

## Retrospective Cohort Study

# Amount of polyhydramnios attributable to diabetes may be less than previously reported

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## Abstract

### AIM

To evaluate the frequency and the quantity of polyhydramnios attributable to diabetes in pregnancy.

### METHODS

The charts of patients with a four-quadrant amniotic fluid index (AFI)  $\geq 20$  cm and either a diagnosis of diabetes or a diabetes screening test during the index pregnancy were retrospectively reviewed. AFI was stratified into 5 categories and the frequency of diabetes was evaluated for each group. The frequency of polyhydramnios attributable to diabetes was compared to the frequency of polyhydramnios in the setting of fetal anomalies or no known cause.

### RESULTS

One thousand five hundred and forty-five patients were included in the study. Eight point five percent ( $n = 131$ ) had diabetes and no other cause for polyhydramnios. Eleven point two percent (173) had antenatally diagnosed anomalies. For all categories of AFI except the largest ( $> 40.9$  cm) the most common cause of polyhydramnios was idiopathic. In patients with diabetes the AFI was most likely to be between 26 cm and 35.9 cm.

### CONCLUSION

The rate of polyhydramnios in this study is 8.5%. Patients with diabetes most commonly have mild polyhydramnios between 26 and 35.9 cm of fluid on a four-quadrant AFI.

**Key words:** Gestational diabetes; Amniotic fluid index; Diabetes in pregnancy; Polyhydramnios

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**Core tip:** A finding of polyhydramnios has been considered an indicator to test the mother for the presence

of diabetes. This is based on reports in the literature of a rate of polyhydramnios due to diabetes between 15% and 25%. This study identified a rate of polyhydramnios associated with diabetes of only 8.5%. This is half of the amount previously reported. Additionally, in patients with diabetes this study found that most had mild polyhydramnios between 26-35.9 cm of fluid on a four-quadrant amniotic fluid index.

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## INTRODUCTION

Polyhydramnios is defined as a 4-quadrant amniotic fluid index (AFI) > 24 cm or a single maximum vertical pocket > 8 cm. Up to 2% of all pregnancies have an excess amount of fluid meeting the criteria for polyhydramnios<sup>[1,2]</sup>. It is reported in the literature that approximately sixty percent of polyhydramnios is idiopathic; twenty percent of polyhydramnios can be attributed to poorly controlled or undiagnosed diabetes and the remainder of cases of polyhydramnios are associated with fetal anomalies<sup>[2-4]</sup>. Several adverse outcomes have been associated with polyhydramnios including preterm labor and rupture of membranes. The primary goal of the study was to evaluate the frequency of polyhydramnios associated with diabetes. Subjectively due to the large of amount of polyhydramnios seen in our clinics and our mainly Hispanic population with a high endemic rate of diabetes, we hypothesized that the frequency of polyhydramnios attributable to diabetes would be greater than the twenty percent quoted in the literature. The secondary goal was to identify a quantity of polyhydramnios associated with diabetes in comparison to other causes. In our review of the literature, no studies have evaluated differences in the quantity of fluid stratified by causation. We hypothesized that the quantity of polyhydramnios associated with diabetes would be different than the quantity of polyhydramnios associated with fetal anomalies or due to an idiopathic process.

## MATERIALS AND METHODS

This retrospective cohort study was carried out at the University of New Mexico teaching hospital in Albuquerque, New Mexico, United States of America. This study was reviewed by the Human Research Review Committee (HRRRC) at the University of New Mexico and was assigned HRRRC#10-418. Patients receiving an ultrasound in the prenatal diagnosis unit from 2009-2012 were included in the study. All patients included in the study were > 28 wk of gestation. The gestational age was chosen so that the majority of patients would have

Table 1 Demographics

	Data
Hispanic	92% (1426)
Native American	6.7% (105)
Other	1% (14)
Age (yr)	33 ± 5.2
BMI	31 ± 6.1
EGA at diagnosis (wk)	32 ± 2.1

BMI: Body mass index; EGA: Emirates Global Aluminium.

received screening for gestational diabetes which is traditionally performed between 24-28 wk.

The 4-quadrant AFI for each patient was measured by a registered diagnostic sonographer using the method initially described by Phelan *et al*<sup>[5]</sup> in which the maternal abdomen is divided into 4 quadrants using the linea nigra as a midline and the umbilicus to define the crossing X-axis. The largest vertical pocket of fluid in each quadrant was measured and the sum of the four measurements was used as the AFI. Associated images of quadrant measurements were reviewed for each patient by a board certified perinatologist.

Patients were included in the study if they received prenatal care at the University of New Mexico, had been tested for diabetes or had a diagnosis of preexisting diabetes, and if on any ultrasound after 28 wk a 4-quadrant AFI was 20 cm or greater. The lower limit of 20 cm of fluid was chosen because this was the cutoff used in the first paper describing the four-quadrant AFI<sup>[5]</sup>. The frequency of polyhydramnios attributable to diabetes was compared to the frequency associated with fetal anomalies and in patients with no known cause of polyhydramnios.

In the planned secondary analysis, the AFI was stratified into 5 groups; Group A = 20-25.9 cm; Group B = 26-30.9 cm; Group C = 31-35.9 cm; Group D = 36-40.9 cm and Group E > 40.9 cm. The frequency of diabetes was evaluated for each group.

## Statistical analysis

Statistical analysis was performed using SAS version 9.2 (SAS institute, Cary, North Carolina). Categorical variables are listed as frequencies and percentages. Continuous variables are presented as mean with standard deviation. The association between categorical variables was analyzed using  $\chi^2$  and Fisher's exact test. The frequency of polyhydramnios due to diabetes was assumed to be 20%. We found a frequency of 8.5%. A post hoc power analysis indicated a > 80% power to detect the study hypothesis with a significance rate of 0.05 using a sample size of 1545 patients.

## RESULTS

One thousand five hundred and forty-five patients had a 4-quadrant AFI  $\geq$  20 cm. Demographics are shown in

**Table 2 Results of primary analysis: Quantity of fluid stratified by causation**

Amniotic fluid index (n)	Diabetic n (%)	Anomalies n (%)	Idiopathic n (%)	P value for incidence of diabetes
A: 20-25.9 cm (1261)	7.06 (89)	7.1 (90)	85 (1082)	
B: 26-30.9 cm (199)	15.08 (30)	20.6 (41)	64 (128)	P = 0.0002 (B compared to A)
C: 31-35.9 cm (53)	18.87 (10)	41.5 (22)	39 (21)	P = 0.002 (C compared to A)
D: 36-40.9 cm (18)	5.56 (1)	38.8 (7)	55 (10)	P = 0.9 (D compared to A)
E: > 40.9 cm (14)	7.14 (1)	92.9 (13)	0 (0)	P = 0.9 (E compared to A)
				P = 0.85 (E compared to D)

Table 1. The majority of patients in the study (92%) were Hispanic. The mean BMI for study was 31 (range 18-52). 8.5% ( $n = 131$ ) of patients were diabetic. Ninety-four patients had gestational diabetes. Thirty-seven patients had pre-existing diabetes. One hundred and seventy-three (11.2%) patients had antenatally diagnosed anomalies. There were no fetal anomalies in the patients with diabetes. The mean gestational age at diagnosis of polyhydramnios was 32 completed weeks.

The difference between the incidence of diabetes in Group A with an AFI between 20-25.9 cm and Group B with an AFI between 26-30.9 cm was statistically significant ( $P = 0.0002$ ). The difference in incidence of diabetes between Group A and Group C (AFI between 31-35.9 cm) was also statistically significant ( $P = 0.002$ ). The difference between the incidence of diabetes in Groups D and E was not significant in comparison to Group A ( $P = 0.9$ ) or in comparison to each other ( $P = 0.85$ ). There was no difference in AFI between preexisting and gestational diabetics ( $P = 0.6$ ). These results are shown in tabular form in Table 2.

For all categories of AFI except the largest (> 40.9 cm) the cause was most likely to be idiopathic. At mild levels of polyhydramnios between 26-30.9 cm and 31-35.9 cm the frequency of anomalies was higher than the frequency of diabetes, though the frequency of diabetes was statistically different than in the 20-25.9 cm group. Cases of diabetes clustered between 26 cm and 35.9 cm as shown in Table 2. In the 36-40.9 cm grouping, the rate of diabetes began to taper off and was significantly less than the rate of anomalies. In the > 40.9 cm grouping, no cases were idiopathic, 92.9% was due to fetal anomalies and 7% due to diabetes though this actually amounted to a single patient with diabetes in that grouping.

## DISCUSSION

In 1970 Queenan *et al*<sup>[3]</sup> reported on 358 patients with clinically diagnosed polyhydramnios. Thirty-four percent was idiopathic and 24.6% was due to diabetes. This was the initial study to report the association of diabetes with polyhydramnios and is the basis for the recommendation to rule out diabetes when polyhydramnios is discovered. In 1987, Hill *et al*<sup>[6]</sup> reported on 102 cases of mild to severe polyhydramnios. In 66.7% of those patients no cause was found. Fourteen point seven percent was due to either gestational or preexisting diabetes.

In our study 8.5% of polyhydramnios was associated with diabetes and 11.2% was due to an anomalous fetus and in 74% of our patients no cause was found. The

percentage of polyhydramnios attributable to diabetes is lower in our study than previously reported. The lower limit of polyhydramnios in our study was 20 cm of fluid; If the lower limit was defined as 25 cm then the amount of polyhydramnios attributable to diabetes is even lower at 2.7%. This finding was surprising because the population, which is predominantly Mexican-Hispanic, has a high rate of endemic diabetes and we hypothesized that the amount would be higher than previously reported. A possible explanation is improved glycemic control during pregnancy in comparison to the 1970's when Queenan first reported this association. A limitation of our study is that due to its retrospective nature we were unable to evaluate the degree of glycemic control for patients in the study.

Our goal was to evaluate diabetes associated polyhydramnios. Between groups D and E the difference in the frequency of diabetes was not significant, however the difference in the frequency of anomalies between group D compared to group E was significant ( $P = 0.008$ ). This may indicate that anomalies are more common than diabetes at extreme levels of polyhydramnios.

To our knowledge no study has looked at the quantity of polyhydramnios associated with diabetes in comparison to other causes. We found that diabetes is most common in the mild range of polyhydramnios between 26 and 35.9 cm on a four-quadrant AFI.

At the lower end in the 20-25.9 cm group the rate of anomalies and the rate of diabetes was the same. Interestingly, recent definitions of polyhydramnios starting at 25 cm of fluid would eliminate this group which contained 68% ( $n = 89$ ) of all the diabetics in the study.

In conclusion, the majority of cases of polyhydramnios associated with diabetes had a 4-quadrant AFI between 26-35.9 cm. Cases above and below that were outliers. The rate of polyhydramnios attributable to diabetes was 8.5%. This is less than reported in previous studies.

## COMMENTS

### Background

Queenan first reported the association between diabetes during pregnancy and polyhydramnios in 1971. He found that approximately 1 in 4 cases of polyhydramnios was due to diabetes. This was during a time when women with diabetes were advised to avoid pregnancy because outcomes were universally poor.

### Research frontiers

The authors hypothesized that the amount of diabetes associated polyhydramnios would be less than the 25% reported by Queenan. Possibly due to improved glycemic control or other factors. This study addresses whether, in

modern times when women with diabetes have excellent pregnancy outcomes, the incidence of polyhydramnios in diabetes remains the same.

### Innovations and breakthroughs

This study shows that the amount of polyhydramnios attributable to diabetes is < 10%. This is significantly lower than previously reported.

### Applications

In the setting of polyhydramnios, the most likely cause is idiopathic, followed by the possibility of an anomaly. The frequency of polyhydramnios associated with diabetes was less than the frequency of polyhydramnios associated with an anomaly.

### Terminology

Amniotic fluid index (AFI): The sum of the measurements of the largest vertical pocket of amniotic fluid in each of the four quadrants of the pregnant uterus; Polyhydramnios: For this study polyhydramnios was defined as a four-quadrant AFI  $\geq$  20 cm.

### Peer-review

The manuscript is interesting and well written.

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