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What is the optimal gestational age for women with gestational diabetes type A1 to deliver?

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Abstract

OBJECTIVE—Gestational diabetes type A1 (A1GDM), also known as diet-controlled gestational diabetes, is associated with an increase in adverse perinatal outcomes such as macrosomia and Erb's palsy. However, it remains unclear when to deliver these women because optimal timing of delivery requires balancing neonatal morbidities from early term delivery against the risk of IUFD. We sought to determine the optimal gestational age (GA) for women with A1GDM to deliver.

STUDY DESIGN—A decision-analytic model was built to compare the outcomes of delivery at 37 through 41 weeks in a theoretical cohort of 100,000 women with A1GDM. Strategies involving expectant management until a later GA accounted for probabilities of spontaneous delivery, indicated delivery, and IUFD during each week. GA associated risks of neonatal complications included cerebral palsy, infant death, and Erb's palsy. Probabilities were derived from the literature, and total quality-adjusted life years (QALYs) were calculated. Sensitivity analyses were used to investigate the robustness of the baseline assumptions.

RESULTS—Our model showed that induction at 38 weeks maximized QALYs. Within our cohort, delivery at 38 weeks would prevent 48 stillbirths but lead to 12 more infant deaths compared to 39 weeks. Sensitivity analysis revealed that 38 weeks remains the optimal timing of delivery until IUFD rates fall below 0.3-fold of our baseline assumption at which expectant management until 39 weeks is optimal.

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CONCLUSION—By weighing the risks of IUFD against infant deaths and neonatal morbidities from early term delivery, the ideal GA for women with A1GDM to deliver is 38 weeks.

Keywords

gestational diabetes; induction; timing of delivery

Introduction

The prevalence of gestational diabetes mellitus (GDM) in the United States is now at approximately 6–7% of the population¹. GDM is on the rise in the United States in concert with the obesity epidemic, and this is concerning because pregnancies complicated by GDM have an increased risk of adverse perinatal outcomes². Studies have shown that women with GDM are more prone to preeclampsia, operative deliveries, and subsequent Type 2 diabetes mellitus. Furthermore, neonates born to mothers with GDM have an increased incidence of shoulder dystocia, macrosomia, hypoglycemia, hyperbilirubinemia, subsequent obesity, and impairment of glucose tolerance². Consequently, there is a higher prevalence of adverse newborn outcomes such as major neurodevelopmental disabilities, Erb's palsy, intrauterine fetal demise, and neonatal death.

Women with GDM undergo glycemic management in order to decrease the rates of these complications³. While some women are successfully managed with diet and exercise (A1GDM), others require medical therapy (A2GDM). In addition to interventions to achieve normal glucose levels and antenatal testing, women with A2GDM are generally delivered by 39 weeks gestation. However, women with A1GDM have much less consistent guidance regarding timing of delivery.

Numerous guidelines have been established on when to deliver women with various conditions or complications such as chronic hypertension, oligohydramnios, and placenta previa⁴. However, it remains unclear what is the ideal gestational age for women with A1GDM to deliver to minimize adverse outcomes for both the mother and the newborn⁵. For example, the most recent recommendations from the NICHD and ACOG do not recommend a specific gestational age other than to discourage delivery prior to 39 weeks' gestation. Therefore, the goal of our study was to perform a decision analysis balancing the tradeoffs of delivering at various gestational ages at term in order to determine the optimal gestational age for women with A1GDM to deliver.

Materials & Methods

A decision-analytic model was created using TreeAge software to compare the outcomes of planning to deliver at 37 through 41 weeks in a theoretical cohort of 100,000 women with A1GDM (Figure 1). Strategies involving expectant management until a later GA accounted for probabilities of spontaneous delivery, indicated delivery, and IUFD during each successive week. GA associated risks of neonatal complications included cerebral palsy, infant death, IUFD, and Erb's palsy. Maternal outcomes in the model included maternal death and mode of delivery. Probabilities were derived from the literature, and total quality-adjusted life years (QALYs) were calculated using both utilities from the maternal and

neonatal perspective from the literature. Utilities are measures of quality of life in various health states that range from 0 for death to 1 for optimal health. For baseline reference in this model, the maternal utility for an uncomplicated vaginal delivery was set at 1. Sensitivity analyses were used to investigate the robustness of the baseline assumptions.

Probabilities

All probability inputs in the model were derived from the literature (Table 1). The baseline probabilities for cesarean deliveries with expectant management and cesarean deliveries after induction at various GAs from 37 weeks to 41 weeks were derived from a 2006 retrospective cohort study comparing the outcomes of women who were induced and those who were expectantly managed⁶. Baseline probabilities for maternal deaths from cesarean and vaginal deliveries were derived from a 2003 case-control study on pregnancy-related deaths⁷. Regarding neonatal outcomes, the gestational age-specific probabilities for macrosomia (defined as a birthweight of greater than 4000 g) were derived from a 2008 retrospective cohort study on perinatal outcomes in low-risk term pregnancies⁸. Since women with GDM are more likely to have cesarean deliveries and macrosomic infants, these were each accounted for with an odds ratio of 2.2 from a 2009 retrospective cohort study on perinatal mortality among women with A1GDM⁹. In our model, macrosomia was considered as an intermediate outcome in the decision analytic model - one that would impact downstream outcomes such as cesarean deliveries and brachial plexus injuries. Therefore, we did not consider macrosomia alone as an outcome as it did not impact maternal or neonatal utilities, and thus would not affect calculation of QALYs. Since literature for A1GDM-specific women was limited, probabilities for infant deaths (defined as infants who die within one year of birth) in women with GDM were derived from a 2012 retrospective cohort study on the risks of stillbirth and infant death in women with GDM¹⁰. IUFD rates were calculated using values from the literature and then extrapolated to women with A1GDM with an odds ratio of 1.08 from a 1997 retrospective cohort study comparing the outcomes of women with GDM to those of the general obstetric population^{11,12}. Cerebral palsy probabilities and Erb's palsy probabilities were both derived from the literature^{13,14}.

Utilities

Utilities from the maternal and neonatal perspective were all derived from the literature (Table 1). The maternal utility for a vaginal delivery was set at 1, while the utility of a cesarean delivery was set at 0.996 based on literature concerning maternal preferences in mode of delivery¹⁵. Maternal death utility was assumed to be 0 from the maternal perspective. The utility of maternal death from the neonatal perspective was not accounted for because of controversy over how to determine this value. The utility for cerebral palsy from the maternal perspective was derived from a 2002 study on maternal preferences¹⁶. The maternal utilities for IUFD and infant death were derived from a 2000 cross-sectional study of 534 patients in California¹⁷. There were no maternal or neonatal utility values found for Erb's palsy, so we assumed Erb's palsy to be similar to mild cerebral palsy^{16,18}. Utility values were applied over the lifetime of either the mother (life expectancy = 56.75, assuming delivery at age 25) or the infant (life expectancy = 78.5)¹¹. When the infant had cerebral palsy the life expectancy for the infant was changed to 66.562¹⁹.

Analysis

Baseline analysis used literature-derived probabilities of adverse perinatal maternal and neonatal outcomes at each gestational week to compare planning to deliver women with A1GDM at 37, 38, 39, 40, and 41 weeks gestation. QALYs for each management strategy were then calculated.

Sensitivity analysis was used to evaluate the robustness of this model. With sensitivity analysis, we were able to vary variables individually to determine thresholds in which the optimal strategy would differ from our original result.

Monte Carlo analysis was also performed to further evaluate the robustness of this model. In this analysis, distributions of the probabilities, rather than the means of the probabilities, were used to run a theoretical cohort of 100,000 women through the model. This sort of analysis provides us with proportions of when each outcome was optimal. By sampling distributions we incorporated the uncertainty underlying the model inputs in order to produce confidence estimates regarding the outcomes examined.

Results

Both maternal and neonatal outcomes were predicted in our theoretical model of 100,000 women with A1GDM. We found that planned delivery of these women at 38 weeks gestation was the optimal timing of delivery, which maximized QALYs. In our theoretical cohort, delivering at 38 weeks resulted in 48 fewer stillbirths but 12 more infant deaths compared to delivery at 39 weeks (Table 2). Additionally, delivering women at 38 weeks compared to 39 weeks reduced the maternal death rate from 16.2 per 100,000 women to 15.4 per 100,000 women while also decreasing the number of cesarean deliveries performed. Even though delivering these women at 38 weeks led to 21 more potential cases of cerebral palsy, this outcome did not outweigh the perinatal mortality differences enough to drive the optimal strategy to plan delivery at 39 weeks gestation. Overall, induction of women at 38 weeks gestation led to 5,705,614 QALYs as compared to 5,704,490 QALYs for women at 39 weeks gestation, a difference of 1124 total QALYs for this population.

Univariate sensitivity analyses were run on all variables to determine which variables had the largest impact on establishing the optimal strategy of delivering women with A1GDM at 38 weeks. Our model remained fairly robust for all variables. For infant deaths, our model remained robust until the infant death rates rose to a threshold of 3.73 times above our baseline rate (Figure 2A). Above this threshold, expectant management until 39 weeks gestation was the optimal strategy. When cerebral palsy rates were varied, our model remained optimal until cerebral palsy rates decreased to 0.32 times below our baseline rate, after which delivery at 37 weeks was favored, or increased beyond 3.79 times above our baseline rate, when delivery at 39 weeks became optimal (Figure 2B). IUFD rates, when varied, also had effects on our model (Figure 2C). With an IUFD rate of 0.3 times below our baseline rate, delaying delivery until 39 weeks was preferred; in contrast, with an IUFD rate of 1.90 times above our baseline rate, the optimal strategy was to deliver at 37 weeks.

Monte Carlo simulation was also used to determine the robustness of our model. When 10,000 theoretical women were ran through the model, the strategy to deliver at 38 weeks gestation was optimal 100% of the time.

Comment

Our model, based on a theoretical cohort of 100,000 women with A1GDM, demonstrated that the optimal time to plan to deliver these women was 38 weeks in order to minimize adverse perinatal maternal and neonatal outcomes. Delivering at 38 weeks gestation remained the optimal strategy until infant death rates rose to a threshold of 3.73 times above our baseline assumptions, cerebral palsy rates increased to 3.79 times above our baseline assumptions, or IUFD rates increased to 1.90 times above our baseline assumption. Additionally, delivering at 38 weeks gestation remained the optimal strategy until cerebral palsy rates decreased to below 0.32 times our baseline assumptions or when IUFD rates decreased to 0.3 times below our baseline assumptions. Maternal outcomes were also improved by planning delivery at 38 weeks as it reduced maternal deaths and also decreased the number of cesareans by 3,200 deliveries in a cohort of 100,000 women. Interestingly, this model demonstrated that the neonatal outcomes, IUFD, and infant death rates at various weeks of gestation, appear to be the main driver of this model as varying the rates of induction of labor and cesarean section did not alter the optimal strategy. Given that current guidelines are to wait until at least 39 weeks' gestation, certainly such practice recommendations should be questioned and examined in future studies.

The literature regarding timing of delivery of women with A1GDM has been quite heterogeneous, and there have been few quality studies to establish the optimal management these patients. A 2009 review article analyzed 4 cohort studies and 1 randomized controlled trial (RCT) on timing of delivery of women with GDM²⁰. The RCT focused specifically on insulin-requiring GDM, and while the results from this study did suggest that these women should be induced at 38 weeks of gestation, the study only included 200 women. Additionally, three of the cohort studies in this review did not differentiate among the classes of GDM, and all four of the cohort studies did not adjust for any confounders. Our study, in contrast, attempted to focus specifically on women with diet-controlled gestational diabetes. To consider the potential uncertainty in our inputs, we performed univariate sensitivity analyses on all our variables and a Monte Carlo simulation.

Since our model was based on a theoretical cohort, there are limitations to this study that must be considered when interpreting our results. Given the intrinsic nature of a decision-analytic model, we were unable to mimic real-world outcomes in that we only included a select group of variables that affected maternal and neonatal outcomes. It is important to note that our model inherently included a population of women with A1GDM without stratification, even though factors such as macrosomia, fetal growth restrictions, poor glycemic control, and concomitant disease would likely affect the optimal gestational age to deliver these women. For instance, preeclampsia was not included in our model and could very well have affected many women in this theoretical model. Preeclampsia was not included because of its potential impact on certain variables, such as IUFD rates. The inclusion of preeclampsia would likely only lead to an earlier gestational age for delivery.

Additionally, we examined maternal and neonatal outcomes that we deemed were most severe and had the largest impact on affecting quality of life for the mother and neonate. Thus, we did not include outcomes such as neonatal hypoglycemia and hyperbilirubinemia, which are more minor and transient in nature. As mentioned before, macrosomia was only considered an intermediate outcome in this decision model because it did not impact maternal or neonatal utilities, and thus would not affect calculation of QALYs. Interestingly, it has been shown that macrosomic fetuses from women with GDM may carry different risks than would macrosomic fetuses in women without GDM and that GDM may be an independent risk factor for short or long term complications related to macrosomia²¹. In light of this, given the scant literature examining this issue, we were able to approximate these risks by using odds ratios of macrosomia in women with GDM compared to women without GDM and odds ratios of complications, such Erb's palsy, in relation to macrosomia or no macrosomia. Sparse literature also resulted in some approximations regarding probabilities of outcomes for women with specifically A1GDM. The infant death rates were derived from a paper that did not differentiate among the different types of GDM; however, macrosomia and IUFD rates were specifically from studies of only women with A1GDM. We did not account for any effects of A1GDM on CP rates. For Erb's palsy and shoulder dystocia rates, we accounted for their probabilities in relation to macrosomia, which was A1GDM-specific. Further, our model did not account for long-term neonatal outcomes, such as childhood obesity as there is no evidence that gestational age itself, controlling for birthweight, would influence these outcomes. Lastly, since our baseline assumptions were based on the literature, we must be aware that these individual studies may be biased or underpowered; however, we were able to account for these potential study limitations through sensitivity analyses and Monte Carlo simulation.

This model contributes to the current literature on gestational diabetes as it offers providers more guidance in determining the optimal time to deliver women with A1GDM to minimize adverse perinatal maternal and neonatal outcomes. Given the national recommendations towards preventing early term deliveries, it appears that at a minimum women with gestational diabetes should be added to the exclusion list and potentially delivered prior to 39 weeks' gestation. Cost-effectiveness models should be constructed to determine whether this management strategy would continue to be optimal from an economic perspective. Additionally, future studies should include a prospective randomized controlled trial to determine whether these simulated results are supported in a clinical scenario.

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References

1. Mission JF, Ohno MS, Cheng YW, et al. Gestational diabetes screening with the new IADPSG guidelines: a cost-effectiveness analysis. *Am J Obstet Gynecol.* 2012; 207:326.e1–326.e9. [PubMed: 22840972]

2. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med*. 2005; 352:2477–2486. [PubMed: 15951574]
3. Landon MB, Spong CY, Thom E, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. *N Engl J Med*. 2009; 361:1339–1348. [PubMed: 19797280]
4. Zlatnik MG, Cheng YW, Norton ME, et al. Placenta previa and the risk of preterm delivery. *J of Maternal-Fetal and Neonatal Medicine*. 2007; 20:719–723.
5. Spong CY, Mercer BM, D'Alton M, et al. Timing of indicated late-preterm and early-term birth. *Am J Obstet Gynecol*. 2011; 118:323–333.
6. Caughey AB, Nicholson JM, Cheng YW, et al. Induction of labor and cesarean delivery by gestational age. *Am J Obstet Gynecol*. 2006; 195:700–705. [PubMed: 16949399]
7. Harper MA, Byington RP, Espeland MA, et al. Pregnancy-related death and health care services. *Am J Obstet Gynecol*. 2003; 102:273–278.
8. Cheng YW, Nicholson JM, Nakagawa S, et al. Perinatal outcomes in low-risk term pregnancies: do they differ by week of gestation? *Am J Obstet Gynecol*. 2008; 199:370.e7. [PubMed: 18928977]
9. Karmon A, Levy A, Holcberg G, et al. Decreased perinatal mortality among women with diet-controlled gestational diabetes mellitus. *International J of Gynecol and Obstet*. 2009:199–202.
10. Rosenstein MG, Cheng YW, Snowden JM, et al. The risk of stillbirth and infant death stratified by gestational age in women with gestational diabetes. *Am J Obstet Gynecol*. 2012; 206:309.e1–309.e7. [PubMed: 22464068]
11. National Center for Health Statistics. Health, United States 2011: With Special Feature on Socioeconomic Status and Health. Hyattsville, MD: 2012.
12. Casey BM, Lucas MJ, McIntire DD, et al. Pregnancy outcomes in women with gestational diabetes compared with the general obstetric population. *Obstet Gynecol*. 1997; 90:869–873. [PubMed: 9397092]
13. Surman, G.; Newdick, H.; King, A., et al. Annual Report 2009, including data for births 1984 to 2003. Oxford: National Perinatal Epidemiology Unit; 2009. 4Child: Four Counties Database of Cerebral Palsy, Vision Loss and Hearing Loss in Children.
14. Volpe KA, Pilliod RA, Yanit KE, et al. Effect of birthweight on the incidence of brachial plexus injury among births with shoulder dystocia. Unpublished results.
15. Caughey AB. Quantitative evaluation of preference for mode of delivery in pregnant Chilean women. *Med Decis Making*. 2003; 23:634.
16. Grobman WA, Dooley SL, Welshman EE, et al. Preference assessment of prenatal diagnosis of Down syndrome: Is 35 years a rational cutoff? *Prenat Diagn*. 2002; 22:1195–1200. [PubMed: 12478632]
17. Kuppermann M, Nease RF, Learman LA, et al. Procedure-related miscarriages and Down Syndrome-affected births: implications for prenatal testing based on women's preferences. *Obstet Gynecol*. 2000; 96:511–516. [PubMed: 11004350]
18. Carroll AE, Downs SM. Improving decision analyses: parent preferences (utility values) for pediatric health outcomes. *J Pediatrics*. 155:21–25.e5.
19. Blair E, Watson L, Badawi N, et al. Life expectancy among people with cerebral palsy in Western Australia. *Dev Med Child Neurol*. 2001; 43:508–515. [PubMed: 11508916]
20. Witkop CT, Neale D, Wilson LM, et al. Active compared with expectant delivery management in women with gestational diabetes. *Obstet Gynecol*. 2009; 113:206–217. [PubMed: 19104376]
21. Esakoff TF, Cheng YW, Sparks TN, et al. The association between birthweight 4000 g or greater and perinatal outcomes in patients with and without gestational diabetes mellitus. *Am J Obstet Gynecol*. 2009; 200:672.e1–672.e4. [PubMed: 19376489]

Figure 1. Decision analytic model for women with A1GDM

Decision-analytic model to determine optimal clinical management of women with A1GDM at 37 weeks gestation. The entire tree is not shown, but one of the expanded branches is shown. IOL, induction of labor; mat death, maternal death; IUFD, intrauterine fetal demise

Figure 2. Univariate sensitivity analyses

2A. 1-way sensitivity analysis of infant deaths demonstrating that delivering at 38 weeks remained the optimal clinical strategy until the infant death rate increased 3.73 times above our baseline rate

2B. 1-way sensitivity analysis of cerebral palsy demonstrating that delivering at 38 weeks remained the optimal clinical strategy until the cerebral palsy rate decreased to 0.32 times below our baseline rate or increased to 3.79 times above our baseline rate

2C. 1-way sensitivity analysis of intrauterine fetal demise demonstrating that delivering at 38 weeks remained the optimal clinical strategy until the intrauterine fetal demise rate decreased to 0.3 times below our baseline rate or increased to 1.90 times above our baseline rate

Table 1

Probabilities and utilities for the A1GDM model

Outcomes	Probabilities	Utilities (maternal, neonatal perspective)	References
Maternal outcomes			
Cesarean delivery in women with GDM		0.996, 1	15
Expectant mgmt (wks of GA: 37, 38, 39, 40)	0.252, 0.252, 0.280, 0.436,		6, 9
After induction (wks of GA: 37, 38, 39, 40, 41)	0.229, 0.229, 0.269, 0.361, 0.414		6, 9
Maternal deaths		0	
Cesarean	0.000359		7
Vaginal	0.000092		7
Neonatal outcomes			
Macrosomia (birthweight > 4000g) in women with GDM (wks of GA: 37, 38, 39, 40, 41)	0.0425, 0.095, 0.158, 0.241, 0.344		8, 9
Shoulder dystocia			
In macrosomic infants	0.06		21
In non-macrosomic infants	0.009		21
Infant deaths from women with GDM (wks of GA: 37, 38, 39, 40, 41)	0.00140, 0.00106, 0.00087, 0.00095, 0.00115	0.92, 0	10, 17
IUFD in women with GDM (wks of GA: 37, 38, 39, 40)	0.000462, 0.000529, 0.000562, 0.000632	0.92, 0	11, 12, 17
Cerebral palsy (wks of GA: 37, 38, 39, 40, 41)	0.0023, 0.0012, 0.0009, 0.0010, 0.0010	0.733, 0.612	13, 16
Erb's palsy in setting of shoulder dystocia		0.78, 0.87	17, 18
In macrosomic infants	0.0612		14
In non-macrosomic infants	0.0295		14

GDM, gestational diabetes; GA, gestational age; IUFD, intrauterine fetal demise

Table 2

Outcomes of theoretical cohort of 100,000 women with A1GDM managed at 37 wks GA

Planned GA of delivery (wks)	Infant death	IUFD	Major neurodevelopmental disability	Erb's palsy	QALYs
37	140	-	230	32	5,704,286
38	109	46	131	44	5,705,614
39	97	94	110	52	5,704,490
40	100	131	114	56	5,702,710
41	102	154	114	56	5,701,658

GA, gestational age; IUFD, intrauterine fetal demise; QALY, quality-adjusted life years