Pregnancy Outcomes in Young Women With Youth-Onset Type 2 Diabetes Followed in the TODAY Study

TODAY Study Group*

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OBJECTIVE

To assess pregnancy outcomes in young women with youth-onset type 2 diabetes followed in the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study.

RESEARCH DESIGN AND METHODS

Pregnancy information (outcome and any maternal or fetal complications) was obtained from the female participants by self-report. Additionally, medical records for the pregnancy and the child's neonatal course were obtained with data abstracted into standardized forms.

RESULTS

Over a maximum of 15 years, 260 pregnancies were reported by 141 women (aged 21.5 ± 3.2 years, BMI 35.6 ± 7.2 kg/m^2, and diabetes duration 8.1 ± 3.2 years). Contraception use prior to pregnancy was reported by 13.5% of the women. Complications were reported by 65% of the women during their pregnancy. Pregnancy loss was observed in 25.3% and preterm birth in 32.6% of pregnancies. HbA_{1c} ≥8% was observed in 31.9% of the pregnancies, and 35% of the pregnancies were complicated by chronic hypertension. Nephropathy prior to pregnancy was observed in 25% of the women. In the offspring, 7.8% were classified as small for gestational age, 26.8% large for gestational age, and 17.9% in the macrosomic range.

CONCLUSIONS

Based on observations from the TODAY cohort, young women with pregestational, youth-onset type 2 diabetes had very high rates of maternal complications stemming from significant socioeconomic disadvantage. The substantial maternal and infant complications seen in these young moms could potentially be avoided with improved contraception rates and reproductive planning.

With the increase in youth-onset type 2 diabetes (1), the number of pregnancies in women complicated by preexisting type 2 diabetes is increasing (2). From 2000 to 2010, the prevalence of pregestational diabetes (including type 2 diabetes) increased by 37% (3). According to the most recent report by the Centers for Disease Control and Prevention (CDC) in 2016, the national prevalence of

Corresponding author: Kimberly L. Drews, today@bsc.gwu.edu

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**Members of the TODAY Study Group Writing Committee are listed in the APPENDIX. A complete list of the TODAY Study Group members can be found in the supplementary material online.*

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pregestational diabetes during pregnancy (type 1 diabetes and type 2 diabetes) was 0.9% (4).

Diabetes during pregnancy has long been associated with morbidity in the mother and offspring, as well as infant mortality. While gestational diabetes is the most common form of diabetes during pregnancy (4), pregestational diabetes has been associated with worse outcomes for both the mother and her offspring (5,6), with type 1 and type 2 diabetes having equal contributions to pregestational diabetes (7). With the overall increase in the incidence of type 2 diabetes, especially in youth, the percentage of pregnancies affected by type 2 diabetes has increased ~85% over an 8-year period (8). Type 2 diabetes during pregnancy has been associated with increased risk for adverse outcomes (9,10). Perinatal mortality in infants born to mothers with adult-onset type 2 diabetes has been reported to be approximately fourfold higher than in infants born to mothers with type 1 diabetes (11).

Few studies have examined the impact of youth-onset type 2 diabetes during pregnancy on maternal and fetal outcomes. In prior reports of pregestational diabetes in pregnancy, the average age of the women at pregnancy onset ranges from 33 to 36 years, with a diabetes duration averaging ~5 years (11,12). The Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study was a multisite intervention study designed to examine the effectiveness of varying approaches to diabetes management on maintenance of glycemic control, followed by an observational follow-up through early adulthood to understand the long-term outcomes of youth-onset type 2 diabetes (13). The TODAY study offers a unique opportunity to understand the impact of type 2 diabetes in women who are younger, with a longer duration of diabetes. We previously reported pregnancy outcomes from the intervention phase of the trial, in which participants' mean maternal age was 18.4 years with a mean diabetes duration of 3.17 years at the time of the first pregnancy (14). The initial report included 63 pregnancies in 46 women in TODAY. In 53 pregnancies with available outcomes, 22.4% of the pregnancies resulted in pregnancy loss. Stillbirth was reported in two pregnancies. Of the 39 live-born infants during the trial, 15% were born preterm and 20.5% were born with a major congenital anomaly.

Since the initial report (14), pregnancy data for an additional 197 pregnancies have been collected prospectively to allow assessment of maternal pregnancy complications and expanded perinatal complications in the offspring in a more structured fashion. Given that more participants in the TODAY cohort experienced glycemic failure (15) since the initial report, it was expected that the prevalence of pregnancy and perinatal complications would increase as a result of worse glycemia; thus, the purpose of the current analysis was to assess pregnancy and perinatal complications associated with preexisting youth-onset type 2 diabetes in women (median age 22.3 years, minimum 14.5 years, and maximum 30.4 years) from the TODAY cohort and their offspring.

RESEARCH DESIGN AND METHODS

The TODAY study has been previously described in detail (16). The study included 699 participants 10–17 years of age diagnosed with type 2 diabetes using prevailing American Diabetes Association criteria, with illness duration of ≤2 years at the time of enrollment (17). Other inclusion criteria included BMI ≥85th percentile for age and sex and confirmed type 2 diabetes (for <2 years' duration) based on fasting C-peptide >0.6 ng/mL and absence of pancreatic autoantibodies (17). Participants were randomized to one of three treatment arms—metformin alone, metformin with rosiglitazone, or metformin plus a lifestyle intervention program—and followed longitudinally for 2–6 years. The primary outcome of the trial was time to treatment failure, defined as a persistently elevated HbA_{1c} (≥8%) over a period of 6 months or inability to wean from insulin after metabolic decompensation. An observational follow-up study (TODAY2) was conducted in two phases. During the first phase, participants were transitioned to standard diabetes care with metformin and insulin if needed for glycemic control. In the second phase of the observational study, all participants were transitioned to local providers within their communities, but continued to have annual visits to collect serum and urine samples, assess microvascular and macrovascular complications, and conduct structured interviews to capture demographic and health information data.

Of the 699 participants, 452 (64.7%) of the cohort were female (16). In the initial phase of the trial, counseling was provided to all females regarding the risks of rosiglitazone use during pregnancy; consent for the study required the use of adequate contraception. Additionally, the female participants were counseled on the risk of pregnancy loss and fetal malformations associated with poor glucose control throughout all phases of the study.

Pregnancy information, including outcome and any maternal or fetal complications, was obtained prospectively from the female participants by self-report at regularly scheduled study visits, which occurred every 3–6 months in the initial phase of the trial and annually in the second phase of the trial. Additionally, participants provided consent to obtain the pregnancy records for the pregnancy, birth, and the baby, from which data were abstracted into standardized forms for reporting maternal and infant health outcomes; medical records were available for review in 97% of the pregnancies reported. All medical records were reviewed and the data abstracted from the records used for analysis. In cases in which a discrepancy arose between the subject report and the record, the medical record information was used for the data collection. Information on mode of delivery (cesarean sections) was only captured from 2014 to 2020. Pregnancy was defined as a reported or documented positive urine pregnancy test.

For maternal pregnancy outcomes, miscarriage was defined as pregnancy loss at <20 weeks, and stillbirth defined as pregnancy loss during or after 20 weeks' gestation in which the infant was not live-born. Pregnancy losses with undetermined gestational age at the time of the loss were classified as unknown losses. Maternal hospitalization was defined as any hospitalization other than a scheduled delivery. Women were considered to have preeclampsia based on stated diagnosis by a physician documented within the medical records reviewed. Hypertension was defined as use of medications, consecutive measures ≥130 mmHg systolic and/or ≥80 mmHg

diastolic, or stated diagnosis per the physician notes. Those with documented hypertension prior to pregnancy during analysis were subtracted from the total number with hypertension to determine the number women with gestational hypertension. Microalbuminuria was defined as urine albumin-to-creatinine ratio >30 mg/g on two occasions prior to the pregnancy. Macroalbuminuria was defined as one urine albumin-to-creatinine ratio >300 mg/g prior to pregnancy. Micro- and macroalbuminuria during pregnancy excludes women diagnosed prior to the pregnancy. HbA_{1c} >8% was defined as one elevated value at any point in the pregnancy. Documentation of the diagnosis by a physician in the medical records also was sufficient to meet the criteria for these conditions.

Preterm deliveries were classified as delivery of a live infant between 20 and 37 weeks' gestation and term as ≥37 weeks' gestation. Very low birth weight was defined as <1,500 g, low birth weight 1,500–2,499 g, normal birth weight 2,500–3999 g, and macrosomia as ≥4,000 g, according to the World Health Organization standards. Birth weight classification was described as small for gestational age (SGA) (<10th percentile), appropriate for gestational age (10–90th percentiles), and large for gestational age (LGA) (>90th percentile) adjusted for infant sex and race, according to the criteria established by Alexander et al. (18). For neonatal complications such as hypoglycemia and respiratory distress, physician documentation within the medical record was the criteria used to define these conditions.

Statistical Analysis

Prevalence of adverse maternal and fetal outcomes is reported based upon all pregnancies, known outcomes, or live births. Descriptive statistics reported are frequencies, percentages, means, and SDs. Comparisons between groups for continuous variables were conducted using two-sided *t* tests when the assumption of approximate normality was satisfied and using the Wilcoxon rank sum test otherwise. For noncontinuous outcomes, χ^2 tests or Fisher exact tests were used to compare groups. *P* values <0.05 were considered statistically significant. Given the descriptive and exploratory nature of the analysis, no adjustments were made for multiple comparisons for overall testing; however, Bonferroni adjustments were used for pairwise comparisons when the overall test indicated statistical significance. Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

In the 15 years of the combined TODAY study data collection, 260 pregnancies were reported by 141 young women (Supplementary Fig. 1). Baseline characteristics were similar between the women who reported pregnancies and those who did not, with the exception that those reporting a pregnancy had lower household income at baseline with a higher proportion of non-Hispanic Black race/ethnicity (Supplementary Table 1).

A full description of the cohort is contained in Table 1. The average age at first pregnancy was 20.5 ± 3.2 years with an average duration of diabetes prior to the pregnancy of 7.3 ± 3.4 years. Overall, the non-Hispanic Black group accounted for the most pregnancies. The majority of participants who experienced a pregnancy came from a low-income household, with 62.1% having an income <$25,000. Educational attainment was also low for the women who experienced a pregnancy, with 22.7% having less than a high school education and 54% having only a high school degree or equivalent. Prior to first pregnancy, 36.9% of the women had hypertension, and 24% had diabetic nephropathy. Preconception counseling was reported in 16.3% of women prior to first pregnancy, and only 14.9% used any method of contraception prior to the first pregnancy. In comparing women with different reported numbers of pregnancies, no difference was appreciated in any of the measures.

Maternal complications were experienced in 65% of the reported pregnancies. In women with gestation ≥20 weeks, hospitalization at some point in the pregnancy not directly linked to delivery was reported in 35.3% of the young women (Table 1). Preeclampsia was the most common complication, reported in 20.1% of pregnancies, followed by hypertension in 16.8%. An HbA_{1c} >8% was documented on at least one occasion in 31.9% of pregnancies. Of the 174 pregnancies resulting in live birth, 73.9% of the women received insulin for glycemic control during the pregnancy, with 20.1% reporting use of metformin during the pregnancy. Only 6.5% of the women with gestation ≥20 weeks received therapy with acetylsalicylic acid for preeclampsia prophylaxis. Antihypertensive therapy was used by 15.8% of the women with gestation ≥20 weeks.

A full-term delivery was achieved in 62.5% of pregnancies, with 32.6% of pregnancies resulting in preterm delivery in pregnancies ≥20 weeks' gestation (Table 1). The rate of known miscarriage for the entire study was 12.3%. The rate of known stillbirth in the cohort was 3%. Approximately 10% of pregnancy loss could not be classified due to inadequate records related to the timing of the loss. The HbA_{1c} was significantly higher in pregnancies complicated by miscarriage and preterm delivery compared with full-term deliveries (Supplementary Table 2).

The average birth weight for the entire offspring cohort was 3.201 ± 0.847 kg, with an overall birth weight *z*-score (adjusted for gestational age and sex) of −0.329 ± 0.847 (Table 2). The overall negative *z*-score was driven by very low birth weight *z*-scores in the preterm infants (Supplementary Fig. 2). In the offspring, 7.8% were classified as SGA, while 26.8% were classified as LGA. Macrosomia was reported in 17.9% of the infants.

The offspring complication reported most frequently was neonatal hypoglycemia, affecting 29.4% of infants overall and 42.2% in preterm births (Table 3). Cardiac anomalies were found in 10% of infants. Respiratory distress affected 18.6% of infants, again with higher frequency in those born preterm. Other complications and congenital anomalies were noted in 10% of infants, including anencephaly, renal anomalies, and complications related to prematurity. Neonatal hypoglycemia, respiratory distress, and cardiac anomalies were associated with suboptimal glycemic control (as evidenced by a documented HbA_{1c} >8%) during pregnancy ($P < 0.05$) (Table 4).

CONCLUSIONS

In the 15 years encompassing all phases of the TODAY study, young women have reported 260 total pregnancies, making it the largest collection of pregnancy outcomes in a multiethnic cohort of

Table 1—Characteristics at the start and during pregnancy and pregnancy outcome

	All (*N* = 260)				Gestation ≥20 weeks (*N* = 184)			
		Pregnancy order				Pregnancy order		
	All	1 (*N* = 141)	2 (*N* = 71)	≥3 (*N* = 48)	All	1 (*N* = 98)	2 (*N* = 55)	≥ 3 (*N* = 31)
Characteristics at start of pregnancy								
Age (years)	21.5 (3.16)	20.5 (3.08)	22.1 (2.65)	23.7 (2.79)	21.6 (3.09)	20.5 (3.04)	22.2 (2.57)	24.0 (2.46)
Diabetes duration (years)	8.1 (3.20)	7.3 (3.37)	8.4 (2.78)	9.9 (2.48)	8.0 (3.22)	7.2 (3.47)	8.4 (2.80)	9.6 (2.36)
BMI*	35.6 (7.16)	35.4 (7.17)	36.0 (7.26)	35.9 (7.11)	35.5 (6.97)	35.3 (6.70)	35.8 (7.70)	35.6 (6.75)
Race/ethnicity								
Non-Hispanic Black	39.2	41.9	43.8	41.2	38.0	40.8	36.4	32.3
Hispanic	29.6	34.9	18.8	29.4	29.3	30.6	30.9	22.6
Non-Hispanic White	15.0	9.3	18.8	5.9	16.8	16.3	14.5	22.6
Other	16.2	14.0	18.8	23.5	15.8	12.2	18.2	22.6
Income*								
<$25,000	62.1	62.9	57.4	66.7	64.1	64.8	58.7	71.4
$25,000–49,999	4.7	4.8	3.3	6.7	3.4	4.2	2.2	3.6
≥$50,000	0.9	0.0	1.6	2.2	0.0	0.0	0.0	0.0
Refused/unknown	32.2	32.4	37.7	24.4	32.4	31.0	39.1	25.0
Education (%)*								
Less than high school	22.7	26.7	16.4	22.2	23.4	26.8	17.4	25.0
High school degree or equivalent	54.0	49.5	55.7	62.2	55.2	52.1	54.3	64.3
Some college	2.8	1.9	1.6	6.7	0.7	0.0	0.0	3.6
College degree or higher	3.8	5.7	3.3	0.0	4.1	5.6	4.3	0.0
Refused/unknown	16.6	16.2	23.0	8.9	16.6	15.5	23.9	7.1
HbA_{1c} (%)*	8.7 (2.78)	8.9 (2.80)	8.6 (2.82)	8.1 (2.65)	8.3 (2.60)	8.4 (2.58)	8.3 (2.70)	8.0 (2.54)
HbA_{1c} (mmol/mol)*	71.6 (30.41)	74.1 (30.59)	70.5 (30.77)	65.3 (28.96)	67.5 (28.41)	68.7 (28.17)	68.7 (28.17)	63.5 (27.78)
Diabetes complications and comorbidities*								
Hypertension	35.0	36.9	36.6	27.1	34.2	34.7	40.0	22.6
Microalbuminuria	25.0	24.1	29.6	20.8	27.2	24.5	34.5	22.6
Macroalbuminuria	7.3	5.7	8.5	10.4	7.6	5.1	10.9	9.7
LDL dyslipidemia	17.7	14.2	22.5	20.8	17.4	12.2	25.5	19.4
Triglyceride dyslipidemia	35.4	31.2	42.3	37.5	35.9	30.6	47.3	32.3
Preconception counseling	20.0	16.3	22.5	27.1	23.9	21.4	25.5	29.0
Contraception	13.5	14.9	12.7	10.4	14.1	15.3	12.7	12.9
Gestational age prenatal care initiated (weeks)	10.6 (8.73)	11.3 (9.60)	9.2 (5.43)	10.6 (9.78)	11.1 (9.13)	11.9 (10.05)	9.4 (5.57)	11.2 (10.51)
Characteristics during pregnancy								
Medications during pregnancy								
Prenatal vitamins	78.1	78.0	77.5	79.2	93.5	96.9	89.1	90.3
Metformin	21.9	22.0	23.9	18.8	20.1	21.4	21.8	12.9
Insulin	67.3	71.6	67.6	54.2	73.9	79.6	72.7	58.1
Sulfonylurea	5.0	4.3	4.2	8.3	7.1	6.1	5.5	12.9
Other diabetes medications	0.8	1.4	0.0	0.0	1.1	2.0	0.0	0.0
Statins	0.4	0.0	1.4	0.0	0.0	0.0	0.0	0.0
ACE inhibitors	4.2	5.0	4.2	2.1	3.3	4.1	3.6	0.0

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Table 1—Continued

	All (*N* = 260)				Gestation ≥20 weeks (*N* = 184)			
		Pregnancy order				Pregnancy order		
	All	1 (*N* = 141)	2 (*N* = 71)	≥3 (*N* = 48)	All	1 (*N* = 98)	2 (*N* = 55)	≥ 3 (*N* = 31)
Other antihypertensive medications	8.8	9.2	11.3	4.2	12.5	13.3	14.5	6.5
Acetylsalicylic acid	4.6	3.5	7.0	4.2	6.5	5.1	9.1	6.5
Maternal hospitalization	27.7	31.2	22.5	25.0	35.3	39.8	29.1	32.3
Preeclampsia	14.2	14.2	16.9	10.4	20.1	20.4	21.8	16.1
Maternal hypertension#	11.9	10.6	14.1	12.5	16.8	15.3	18.2	19.4
Microalbuminuria (30 mg/g ≤ UACR < 300 mg/g)#	7.7	12.1	4.2	0.0	10.9	17.3	5.5	0.0
Macroalbuminuria/proteinuria (UACR ≥300 mg/g)#	5.0	7.8	2.8	0.0	6.5	10.2	3.6	0.0
HbA_{1c} >8.0% (64 mmol/mol)	31.9	30.5	32.4	35.4	32.1	31.6	30.9	35.5
Other complications**	4.6	5.7	2.8	4.2	6.0	8.2	3.6	3.2
Pregnancy outcome								
Unknown outcome	3.4	5.0	1.4	0.0	0.0	0.0	0.0	0.0
Voluntary or elective termination	4.8	3.5	8.5	4.2	0.5	0.0	1.8	0.0
Preterm delivery	23.8	21.3	26.8	22.9	32.6	30.6	34.5	35.5
Term delivery	42.8	44.7	45.1	41.7	62.5	64.3	58.2	64.5
Miscarriage or fetal death (stillbirth)	25.3	25.5	18.3	31.3	4.3	5.1	5.5	0.0
Unknown pregnancy loss	9.3	8.5	7.1	16.7	0.0	0.0	0.0	0.0
Fetal death (stillbirth)	3.7	3.5	4.2	0.0	4.3	5.1	5.5	0.0
Miscarriage	12.3	13.5	7.0	14.6	0.0	0.0	0.0	0.0

Data are mean (SD) or percent. UACR, urine albumin-to-creatinine ratio. *Data are as of the visit prior to start of pregnancy other than age and diabetes duration. **Other complications included heart failure, tachycardia, twin-to-twin transfer syndrome, and placenta abruption. #Does not include participants with preexisting diagnosis. ##Pregnancy order for all pregnancies, not just pregnancies of at least 20 weeks' gestation.

women with pregestational youth-onset type 2 diabetes. Furthermore, the women in TODAY had longer average diabetes duration at the time of pregnancy than other cohorts involving preestational type 2 diabetes (11,12,19,20). The women in TODAY uniquely demonstrate significant socioeconomic disadvantage, high BMI, and suboptimal glycemic control, along with very low rates of contraceptive use and preconception counseling. These pregnancy outcomes from TODAY extend our previous findings to demonstrate that pregnancy and offspring complications are common in young women with type 2 diabetes and have increased significantly from the previous report (14).

The average age at first pregnancy in the TODAY cohort was 21.6 years compared with the national average in the U.S. of 29.1 years (21) and the averages in Sub-Saharan Africa and Latin America of 20.9 and 21.7 years, respectively (22). Relative socioeconomic disadvantage in the young women in TODAY contributes to inadequate contraceptive use and preconception counseling, as evidenced by the high rates of suboptimal glycemic control during pregnancy, leading to adverse pregnancy outcomes.

Maternal complications during pregnancy, including hypertension and preeclampsia, are more common in women who have pregestational diabetes (23). The rates of maternal chronic hypertension in the TODAY cohort were almost triple those most recently reported in the National Pregnancy in Diabetes (NPID) cohort, a population-based cohort in the U.K., which included 8,685 women (median age of 34 years [range 27–41]) (7); however, the diabetes duration at time of pregnancy was over twice as long in the young women in TODAY. Maternal hypertension is a significant risk factor for preeclampsia, which affects ∼2–7% of all pregnancies and 10–14% of pregnancies complicated by pregestational type 2 diabetes (24). In TODAY, the prevalence of preeclampsia was 20.1%, which is more consistent with rates reported in pregnancies complicated by pregestational type 1 diabetes. This higher rate of preeclampsia in TODAY is perhaps related to the higher BMI, HbA_{1c}, and hypertension rates when compared with other cohorts with type 2 diabetes–exposed pregnancies (9,25,26).

Table 2—Live offspring characteristics

	Preterm (<37 weeks' gestation) (*N* = 64)		Term (≥37 weeks' gestation) (*N* = 115)		Overall (*N* = 179)	
	N	Mean ± SD or %	*N*	Mean ± SD or %	*N*	Mean ± SD or %
Infant sex						
Female	28	43.8	61	53.0	89	49.7
Male	36	56.3	54	47.0	90	50.3
Infant birth weight (kg)	63	2.759 ± 1.012	113	3.448 ± 0.619	176	3.201 ± 0.847
Birth weight *z*-score	63	−1.408 ± 2.386	113	0.273 ± 1.27	176	−0.329 ± 1.924
Birth weight percentile	63	31.9 ± 36.88	113	55.5 ± 33.57	176	47.0 ± 36.49
SGA (<10th percentile)*	7	10.9	7	6.1	14	7.8
LGA (>90th percentile)*	13	20.3	35	30.4	48	26.8
Birth weight categories						
Unknown	1	1.6	2	1.7	3	1.7
Very low (<1,500 g)	9	14.1	0	0	9	5.0
Low (1,500–2,499 g)	17	26.6	4	3.5	21	11.7
Normal (2,500–3,999 g)	30	46.9	84	73.0	114	63.7
Macrosomia (≥4,000 g)	7	10.9	25	21.7	32	17.9

*Based upon the criteria of Alexander et al. (18).

One of the most striking findings in the TODAY cohort was the high rate of pregnancy loss (25%), excluding elective terminations, compared with the national rate of uninduced pregnancy loss in the U.S. of 19.7% (27). Furthermore, stillbirth in TODAY (3.7%) is more than triple the national rates reported by the CDC (1%) (28). The U.K. NPID cohort reported stillbirth in women with type 2 diabetes at 1.3% (7), while other groups reported rates similar to those in TODAY (19). However, in the NPID cohort, the mean HbA_{1c} was 6.9% in the first trimester and 6.0% in the third trimester (7); therefore, the higher average glycemia during pregnancy in TODAY, a likely consequence of very low rates of preconception counseling, may explain the higher rates of stillbirth.

Preterm birth was documented in ∼33% of the pregnancies in TODAY, which is more than triple that in the general U.S. population (9.5%) per the most recent CDC report (21) and higher than reported in NPID (23.4%) (7). The high rates of maternal complications, including preeclampsia and hypertension as well as inadequate glycemic control, prior to contraception significantly contribute to the high rate of preterm births.

In TODAY, 7.8% of the infants were classified as SGA, while 26.8% were LGA, compared with national averages of 1.5% (29) and ∼9% (30), respectively. These rates may be underreported as they are based on World Health Organization guidelines, which have demonstrated underreporting of SGA, especially in preterm infants. Rates of LGA and SGA in TODAY were similar to women from the NPID cohort with type 2 diabetes (7). Within the NPID cohort, risk factors associated with LGA included third trimester HbA_{1c} and younger age (7). In TODAY, the high rates of chronic hypertension combined with inadequate prepregnancy counseling leading to hyperglycemia, specifically later in pregnancy, may have had the greatest impact on birth weight (31).

Diabetes during pregnancy is also known to be associated with risks of morbidity in infants, including perinatal complications. One of the greatest risks is hypoglycemia due to neonatal hyperinsulinemia (32). The rate of hypoglycemia in the infants born during the TODAY follow-up study—approaching 30%—almost doubled from the initial report by Klingensmith et al. (14). While the percentage of young women with HbA_{1c} ≥8% is similar between the two reports, prenatal records were not as

Table 3—Number and type of offspring complications for live births overall and by term status

	Preterm (*N* = 64)	Term (*N* = 115)	*P* value	Overall (*N* = 179)
Neonatal hypoglycemia	27 (42.2)	25 (22.1)	0.0049	52 (29.4)
Respiratory distress requiring surfactant or ventilation	23 (35.9)	10 (8.9)	<0.0001	33 (18.6)
Neonatal hypocalcemia*	4 (6.3)	3 (2.7)	0.2609	7 (4.0)
Shoulder dystocia*	3 (4.7)	2 (1.8)	0.3551	5 (2.8)
Cardiac anomaly	12 (18.8)	6 (5.4)	0.0048	18 (10.2)
Other congenital anomalies#	10 (15.6)	8 (7.3)	0.0811	18 (10.3)

Data are *N* (%) unless otherwise indicated. **P* value from Fisher exact test. #Other congenital anomalies include anencephaly, congenital hemivertebra, multicystic dysplastic kidney, butterfly vertebra, asymmetrical crying face, duplex ureters, pelvic kidney, and macroglossia.

Table 4—Complications and outcomes by glycemic control (HbA_{1c} ≤8% vs. >8%) during pregnancy as extracted from obstetric chart

	During pregnancy loss of glycemic control				
	HbA_{1c} ≤8%#		HbA_{1c} >8%#		
	N	%	*N*	%	*P* value
Maternal	121		59		
Hospitalization	37	30.6	27	45.8	0.0458
Preeclampsia	17	14.1	19	32.2	0.0043
Gestational hypertension	20	23.3	11	33.3	0.2622
Microalbuminuria (30 mg/g ≤ UACR < 300 mg/g)*	6	6.12	4	12.9	0.2512***
Macroalbuminuria/proteinuria (UACR ≥300 mg/g)*	8	6.84	4	8.51	0.7441***
Other complications	8	6.61	3	5.08	1.0000***
Neonatal	117		59		
SGA (<10th percentile)**	8	6.9	5	8.8	0.7606***
LGA (>90th percentile)**	29	25.0	19	33.3	0.2499
Hypoglycemia	28	23.9	24	42.1	0.0140
Respiratory distress requiring surfactant or ventilation	16	13.7	16	28.1	0.0214
Hypocalcemia	3	2.6	4	7.1	0.2167***
Shoulder dystocia	2	1.7	3	5.3	0.3329***
Caudal regression	0	0.0	0	0.0	–
Cardiac anomaly	6	5.2	11	19.3	0.0033
Other congenital anomalies	10	8.6	7	12.7	0.4019

UACR, urine albumin-to-creatinine ratio. *Excludes participants with existing diagnosis. **Based upon the criteria of Alexander et al. (18). ***P value from Fisher exact test. #Equivalent to HbA_{1c} of 64 mmol/mol.

readily available for offspring in the earlier analysis, which may have resulted in underreporting of hypoglycemia cases. In adolescents with type 1 diabetes who experienced pregnancy, the reported rate of hypoglycemia was even higher, at 60.9% (33). Cardiac anomalies were also more prevalent in the infants born to mothers who experienced an HbA_{1c} ≥8% during their pregnancy. It is well established that cardiac anomalies are directly linked to hyperglycemia during pregnancy, particularly during organogenesis in the first trimester (34). The TODAY cohort is notable for inadequate contraceptive use, unplanned pregnancies, and later establishment of prenatal care, likely in part related to the significant psychosocial stressors in the lives of these young women and similar to adolescents with type 1 diabetes who experience pregnancy.

The present analysis has several strengths, including a well-characterized cohort of youth-onset type 2 diabetes with known duration of diabetes. While no data were collected directly by the study during the pregnancy, detailed medical records, including medical summaries and laboratory results, were systematically collected and abstracted. A few limitations are also acknowledged. The HbA_{1c} measures were not collected at consistent times during the pregnancy, making it difficult to determine the glucose control during each trimester. Also, some information from the earliest pregnancies, including mode of delivery, was missing. While every effort was made to obtain pregnancy records, they were not obtained in 20 pregnancies. Infant outcomes were also only obtained at birth; therefore, early neonatal deaths could not be ascertained.

In conclusion, the TODAY cohort demonstrated that young women with pregestational youth-onset type 2 diabetes demonstrate high rates of complications when compared with older women with pregestational type 2 diabetes, though the TODAY women had higher BMI and longer diabetes duration at the time of pregnancy. The inadequate glycemic control seen on average in this adolescent population with type 2 diabetes, combined with inadequate access to effective contraception and preconception counseling, likely contributes to the significant prenatal hyperglycemia and resulting complications. The key to improving pregnancy outcomes in young women with youth-onset type 2 diabetes is to aggressively and adequately treat the type 2 diabetes in youth and to identify barriers to adequate contraceptive use and access to prepregnancy counseling.

APPENDIX

Today Study Group Writing Committee. Jeanie B. Tryggestad (University of Oklahoma Health Sciences Center, Oklahoma City, OK), Megan M. Kelsey (University of Colorado Anschutz Medical Campus, Children's Hospital Colorado, Aurora, CO), Kimberly L. Drews (The Biostatistics Center, George Washington University, Rockville, MD), Steven D. Chernausek (University of Oklahoma Health Sciences Center, Oklahoma City, OK), Elia N. Escaname (UT Health San Antonio, San Antonio, TX), Elvira Isganaitis (Joslin Diabetes Center and Harvard Medical School, Boston, MA), Sarah Macleish (Rainbow Babies and Children's Hospital and Case Western Reserve University School of Medicine, Cleveland, OH), Siripoom McKay (Baylor College of Medicine, Houston, TX), Jennifer Sprague (Washington University School of Medicine, St. Louis, MO), and Steve Willi (Children's Hospital of Philadelphia, Philadelphia, PA).

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Author Contributions. J.B.T. wrote the manuscript. K.L.D. conducted the statistical analyses and wrote sections of the manuscript. M.M.K., K.L.D., S.D.C., E.N.E., E.I., S.Ma., S.Mc., J.S., and S.W. wrote sections of, reviewed, and edited the manuscript. K.L.D. is the guarantor of this work and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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