

A CASE CONTROL STUDY OF PLACENTAL PATHOLOGY IN WOMEN DIAGNOSED WITH HYPERGLYCEMIA BEFORE AND DURING PREGNANCY

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Introduction

- An estimated 8 million women in the United States have some form of diabetes and approximately 1% of these women will have diabetic complications during pregnancy.[1, 2]
- Diabetes may cause pathology in the placenta, the filter between the maternal environment and the fetal environment, and can have a negative effect on the pregnancy.
- The aim of this study is to evaluate placental pathology in pregnancies affected by pregestational and gestational diabetes compared to a control population with normal blood glucose, from a single academic institution. The study hopes to shed light on the continuum of placental pathology in pregnancies complicated by diabetes.

Materials and Methods

- This is a retrospective case control study on patients seen and managed through the University of Arkansas for Medical Sciences clinics from January 2007 till December 2016.
- Pregnancies complicated by diabetes (pregestational and gestational) were identified through the delivery record and patient information and pregnancy complications were extracted from the medical record.
- A convenient sample of control patients in 2010 were selected due to the medical center's policy of not routinely sending normal placentas for pathologic examination
- 12 elements of the placental pathologic report were evaluated.
- All data was summarized by diabetes/control grouping as the mean and standard deviation for continuous measures and frequency and percentage for categorical variables. For highly skewed continuous measures, descriptive statistics are reported as median with the first and third quartiles. Depending on the continuous outcome distribution, statistical analysis utilized either two-sample t-test or Wilcoxon rank-sum test. For binary response, chi-square test statistic or Fisher's exact test was used as appropriate.



References

- J. Lethbridge-Cejku, M., J.S. Schiller, and L. Bernadel, *Summary health statistics for U.S. adults: National Health Interview Survey, 2002*. Vital Health Stat 10, 2004(222): p. 1-151.
- Martin, A., et al., *Births: final data for 2002*. Natl Vital Stat Rep, 2003. 52(10): p. 1-113.

Results

Table 1: Maternal and Infant Demographic Characteristics

Maternal Measure	Diabetes (N = 485)	Control (N = 106)	p-value
Maternal age (years), mean ± sd	30.0 ± 6.1	27.5 ± 6.0	<0.0001
Gravidity, median [Q1, Q3]	3 [2, 4]	2 [1, 3]	<0.0001 ^a
Parity, median [Q1, Q3]	1 [1, 2]	1 [0, 1]	<0.0001 ^a
BMI at delivery (kg/m ²), mean ± sd	37.8 ± 8.6	31.9 ± 8.0	<0.0001
Hypertension			< 0.0001
No Hypertension	295 (60.8%)	99 (93.4%)	
Chronic Hypertension	154 (31.8%)	4 (3.8%)	
Gestational Hypertension	36 (7.4%)	3 (2.8%)	
Current Smoker N (%)	76 (15.7%)	11 (10.4%)	0.16
Delivery method, N (%)			0.002
Vaginal	227 (46.8%)	68 (64.2%)	
Primary cesarean section	107 (22.1%)	21 (19.8%)	
Repeat cesarean section	151 (31.1%)	17 (16.0%)	
Infant Measure			
Gestational age (weeks) mean ± sd	37.0 ± 2.8	38.9 ± 1.5	<0.0001
Birthweight (grams), mean ± sd	3230.8 ± 791.5	3322.7 ± 532.8	0.16
Apgar 1, median [Q1, Q3]	8 [7, 9]	8 [7, 9]	0.009 ^a
Apgar 5, median [Q1, Q3]	9 [8, 9]	9 [9, 9]	0.08 ^a
Male Sex (%)	246 (51.0%)	58 (55.2%)	0.44

^aDenotes statistical test based on Wilcoxon two-sample test

Table 2: Comparison of placental pathology between Diabetics and Controls

Placental Pathology	Diabetes N (%)	Control N (%)	p-value
Villous maturation			<0.0001^a
Delayed	40 (8.3%)	2 (1.9%)	
Normal	395 (81.6%)	103 (91.2%)	
Accelerated	49 (10.1%)	1 (0.9%)	
Thrombus	66 (13.6%)	16 (15.1%)	0.69
Intervillous thrombus	58 (12.0%)	13 (12.3%)	0.93
Subchorionic thrombus	7 (1.4%)	1 (0.9%)	1.0 ^a
Decidual vasculopathy	103 (21.2%)	23 (21.7%)	0.92
Intravillous hematoma	5 (1.0%)	1 (0.9%)	1.0
Intraparenchymal hematoma	0	0	---
Placental disc hematoma	5 (1.0%)	(0%)	0.59 ^a
Infarction	48 (9.9%)	11 (10.4%)	0.88
Placental weight			0.0009
Normal	350 (72.2%)	83 (78.3%)	
Increased	109 (22.5%)	10 (9.4%)	
Decreased	26 (5.4%)	13 (12.3%)	
True knots	2 (0.4%)	3 (2.8%)	0.04 ^a
Number of vessels			0.70^a
2 VC	8 (1.7%)	2 (1.9%)	
3 VC	477 (98.4%)	104 (98.1%)	
Umbilical vasculitis	39 (8.0%)	21 (19.8%)	0.0003
Acute chorioamnionitis	80 (16.5%)	30 (28.3%)	0.005
Chorioangioma	14 (2.9%)	1 (0.9%)	0.49 ^a
Chorangioma	2 (0.4%)	0 (0%)	1.0 ^a

^aDenotes p-value based on Fisher's exact test

Results and Conclusions

- The subjects affected by diabetes were older, had higher gravidity, larger BMI at delivery, delivered at an earlier gestational age, had a higher rate of chronic hypertension, and gestational hypertension compared to the control subjects.
- Out of 12 histologic elements investigated between groups, delayed or accelerated villous maturation and increased placental weight were the only statistically significant findings noted to be increased in diabetic placentas.
- The control group did have statistically more chorioamnionitis, umbilical vasculitis and true knots.
- Although the control group was not low risk as evidence by these pathologic findings; this would only have caused a dilution in the hypoxic villous maturation between groups which remained statistically significant.
- Placentas of pregnancies complicated by diabetes display villous maturation abnormalities, a measure of hypoxia, much more frequently than placentas from pregnancies without this diagnosis.
- The increased incidence of obesity and hypertensive disorders commonly found in this group may have contributed to this finding.