



# Fetal Outcomes After Diabetic Ketoacidosis During Pregnancy

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Historical literature reports risk of fetal demise after diabetic ketoacidosis (DKA) in pregnancy as high as 25–60% (1,2). However, estimates have generally been based on small sample sizes, with limited investigation of other fetal outcomes or risk factors associated with poor fetal outcomes. We aimed to provide an updated assessment of the incidence and risk factors for fetal demise and other adverse outcomes in women with DKA during pregnancy.

This retrospective cohort study included pregnancies between 1996 and 2015 with at least one DKA event in women with type 1 diabetes at one of three teaching hospitals in Boston. Data were collected through medical record review. Pregnancies were excluded if information on birth status (live or demise) and gestational age at birth or demise were unknown.

Among the 77 DKA events in 64 pregnancies in 62 women included in the study, fetal demise, preterm birth, and neonatal intensive care unit (NICU) admissions occurred in 15.6%, 46.3%, and 59% of pregnancies, respectively. Mothers presented in DKA between 5 and 38 weeks of gestation. Fetal demise occurred at the time of or within 1 week of the DKA event and between 1 and 11 weeks

afterward in 60% and 40% of cases, respectively.

Maternal ICU admission ( $P = 0.024$ ) and higher serum osmolality ( $P = 0.045$ ) during the DKA event were associated with increased risk of fetal demise (Table 1). Maternal smoking ( $P = 0.0005$ ) and higher pre-DKA HbA<sub>1c</sub> levels ( $P = 0.032$ ) were associated with higher risk of preterm birth. Maternal smoking ( $P = 0.0077$ ), preeclampsia during pregnancy ( $P = 0.031$ ), higher anion gap during the DKA event ( $P = 0.019$ ), and preterm birth ( $P = 0.0003$ ) were associated with higher risk of NICU admission.

The risk of fetal demise after DKA during pregnancy has decreased over time but remains substantially higher than the baseline risk (2–3%) in women with type 1 diabetes (3). Risks of preterm birth and NICU admissions were also elevated compared with the general population of pregnant women with diabetes (33% [4] and 47% [5], respectively). Factors associated with increased risk of fetal demise were primarily characteristics of the DKA event severity (e.g., maternal ICU admission and higher serum osmolality), lending support to a direct causal relationship. Factors associated with increased risk of preterm birth and NICU admissions, on

the other hand, were more indicative of the mother's overall health status and health behaviors. This finding suggests that the observed increased risk of preterm birth among women with DKA during pregnancy could be due to the higher prevalence of risk factors in this population.

DKA during pregnancy poses a risk to the fetus both at the time of the event and following. Further research is needed to identify effective methods for prevention, early recognition, and timely treatment of DKA in pregnancy to mitigate risk of fetal demise and other adverse fetal outcomes.

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**Table 1—Risk factors for fetal demise in pregnancies complicated by DKA**

	Pregnancies with live births	Pregnancies with fetal demise	<i>P</i> value
Total pregnancies, <i>N</i>	54	10	
DKA events, <i>n</i>	65	12	
Multiple pregnancies, <i>n</i>	2	0	
>1 DKA event, <i>n</i>	7 (13.0)	2 (20.0)	0.6222
Gestational age at DKA event (all events), weeks, mean (SD)	24.7 (9.2)	19.5 (11.8)	0.2825
Gestational age at DKA event, weeks, mean (SD)	24.7 (9.3)	21.3 (12.1)	0.6571
Maternal age, years			0.2677
<20	3 (5.6)	1 (10.0)	
20–35	41 (75.9)	9 (90.0)	
>35	10 (18.5)	0 (0)	
Race†			0.4748
White	32 (60.4)	4 (44.4)	
Hispanic	12 (22.6)	2 (22.2)	
Black	9 (16.98)	3 (33.3)	
Mother's marital status, single vs. not†	26 (49.1)	6 (60.0)	0.7323
Median income by zip code, USD, mean (SD)*†	64,924 (21,510)	54,069 (17,526)	0.0949
Preexisting diabetes	51 (94.4)	10 (100)	1
Insulin injection†			1
None (new-onset type 1 diabetes)	4 (7.6)	0 (0)	
Injection	37 (69.8)	8 (80.0)	
Pump	12 (22.6)	2 (20.0)	
Fetal sex‡			0.4543
Unknown (demise before sex known)	0 (0)	2 (20.0)	
Male	35 (64.8)	4 (40.0)	
Female	19 (35.2)	4 (40.0)	
Decade of DKA occurrence			0.6774
1996–1999 (4 years)	6 (11.1)	0 (0)	
2000–2009 (10 years)	28 (51.9)	7 (70.0)	
2010–2015 (6 years)	20 (37.0)	3 (30.0)	
Presence of diabetic gastroenteropathy	11 (20.4)	2 (20.0)	1
ICU admission during DKA hospitalization**	2 (3.7)	3 (30.0)	0.0240
Ever smoked	12 (22.2)	4 (40.0)	0.2517
Chronic hypertension	8 (14.8)	0 (0)	0.3373
Preeclampsia	12 (22.2)	0 (0)	0.1863
Gestational hypertension	4 (7.4)	0 (0)	1
Contributing factors			
Nonadherence	19 (35.2)	3 (30.0)	1
Gastrointestinal symptoms	9 (16.7)	1 (10.0)	1
Beta sympathomimetics	1 (1.9)	0 (0)	1
Pump failure	4 (7.4)	2 (20.0)	0.2337
Infection	5 (9.3)	0 (0)	1
Glucocorticoid use	1 (1.9)	0 (0)	1
Other	6 (11.1)	2 (20.0)	0.5999
Unknown	13 (24.1)	2 (20.0)	1
Gravida, mean (SD)	2.8 (1.8)	2.2 (1.5)	0.2510
Para, mean (SD)	1.1 (1.4)	0.8 (1.0)	0.7287
Maximum anion gap, mEq/L, mean (SD)†	21.0 (4.7)	20.8 (3.8)	0.9520
Maximum BUN, mg/dL, mean (SD)†	12.4 (4.2)	12.1 (4.8)	0.8054
Maximum creatinine, mg/dL, mean (SD)*	0.74 (0.25)	0.9 (0.4)	0.1003
Maximum glucose, mg/dL, mean (SD)*†	323.3 (118.3)	431.8 (180.0)	0.1120
Maximum osmolality, osmol/kg, mean (SD)**†	295.8 (7.0)	301.8 (10.1)	0.0448
Maximum potassium, mmol/L, mean (SD)	4.4 (0.7)	4.5 (0.5)	0.3081
Minimum potassium, mmol/L, mean (SD)*†	3.5 (0.3)	3.7 (0.3)	0.0733
Minimum phosphate, mg/dL, mean (SD)†	2.4 (0.9)	2.3 (1.1)	0.7066
Pre-DKA HbA <sub>1c</sub> , mean (SD)†			0.4732
%	8.1 (1.9)	9.0 (3.1)	
mmol/mol	65.5 (20.3)	75.0 (10.0)	

Data are *n* (%) unless otherwise indicated. \*Fisher exact test  $P < 0.20$ . \*\*Fisher exact test significant with  $P < 0.05$ . †Missing: one each maximum blood urea nitrogen (BUN), maximum glucose, maximum osmolality, minimum potassium, pre-DKA HbA<sub>1c</sub>, median income, insulin injection, and marital status; two each maximum anion gap and race; 13 minimum phosphate. ‡*P* value only includes male vs. female, excludes two fetuses with unknown sex due to early gestational age at fetal demise. USD, U.S. dollars.

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