introduction

Gestational Diabetes Mellitus (GDM) is a type of diabetes that is initially diagnosed during pregnancy, and its incidence is increasing globally.[1-3] According to the International Diabetes Federation (IDF) 10th Atlas, 16.7% (21.1 million) of live births, one in every six births, have

faced some form of hyperglycemia during pregnancy. A significant proportion of these women (approximately 80.3 %) had GM.[4,5] Studies have consistently demonstrated a correlation between pre-pregnancy body mass index (BMI), number of pregnancies and gravidity, family history of diabetes, prior history of GDM, advanced maternal age, and increased risk of developing GDM.[6,7] GDM can lead to adverse outcomes in both mothers and newborns.[8,9] These outcomes include pregnancy-induced hypertension, preterm labor, the need for cesarean delivery, preeclampsia, macrosomia, and neonatal complications such as respiratory distress syndrome (RDS) and hypoglycemia.[10-12] In the long-term complication, women who have experienced GDM during pregnancy are at a higher risk of developing diabetes mellitus type 2.[13] Additionally, newborns are at elevated risk of developing overweight or obesity in adulthood.[14] Poor glycemic control in mothers during the perinatal period is associated with an increased risk of mortality, as evidenced by a study that reported a high mortality rate of 42.9%.[15] Proper screening and management of GDM can lead to improved outcomes in both mothers and newborns by regulating blood glucose levels. In a study conducted in 2010, the prevalence of GDM among 406 pregnant women (24-28 weeks) in our country was 2.4%.[16] According to a 2020 study by Wurihah, et al. gestational diabetes has adverse effects on pregnancy and childbirth, is a risk factor for miscarriage, preterm labor, stillbirth, and macrosomia, and increases the frequency of cesarean section.[17] The primary motivation for our study was the lack of studies examining the complications of pregnancy, childbirth, and maternal outcomes in women with gestational diabetes mellitus. Thus, our study aimed to determine the maternal outcomes in women with GDM.

Materials and Methods

Research Design

A multicenter, age—and pre-pregnancy BMI-matched prospective cohort study was carried out in five maternity hospitals in Ulaanbaatar, the capital of Mongolia. The study included 418 participants (24-28-week pregnant women) who were under care during pregnancy at the district's health center between February and April 2022. The inclusion criteria were age > 18 years, singleton fetuses, no diabetes mellitus (type 1, type 2, or other types), and any chronic disease.

$$\textit{Sample one } (exposed) = \frac{(Z_{\alpha/2} + Z_{\beta})p(1-p)(r+1)}{(d)^2 r}$$

$$= \frac{(1.96^2 + 0.84)2 \times 0.024 \times (1 - 0.024) \times (1 + 1)}{(0.11)^2 \times (1)} = 30$$

The sample size was estimated using the following parameters: a confidence level of 95% on both sides, a power of 80%, and an exposed-to-non-exposed ratio of 1:1. The prevalence of gestational diabetes in Mongolia was 2.4%.[16] We used the odds ratio leading to pregnancy-induced hypertension from the study by Wurihan, et al. (2020).[17] We increased the sample size by 10% (lost follow-up/non-response). The final minimum sample size for the exposed and non-exposed groups is 33.

Data Collection

Structured questionnaires, physical examination, and an oral glucose tolerance test (75 g, oral glucose, capillary) were performed. Blood glucose levels were determined at 0, 60, and 120 min after the test. GDM status was diagnosed according to the American Diabetes Association (ADA, 2022) criteria when at least one of the following conditions was set: fasting 5.1 mmol/l, 1-hour glucose >10.0 mmol/l, or 2-hour glucose 8.5 mmol/l. Women who were eligible and ineligible for the study and had a positive or negative outcome in their oral glucose tolerance test (OGTT) were defined as GDM and non-GDM groups, respectively. The GDM group met the inclusion and exclusion criteria and had a positive OGTT result. In contrast, the non-GDM group were women in the same age group and with a pre-pregnancy body mass index who had negative OGTT results. The GDM and non-GDM groups were followed from pregnancy to delivery. Maternal and neonatal delivery outcome data (maternal and neonatal complications) were extracted from the clinical records of five maternity hospitals. Birth weight was classified as macrosomia (≥ 4000 g) or low (< 2500 g) based on the World Health Organization (WHO) definition. Preterm birth was defined as birth before the gestational age of 37 weeks. Preeclampsia was defined as the onset of a new episode of hypertension during pregnancy, characterized by persistent hypertension (diastolic blood pressure≥90 mm Hg) and proteinuria (>0.3g/24 hours) based on the WHO criteria. Induction of labor was defined as the process of artificially stimulating the uterus to start labor. It includes oxytocin,

prostaglandins, or manually rupturing the amniotic membranes. The newborn's Apgar scores were assessed one and five minutes after delivery. The evaluation consisted of rating the breathing effort, heart rate, skin color, muscle tone, and reflexes, with each category scored on a scale of 0 to 2 points. A total score of 7 or more was considered normal.

Statistical Analysis

Categorical variables are presented as frequencies (%, percentage), and continuous variables are expressed as mean (SD, standard deviation). Pearson's Chi-square test was used to compare the differences in the proportions of general characteristic variables. An independent sample t-test was performed to compare the differences in the means of the maternal and neonatal outcome data. Logistic regression analysis was used to estimate the odds ratios (ORs) with 95% confidence intervals (CIs) for the maternal outcomes associated with GDM. SPSS 27 was used for statistical analyses, and P<0.05 was considered statistically significant.

Ethical Statement

The study was approved by the Research Ethics Control Committee of the Mongolian National University of Medical Sciences (approval number: 2022/3–02). All participants provided written informed consent prior to participating in the study.

Results

This study included 418 pregnant women who received antenatal care in district hospitals. Of these, 376 participants completed the baseline survey. Based on the GDM diagnosis criteria, 13% (n=49) of the pregnant women had GDM (Figure 1). The participants were allocated into two groups based on age and pre-pregnancy body mass index (BMI): the GDM group, consisting of 49 individuals, and the non-GDM group, comprising 71 individuals. The study was followed up with participants until delivery. Included in the final analysis were 38 women with and 38 women without gestational diabetes mellitus, comprising the GDM and non-GDM groups, respectively. The participants were from the four districts of Ulaanbaatar, Mongolia: 42.1% (n=32) Bayanzurkh, 15.8% (n=12) Chingeltei, 40.8% (n=31) Songinokhairkhan, and 1.3% (n=1) Baganuur.

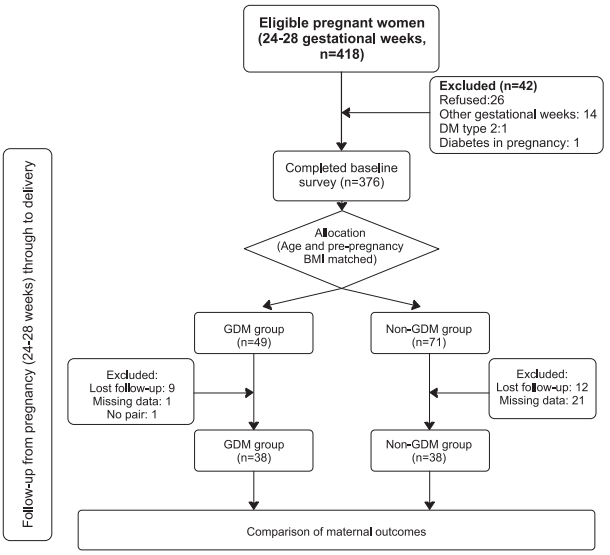

Figure 1. Flow chart of study

The general characteristics and outcomes of maternal delivery are illustrated in Table 1 based on the status of gestational diabetes mellitus (GDM). The mean age was 35.03±3.8 years in the GDM group and 35.08±3.9 years in the non-GDM group. Similarly, the mean pre-pregnancy BMI was 26.23±3.6 kg/m2 in the GDM group and 26.18±3.7 kg/m2 in the non-GDM group. The mean gravidity and parity in the GDM and non-GDM groups were 4.26±1.3, 3.84±1.5 and 2.24±1.0, 2.34±0.9, respectively (P=0.14, P=0.65). The mean gestational weight gain in the GDM and non-GDM group was 11.6±5.5 kg and 8.4±4.1 kg, respectively (P=0.005). Women with GDM had more extended hospital stays (4.9±4.6 days vs 3.0±1.7 days; p=0.018) than those without GDM.

The GDM group was more likely to be affected by pregnancy-induced hypertension and preeclampsia (P<0.05). Moreover, the mean gestational age at delivery was 37.7±0.9 weeks for the GDM group and 38.4±1.9 weeks for the non-GDM group. This indicates that women with GDM tend to give birth earlier than those without (P=0.05). A higher percentage of women with GDM than those without GDM underwent cesarean delivery (52.6% vs. 28.9%). In women with GDM, induction of labor was more common during vaginal type of delivery (P<0.05). There was no statistically significant difference between the GDM and non-GDM groups in preterm delivery and cesarean delivery (elective and emergency).Table 2 shows neonatal outcomes by GDM status. Regarding the sex, 61.8% (n=47) were boys and

Table 1. Maternal demographics and outcomes by GDM status, Ulaanbaatar, Mongolia

Variables	Total Mean±SD or n (%)	GDM Mean±SD or n (%)	Non-GDM Mean±SD or n (%)	P-value
Total	76 (100)	38 (50%)	38 (50%)	
Maternal age (year)	35.05±3.8	35.03±3.8	35.08±3.9	0.95
Pre-pregnancy BMI (kg/m^2)	26.21±3.7	26.23±3.6	26.18±3.7	0.95
Gravidity	4.05±1.2	4.26±1.3	3.84±1.5	0.14
Parity	2.29±1.0	2.24±1.0	2.34±0.9	0.65
Hospital of Birth				
Urguu maternity hospital	15(19.7)	9(23.7)	6(19.7)	
Khuree maternity hospital	16(21.1)	8(21.1)	8(21.1)	
Amgalan maternity hospital	20(26.3)	9(23.7)	11(28.9)	
National Center for Mothers and Newborn II	6(7.9)	3(7.9)	3(7.9)	
National Center for Maternal and Child Health	19(25.0)	9(23.7)	10(26.3)	
Gestational weight gain (kg)	9.9±5.1	11.6±5.5	8.4±4.1	0.005
Pregnancy-Induced hypertension	12(15.8)	10(26.3)	2(5.3)	0.012
Preeclampsia	15(19.7)	11(28.9)	4(10.5)	0.044
Length of hospital stay (day)	4.0±3.6	4.9±4.6	3.0±1.7	0.018
Gestational age at delivery (week)	38.0±1.5	37.7±0.9	38.4±1.9	0.050
Preterm delivery (<37 week)	17(22.7)	10(27.0)	7(18.4)	0.373
Type of labor				0.036
Vaginal	45(59.2)	18(47.4)	27(71.1)	
Cesarean	31(40.8)	20(52.6)	11(28.9)	
Cesarean delivery				0.320
Elective	15(48.4)	11(55.0)	4(36.4)	
Emergency	16(51.6)	9(45.0)	7(63.6)	
Induction of labor	32(65.3)	16(84.2)	16(53.3)	0.027

**Based on Chi-Squared or T-test; N/A, not available*
**BMI Body Mass Index; GDM gestational diabetes mellitus; SD Standard Deviation*

38.2% (n=29) were girls. Mean birthweight and birth length in the GDM and the non-GDM group were 3s670.7±572.9 g and 52.0±2.7cm; 3386 ±590.2 g and 50.6±2.9 cm, respectively. 1-min Apgar Score was lower in the GDM group than in the non-GDM group (P<0.05). There was no statistically significant difference between the GDM and non-GDM groups in macrosomia or 5-min Apgar scores (P>0.05).Table 3 used univariate and multivariate logistic regression models to determine the association between women with gestational diabetes mellitus (GDM) and delivery outcomes. According to univariate analysis, women with GDM had a significantly higher risk of developing pregnancy-induced hypertension, cesarean delivery, and labor induction compared to women without GDM. The results remained significant after adjusting for maternal age and pre-pregnancy BMI. No statistically significant associations were found between GDM and preterm delivery, macrosomia, or neonatal complications. On multivariate analysis, the risk of cesarean delivery was 2.83 times higher in women with GDM than in the non-GDM group (adjusted OR [aOR] =2.83, 95% confidence interval [CI] =1.07-7.47). Women with GDM had a 6.9 times higher risk of developing pregnancy-induced hypertension than those without gestational diabetes mellitus (aOR=6.91, 95% confidence interval [CI]=1.35-35.23). The probability of labor-induced childbirth

Table 2. Neonatal outcomes by GDM status

Outcomes	Total Mean±SD or n (%)	GDM Mean±SD or n (%)	Non-GDM Mean±SD or n (%)	P-value
Newborn gender				0.813
Boy	47(61.8)	24(63.2)	23(60.5)	
Girl	29(38.2)	14(36.8)	15(39.5)	
Birth length (cm)	51.3±2.9	52.0±2.7	50.6±2.9	0.045
Birthweight (g)	3528.6±595.1	3670.7±572.9	3386.5±590.2	0.036
Macrosomia (≥4000g)	16(21.1)	10(26.3)	6(15.8)	0.260
1-min Apgar Score	6.8±0.4	6.7±0.4	6.9±0.5	0.031
5-min Apgar score	7.7±0.5	7.6±0.5	7.8±0.6	0.096
RDS	10(13.2)	6(15.8)	4(10.5)	

**Based on Chi-Squared, T-test*
**G gram; GDM gestational diabetes mellitus; SD Standard Deviation; RDS respiratory distress syndrome*

was 5.04 times higher in the GDM group than in the non-GDM group (aOR=5.04, 95% confidence interval [CI]=1.14-22.24). Moreover, increased age and pre-pregnancy BMI were correlated with cesarean delivery, preterm delivery, and neonatal complications but no significant association.

Discussion

Gestational diabetes is a common metabolic disorder that occurs during pregnancy and has significant adverse consequences for both the mother and fetus. An increasing number of studies have been conducted to investigate the risk factors associated with gestational diabetes mellitus, which have been linked to an increased risk of adverse fetal and neonatal outcomes such as macrosomia, neonatal hyperbilirubinemia, respiratory distress syndrome (RDS), hypoglycemia, birth injury, and perinatal mortality. Furthermore, gestational diabetes has been associated with maternal complications, including pregnancy-induced hypertension (PIH), cesarean delivery, and increased risk of type 2 diabetes later in life.[11,18,19] Therefore, in our study, we compared women with and without gestational diabetes according to their pre-pregnancy body mass index and age to investigate the complications of gestational diabetes during pregnancy and delivery.

Advanced maternal age and overweight/obesity are not the only risk factors for GDM. However, they are also associated with adverse pregnancy outcomes, including preterm birth, small for gestational age, macrosomia, preeclampsia, increasing cesarean rate, and pregnancy-induced hypertension.[20-22] The mean age of the women diagnosed with GDM in our study was 35.05±3.8 years (28-45 years old), which was higher than the results of Turki Gasim and Bhat Mamta, et al.'s study, the mean age was 32.4±7.5 years and 26.63±4.54 years, respectively.[23,24] The mean pre-pregnancy body mass index (BMI) of the women diagnosed with gestational diabetes in our study was 26.23±3.68 kg/m2, which indicates that being overweight and obese in pre-pregnancy may be a development for gestational diabetes during pregnancy. According to a study by Tahmineh Ezazi Bojnordi, the mean pre-pregnancy body mass index (BMI) was 25.74 ± 4.73 kg/m2 in GDM women.[25] Shin, et al. analyzed 219868 pregnant women from the Pregnancy Risk Assessment Monitoring System (PRAMS) between 2004 and 2011. This study showed that a high pre-pregnancy BMI (obese) increased the risk of gestational diabetes, pregnancy-induced hypertension, and large-for-gestational age.[26] These results are similar to those of the present study.

The World Health Organization (WHO) suggests that the ideal cesarean delivery rate for all countries is between 10% and 15%.[27,28] According to research from the WHO, the prevalence of cesarean delivery was 21.1% in 2018 (1 in 5 of all childbirths) and is continuously increasing worldwide.[29] The global rate of cesarean sections has significantly increased from approximately 7% in 1990 to 21% today. Calculations show that this trend

Table 3. Correlation between delivery outcomes and GDM, Ulaanbaatar, Mongolia, 2022

Delivery outcome variables	cOR*	CI	P value	aOR&	CI	P-value
Cesarean delivery						
Age	1.07	0.94-1.21	0.291	1.06	0.93-1.20	0.383
Pre-pregnancy BMI	1.1	0.96-1.25	0.58	1.09	0.95-1.25	0.202
GDM	2.72	1.06-7.03	0.38	2.83	1.07-7.47	0.035
Preterm delivery						
Age	1.04	0.91-1.20	0.562	1.11	0.95-1.30	0.168
Pre-pregnancy BMI	1.12	0.96-1.30	0.143	1.02	0.89-1.18	0.738
GDM	1.64	0.55-4.90	0.376	1.65	0.54-5.03	0.377
Macrosomia						
Age	0.91	0.79-1.06	0.247	0.89	0.76-1.04	0.143
Pre-pregnancy BMI	1.14	0.98-1.34	0.089	1.17	0.99-1.34	0.055
GDM	1.91	0.61-5.91	0.265	1.93	0.59-6.25	0.272
Neonatal complications						
Age	1.13	0.95-1.35	0.176	1.12	0.94-1.34	0.208
Pre-pregnancy BMI	1.06	0.89-1.27	0.511	1.04	0.86-1.25	0.689
GDM	1.59	0.41-6.17	0.5	1.64	0.41-6.51	0.48
Induction of labor						
Age	0.87	0.74-1.03	0.101	0.86	0.71-1.03	0.096
Pre-pregnancy BMI	0.99	0.84-1.16	0.883	1.02	0.85-1.22	0.868
GDM	4.67	1.12-19.43	0.034	5.04	1.14-22.24	0.033
Pregnancy-Induced hypertension						
Age	0.86	0.72-1.03	0.096	0.84	0.69-1.02	0.085
Pre-pregnancy BMI	0.99	0.84-1.17	0.933	1.01	0.84-1.21	0.92
GDM	6.43	1.30-31.73	0.022	6.91	1.35-35.23	0.02
Preeclampsia						
Age	0.98	0.85-1.14	0.833	0.97	0.83-1.14	0.729
Pre-pregnancy BMI	1.07	0.92-1.25	0.36	1.08	0.92-1.27	0.333
GDM	3.46	0.99-12.10	0.052	3.49	0.99-12.03	0.052

**Binary Logistic Regression, &adjusted for maternal age and pre-pregnancy BMI*
**GDM, gestational diabetes mellitus*

will continue for the next ten years. The cesarean section rate in Mongolia increased by 25.4% in 2016, to 25.8% in 2018, and 26.4% in 2020.[30-32] The prevalence of cesarean delivery is strongly associated with GDM in pregnant women. The Cesarean delivery rate in pregnant women with GDM ranges from 50.8 to 59.9%.[33,34] Eshetu, et al. reported that the cesarean rate was 57.8% in diabetic women.[35] Our study showed similar results, with a cesarean delivery rate of 52.6%. Moreover, according to a study by Oleirich, et al. in 2019, the cesarean section rate in patients with GDM was 40.3% (aOR 1.25, 95% CI 1.18-1.31), which was lower than our result.[36]

This study found that women with GDM were not only at an increased risk of preeclampsia but also 6.9 times at a high risk of pregnancy-induced hypertension. Pregnancy-induced hypertension, often referred to as gestational hypertension, is a condition in which women who are previously normotensive experience high blood pressure after 20 weeks of gestation.[37,38] Preeclampsia is a common condition during pregnancy that is distinguished

by the onset of hypertension and the presence of protein in the urine.[39] This result is consistent with those of several other studies that have reported that GDM increases the risk of PIH and preeclampsia. A study conducted in Eastern Ethiopia found that mothers with gestational diabetes mellitus (GDM) were three times more likely to develop preeclampsia than those who did not have GDM.[40]

Moreover, according to Ajazi, women with GDM are 2.37 more likely to develop preeclampsia compared to non-GDM.[41] The results of this study were lower than those of the current study. In contrast, gestational diabetes, pregnancy-induced hypertension, and preeclampsia are common complications that can occur during pregnancy; however, their relationship is not fully understood. Moreover, women with PIH should be screened for OGGT to detect gestational diabetes mellitus.[42]

Labor induction was more common in women with GDM than in those without GDM in our study. In a study by the Indian researcher Bhat Mamta, et al. 58.7% of women with gestational diabetes were induced to give birth.[24] Moreover, a study conducted on Saudi women with GDM demonstrated that women with GDM had 2.7 times more GDM than the control group. [23] These results were lower than ours. In this study, 26.3% of the women with GDM had a newborn weight of > 4000 g. According to Gasim, et al. 12.7% of women with GDM had newborn macrosomia.[23] Other studies have shown that 12.7% and 6.2% of women with GDM had newborn macrosomia, respectively.[23, 43] These results were lower than our study.[23], 43 The results of these studies may be lower than ours because of the small sample size. Howard Berger, et al. investigated the timing of labor among pregnant women with diabetes mellitus. They concluded that induction of labor in gestational diabetes and pre-gestational diabetes pregnancies can prevent stillbirth, excessive fetal growth, and some potential complications. So, in our study, labor induction is required more frequently in the GDM group.[44]

This study has several limitations. First, the sample size was small. Second, we extracted maternal and newborn information from clinical records; therefore, there was a limitation on newborn complications, including hypoglycemia and serum bilirubin levels, etc. Moreover, the long-term prognosis of mothers and children has yet to be studied. In the future, research is needed to investigate whether women with gestational diabetes are transitioning to type 2 diabetes and the complications that may arise in infants.

Conclusion

Women with gestational diabetes mellitus (GDM) have more pregnancy complications, including pregnancy-induced hypertension, preeclampsia, labor-induced childbirth, and cesarean delivery, than women without GDM in Mongolia. Therefore, we recommend that our country should screen for GDM during pregnancy in order to identify and manage it early.

Conflict of Interest

The authors declare no conflicts of interest.

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