Sonographic Estimated Fetal Weight among Diabetics at $\geq$ 34 Weeks and Composite Neonatal Morbidity

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Abstract

Objectives The objective was to assess the composite neonatal morbidity (CNM) among diabetic women with sonographic estimated fetal weight (SEFW) at 10 to 90th versus >90th percentile for gestational age (GA).

Study Design The inclusion criteria for this retrospective study were singleton pregnancies at 34 to 41 weeks, complicated by diabetes, and that had SEFW within 4 weeks of delivery. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated.

Results Among the 140 cohorts that met the inclusion criteria, 72% had SEFW at 10th to 90th percentile for GA, and 28% at >90th percentile. Compared with women with diabetes with last SEFW at 10th to 90th percentile, those with estimate > 90th percentile for GA had a significantly higher rate of CNM (13 vs. 28%; OR, 2.65; 95% CI, 1.07–6.59). Among 109 diabetic women who labored, the rate of shoulder dystocia was significantly higher with SEFW at >90th percentile for GA than those at 10th to 90th percentile (25 vs. 2%; $p = 0.002$); the corresponding rate of CNM was 29 versus 10% ($p = 0.02$).

Conclusion Among diabetic women with SEFW > 90th percentile for GA, CNM was significantly higher than in women with estimate at 10 to 90th percentile. Despite the increased risk of CNM, these newborns did not have long-term morbid sequela.

Keywords
- diabetes
- sonographic estimated fetal weight
- composite neonatal morbidity

Of the 3.97 million births in the United States in 2015, over 258,000 (6.5%) were to diabetic women alone.[1] Some of the potential complications of diabetic pregnancies are large for gestational age (LGA), defined as birth weight (BW) above 90th percentile, and fetal macrosomia (BW of 4,000 g or more). Among diabetics, the rate of LGA varies from 5 to 24% and that of macrosomia from 6 to 19%.[2–6] Accelerated fetal growth among diabetics is associated with stillbirth,[7,8] shoulder dystocia,[9] and neonatal brachial plexus palsy.[10,11] To potentially avert the complications, American College of Obstetricians and Gynecologists (ACOG) suggests sonographic estimated fetal weight (SEFW) among gestational and pregestational diabetics in the third trimester.[12,13]

The fetus is regarded as suspected appropriate for gestational age (AGA) when the SEFW is at 10th to 90th percentile for gestational age (GA), and suspected LGA when the SEFW > 90th percentile.[14] While there are publications on morbidity associated with actual BW above 90th percentile for GA or at least 4,000 g,[15–18] BW is unknown to clinicians managing parturients. While SEFW is available to clinicians, there is a paucity of reports on diabetic women with SEFW $\leq$ 90th percentile versus SEFW > 90th percentile for GA and the associated composite neonatal morbidity (CNM). A PubMed search using combinations of terms "diabetes, SEFW, large for gestational age, morbidity, neonatal" indicated that few publications focused on SEFW among diabetic women alone and CNM.[6]

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The purpose for this retrospective study was to compare the CNM among diabetic women, at 34 weeks or more, with SEFW $\leq$ 90th percentile versus SEFW $>$ 90th percentile for GA. The secondary objectives was to determine the CNM among those who labored and had SEFW of 10th to 90th percentile versus SEFW $>$ 90th percentile for GA.

Materials and Methods

An institutional review board approved this retrospective study of all diabetic women who had SEFW within 4 weeks of delivery, and who delivered at a teaching hospital from January 2013 through June 2016. ICD 9 and 10 codes (648.80–3, V12.21, O24.41–2, O99.81, and O24.319), and logbooks on labor and delivery were used to identify women with gestational or pregestational diabetes.

Gestational diabetes was defined by the Carpenter and Coustan criteria, with 1-hour glucose tolerance test value greater than 135 mg/dL, followed by 3-hour glucose tolerance test values greater than 95, 180, 155, and 140 mg/dL, with at least two values being abnormal.[19] A woman was considered to have pregestational diabetes if there was a history of diabetes before pregnancy confirmed by reviewing her medical records. In addition, women who were singletons, nonanomalous, and had adequate dating, had delivered at 34.0 weeks or later, and had SEFW within 4 weeks of delivery were included. Adequate pregnancy dating was defined as a pregnancy dated by last menstrual period and had an ultrasound before 22 $^{0/7}$ weeks that confirmed or revised the estimated due date, or by assisted reproductive technology.[20] Our inclusion of diabetic women with SEFW within 4 weeks of delivery was based on ACOG guideline on ultrasonography, which suggests that estimated fetal weight should be obtained every 3 to 4 weeks.[21]

Women were excluded in the presence of multiple gestation and known fetal anomalies, if deliveries happened before 34 $^{0/7}$ weeks, if pregnancies were managed by private nonteaching obstetricians/gynecologists, or if they did not have an SEFW by either an RDMS (Registered Diagnostic Medical Sonographer) or by a resident physician in obstetrics/gynecology within 4 weeks of delivery.

The ACOG guideline was used for the measurements of fetal biometric parameters. Biparietal diameter (BPD) was measured at the level of the thalami by taking the measurement from the outer edge of the proximal skull to the inner edge of the distal skull. Head circumference (HC) was obtained at the same level of the BPD by measuring the outer perimeter of the calvaria. The abdominal circumference (AC) was measured at the level of the junction of the umbilical vein, portal sinus, and the fetal stomach. The femur length (FL) was calibrated with the beam of insonation being perpendicular to the shaft, excluding the distal femoral epiphysis.[21] SEFW was derived from the regression equation proposed by Hadlock et al:[22] $\log_{10}$ (EFW) = 1.5662–0.0108(HC) + 0.0034(HC)^2 + 0.0468 (AC) + 0.171(FL) − 0.003685(AC)(FL).

For categorizing the fetus, we used the SEFW reported in the last ultrasound examination performed. Suspected LGA was defined as SEFW $>$ 90th percentile for GA, AGA as SEFW 10 to 90th percentile for GA, and fetal growth restriction as SEFW $<$ 10th percentile for GA.[14] Consistent with ACOG guidelines,[23] oligohydramnios was defined as a deepest vertical pocket $\leq$ 2.0 cm or an amniotic fluid index $\leq$ 5.0 cm, and polyhydramnios as a deepest vertical pocket $\geq$ 8.0 cm or amniotic fluid index $\geq$ 24.0 cm.

From each identified chart, data regarding maternal demographics, medical and obstetric history, prenatal course, medication used, sonographic examinations, intrapartum events, mode of delivery, and neonatal outcomes were extracted by a resident physician (L. A.-H.).

The primary outcome we compared among diabetic women with SFFW $\leq$ 90th percentile versus SFFW $>$ 90th percentile for GA was the CNM, defined as any one of the following: shoulder dystocia, Apgar score $<$ 5 at 5 minutes, admission to neonatal intensive care unit (NICU), mechanical ventilation, transient tachypnea of the newborn, respiratory distress syndrome, hypoglycemia, sepsis, seizure, fracture, neonatal brachial plexus palsy, or neonatal death. Shoulder dystocia was defined as failure to deliver the anterior shoulder with downward traction, necessitating additional obstetric maneuvers to effect delivery.[24] Hypoglycemia was defined as a blood glucose value less than 40 mg/dL in the first 24 hours of life.[25] Nomogram by Alexander et al[26] was used to categorize newborns as having BW $\leq$ 90th percentile or BW $>$ 90th percentile for GA.

Descriptive statistics were used to report all variables of interest. Differences in maternal characteristics and clinical outcomes between the two groups were examined using Student's *t*-test, chi-square test, or Fisher's exact test. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated where appropriate. A p-value $<$ 0.05 or 95% CI not crossing integer 1 was considered statistically significant.

Results

During the study period, we identified 321 diabetics that delivered at our institution. Of these, 181 (56%) were excluded, with the three most common reasons being: (1) managed by a private obstetrician/gynecologist (N = 59; 33%), (2) no documented SEFW within 4 weeks of delivery (N = 50; 28%), and (3) multifetal gestation (N = 34; 19%). Of the remaining 140 (43%) diabetics that met all the inclusion criteria, 34% (N = 47) had GDM-A1 (gestational diabetes controlled by diet), 54% (N = 76) had GDM-A2 (gestational diabetes controlled with medication), and 12% (N = 17) had pregestational diabetes. On the last documented sonographic exam, none of the fetuses had SEFW $<$ 10th percentile, 101 (72%) had estimate at 10th to 90th percentile, and the remaining 39 (28%) had an estimate $>$ 90th percentile for GA.

Among women with SEFW at 10th to 90th versus SEFW $>$ 90th percentile for GA, there were no significant differences in the maternal characteristics: age, ethnicity, nulliparity, body mass index at delivery of $<$ 30 kg/m^2 versus $\geq$ 30 kg/m^2, cigarette use, comorbidities (asthma, hypertensive disease of pregnancy, cholestasis, and thyroid disease), and rate of admission for blood glucose control. Marital status did differ between the two groups (►**Table 1**).

Table 1 Maternal characteristics

	SEFW 10th–90th percentile for GA ($N = 101$)	SEFW > 90th percentile for GA ($N = 39$)	*p*-Value	OR	95% CI
Maternal age (y)					
< 20	2 (2%)	3 (8%)	0.53		
20–34	71 (70%)	26 (67%)			
≥ 35	28 (28%)	10 (26%)			
Ethnicity					
Caucasian	9 (9%)	4 (10%)	0.97		
Afro-American	8 (8%)	1 (3%)			
Hispanic	80 (79%)	34 (87%)			
Other	4 (4%)	0 (0%)			
Nulliparous	77 (76%)	32 (82%)	0.13	0.49	0.19–1.23
BMI at delivery (kg/m^2)					
< 30	25 (25%)	10 (26%)	0.91	1.04	0.44–2.45
≥ 30	76 (75%)	29 (74%)			
Married	71 (70%)	35 (90%)	0.02	3.69	1.2–11.32
Cigarette use	4 (4%)	1 (3%)	0.69	0.63	0.06–5.89
Comorbidity					
Asthma	6 (6%)	4 (10%)	0.09		
Chronic hypertension	6 (6%)	2 (5%)			
Cholestasis	3 (3%)	0 (0%)			
Preeclampsia	19 (19%)	5 (13%)			
Thyroid disease[a]	8 (8%)	0 (0%)			
Admission for blood glucose control	6 (6%)	3 (8%)	0.71	1.31	0.32–5.55

Abbreviations: BMI, body mass index; GA, gestational age; SEFW, sonographic estimated fetal weight.
Note: Data presented as *N* (%).
[a]Hypo- or hyperthyroid disease.

There was a significantly higher number of women with GDM-A1 among the women with SEFW at 10th to 90th percentile compared with those with estimates above 90th percentile for GA (39 vs. 21%; OR, 2.43, 95% CI, 1.01–5.84). The time interval between the last SEFW and day of delivery was similar for the two groups (5.0 ± 7.4 days for those with estimate at 10th–90th percentile vs. 6.5 ± 7.5 days for those above 90th percentile for GA; $p = 0.29$). The rate of oligohydramnios was similar (4.0% for those with SEFW at 10th–90th percentile and 10.0% for those with estimates > 90th percentile; OR, 2.77; 95% CI, 0.65–1.68). The rate of polyhydramnios, however, was significantly lower in those with SEFW at 10th to 90th percentile versus those with estimates above 90th percentile for GA (3 vs. 15%; OR, 0.16; 95% CI, 0.03–0.71).

Several intrapartum characteristics—rate of delivery before 37 weeks versus at 37 weeks or later, augmentation/induction, chorioamnionitis, and duration of second stage among those who delivered vaginally—were similar for the two groups. The rate of cesarean delivery (CD) was significantly higher for women with SEFW > 90th percentile (48%) than those with an estimate of 10th to 90th percentile for GA (29%; OR, 2.24; 95% CI, 1.05–4.81). The discordance in the rate of CD was attributable to cesarean for SEFW > 90th for GA (20% of CD; ►**Table 2**).

Among all cohorts, the CNM was significantly higher for newborns that had SEFW > 90th percentile (28%) than those with estimate at 10th to 90th percentile for GA (13%; OR, 2.65; 95% CI, 1.07–6.59). The rate of shoulder dystocia was higher if the SEFW > 90th percentile (15%) rather than 10th to 90th percentile (2%; OR, 9.00; 95% CI, 1.73–46.70) as was of neonatal hypoglycemia (12 vs. 3%, respectively; OR, 4.81; 95% CI, 1.08–21.10). Among the two groups, there were no differences with regard to admission to NICU, mechanical ventilation, transient tachypnea of the newborn, respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, neonatal sepsis, periventricular leukomalacia, seizure, fracture, neonatal brachial plexus palsy, stillbirth, or death (►**Table 3**).

Of the 140 diabetics in the analysis, 78% ($N = 109$) attempted a trial of labor. Among these 109 women, the rate of CNM was significantly higher when the SEFW was

Table 2 Intrapartum characteristics

	SEFW 10th–90th percentile for GA ($N = 101$)	SEFW > 90th percentile for GA ($N = 39$)	*p*-Value	OR	95% CI
Gestational age at delivery (wk)					
34.0–36.6	14 (14)	7 (18)	0.54	1.35	0.50–3.67
≥ 37.0	87 (86)	32 (82)			
Augmentation	25 (24%)	5 (13%)	0.13	0.44	0.15–1.26
Induction	76 (75%)	34 (87%)	0.13	2.23	0.78–6.34
Chorioamnionitis	3 (3%)	3 (7%)	0.23	2.72	0.52–14.11
Stage II duration[a]					
< 2 h	65 (91%)	19 (95%)	0.61	1.75	0.19–15.48
≥ 2 h	6 (9%)	1 (5%)			
Cesarean delivery (CD)[b]	30 (29%)	19 (48%)[c]	**0.03**	**2.24**	**1.05–4.80**
Reasons for CD					
Repeat CD	12 (12%)	8 (20%)			
CPD	9 (9%)	2 (5%)			
NRFHT	6 (6%)	2 (5%)			
SEFW > 90th percentile[d]	0 (0%)	8 (20%)			
Others[e]	3 (3%)	0 (0%)			

Abbreviations: CPD, cephalopelvic disproportion; GA, gestational age; NRFHT, nonreassuring fetal heart tones; SEFW, sonographic estimated fetal weight

Note: Data presented as *N* (%). Bolded if significantly different.

[a]Among women who delivered vaginally.

[b]There were no operative vaginal deliveries.

[c]A woman had more than one indication.

[d]Among eight cesarean for SEFW > 90th percentile for GA, four had SEFW > 4,500 g, one had SEFW > 95th percentile and history of shoulder dystocia, and three had SEFW > 95th percentile but < 4,500 g.

[e]Included for history of shoulder dystocia, active herpes, and malpresentation.

above 90th percentile (29%) as compared with 10th to 90th percentile for GA (10%; OR, 3.47; 95% CI, 1.13–10.64). For women with SEFW above 90th percentile, the likelihood of shoulder dystocia was about 1 in 4 (24%), which was significantly higher than if the estimate was 10th to 90th percentile (2%; OR, 13.83; 95% CI, 2.57–74.18). The rate of hypoglycemia was similar in the women who attempted labor and had SEFW 10th to 90th versus SEFW > 90th percentile for GA (►**Table 4**).

Discussion

The main findings of our study include that the CNM among diabetic pregnancies was significantly higher for those with SEFW > 90th percentile for GA than those at 10th to 90th. The components of the CNM that differed between the two groups were shoulder dystocia and neonatal hypoglycemia. The morbidity and mortality with actual BW above certain thresholds is acknowledged,[15–18,27–29] but the BW is unknown to clinicians until after the delivery. Additionally, most macrosomic newborns are unidentified as having accelerated growth before birth.[30,31] Thus, studies assessing the link between SEFW and adverse outcomes are pragmatic for the management of pregnancy complicated by diabetes.[32–34]

SEFW > 90th percentile has been reported to be associated with shoulder dystocia and is plausible. Regardless of the diabetic status, earlier reports suggest that shoulder dystocia occurred in 12% (95% CI, 7–20%) if the SEFW was above 90th percentile.[34] The plausible reasons that an SEFW above 90th percentile is a risk factor for shoulder dystocia are: (1) it is associated with macrosomia, a known risk factors for impacted shoulder;[32,33] (2) diabetes is a risk factors for shoulder dystocia;[16,24] and (3) there are anthropometric differences among newborns with and without shoulder dystocia and these are attenuated among diabetics pregnancies.[32,35–37]

Previously, Chiossi et al[28] published a bayesian meta-analysis of 27 articles, which reported on morbidity linked with LGA. Compared with non-LGA, those with accelerated growth did not have increased risk of hypoglycemia. Our findings differ from the meta-analysis because we focused only on diabetic women, while the published reports included all women or even excluded diabetic women. The plausible reason for hypoglycemia is explained by the Pedersen hypothesis that maternal hyperglycemia results in fetal hyperglycemia, which stimulates fetal pancreatic islet cell hypertrophy with subsequent increased insulin secretion. Shortly after delivery with separation of the maternal–fetal pair, the neonate is not

Table 3 Neonatal outcomes

	SEFW 10th–90th percentile for GA ($N = 101$)	SEFW > 90th percentile for GA ($N = 39$)	*p*	OR	95% CI
Female	47 (46%)	22 (56%)	0.29	1.48	0.71–3.12
Birth weight > 90th percentile[a]	18 (18%)	29 (74%)	**<0.001**	**13.37**	**5.54–32.27**
CNM	13 (13%)	11 (28%)	**0.03**	**2.65**	**1.07–6.59**
Shoulder dystocia	2 (2%)	6 (15%)	**0.01**	**9.00**	**1.73–46.77**
NICU admission	11 (11%)	9 (23%)	0.07	2.45	0.92–6.49
Apgar score < 5 at 5 minutes	0 (0%)	1 (2%)	0.21	7.91	0.31–188.36
Mechanical ventilation	5 (5%)	5 (12%)	0.11	2.82	0.76–10.35
TTN	2 (2%)	2 (5%)	0.33	2.67	0.36–19.70
RDS	1 (1%)	1 (2%)	0.49	2.63	0.16–43.10
Hypoglycemia	3 (3%)	5 (12%)	**0.03**	**4.81**	**1.08–21.10**
IVH grade 3 or 4	0 (0%)	0 (0%)	0.63	2.56	0.05–131.75
NEC	0 (0%)	0 (0%)	0.63	2.56	0.05–131.75
Sepsis	0 (0%)	1 (2%)	0.21	7.91	0.31–188.36
PVL	0 (0%)	0 (0%)	NC		
Seizure	1 (1%)	1 (2%)	0.49	2.63	0.16–43.1
Fracture—skull, clavicle, humerus, or other	1 (1%)	3 (7%)	0.07	8.33	0.83–82.7
NBPP	0 (0%)	0 (0%)	NC		
Stillbirth	0 (0%)	0 (0%)	NC		
Neonatal Death	0 (0%)	0 (0%)	NC		

Abbreviations: CNM, composite neonatal morbidity; GA, gestational age; IVH, intraventricular hemorrhage; NBPP, neonatal brachial plexus palsy; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; PVL, periventricular leukomalacia; RDS, respiratory distress syndrome; SEFW, sonographic estimated fetal weight; TTN, transient tachypnea of the newborn.
Note: Data presented as *N* (%). Bolded if significantly different.
[a]Using the nomogram published by Alexander et al.[26]

supported by placental glucose transfer and hypoglycemia ensues.[38] In patients with SEFW > 90th percentile, it has been shown that these infants have a higher risk of neonatal hypoglycemia secondary to increased fetal hyperglycemia, and thus hyperinsulinemia[39,40]

The rate of CD was significantly higher among those with SEFW > 90th percentile for GA than those at 10th to 90th. Other investigators have also reported that SEFW among diabetic women is linked with increased rate of CD.[6,41] Our findings differ from other reports in that we were able to specify the reason for increased CD: scheduled cesarean due to SEFW > 90th percentile. Diabetic women who labored had a similar rate of CD, irrespective of SEFW. The practice bulletin on gestational diabetes[12] does suggest that clinical and sonographic estimate have similar accuracy in detection of macrosomia and that either method to assess fetal weight is acceptable. The corollary of the suggestion should not be that with clinical estimates of fetal weight, the excessive

Table 4 Diabetic women who attempted labor

	SEFW 10th–90th percentile for GA ($N = 85$)	SEFW > 90th percentile for GA ($N = 24$)	*p*	OR	95% CI
Cesarean delivery	15 (18%)	4 (17%)	0.91	0.93	0.28–3.13
CNM	9 (10%)	7 (29%)	**0.02**	**3.47**	**1.13–10.64**
Shoulder dystocia	2 (2%)	6 (25%)	**0.002**	**13.83**	**2.57–74.18**
Hypoglycemia	2 (2%)	3 (12%)	0.05	5.92	0.93–37.7

Abbreviations: CNM, composite neonatal morbidity; GA, gestational age; SEFW, sonographic estimated fetal weight.
(CNM consisted of any of the following: shoulder dystocia, Apgar score < 5 at 5 minute, admission to neonatal intensive care unit, mechanical ventilation, transient tachypnea of the newborn, respiratory distress syndrome, hypoglycemia, sepsis, seizure, fracture, neonatal brachial plexus palsy, or neonatal death).
Note: Data presented as *N* (%). Bolded if significantly different.

CD rate would be lowered, without influencing CNM. A randomized trial where women are managed with either sonographic or clinical estimated fetal weight is needed to determine which method lowers CD without altering the CNM.

Despite the increased risk in CNM in patients with SEFW > 90th percentile, we caution clinicians neither to induce for estimated fetal weight alone nor to proceed with CD because of accelerated growth. Indeed, if the SEFW is 4,500 g or greater, ACOG recommends considering CD among diabetics,[13,27,33] and our findings should not be exploited to modify the national guidelines. There are several reasons not to modify the current management of diabetes because of our findings. First, this is a retrospective study with a small sample size. Second, dystocia and other morbidities noted in our analysis do not have long-term sequela. Moreover, none of the newborns had transient or persistent neonatal brachial plexus, which is the real nightmare.[42] Third, the randomized trial by Boulvain et al[43] of early-term induction for LGA included SEFW > 95th percentile for GA and excluded diabetic women on medical treatment. Hence, the findings of the pragmatic trial at 19 centers are not applicable to most diabetic women.

Aside from the small sample size and the retrospective study design, there are other limitations. Since many of the neonatal morbidity outcomes had no or infrequent events, a multivariable regression adjustment for these outcomes is not feasible. Furthermore, residents supervised by maternal–fetal medicine subspecialists managed all of the diabetic women at a tertiary center. Thus, the findings may not be generalizable to other settings. We did not focus on the intrapartum management of blood sugar, which influences the likelihood of neonatal hypoglycemia.[39,40] Residents and RDMS did SEFW, and their accuracy in estimating fetal weight is not equivalent.[44] We recognize that if an RDMS had had consistently performed the SEFW, the outcomes could be different. Lastly, we did not ascertain the diagnostic accuracy of SEFW in identifying newborns with actual BW > 90th percentile for GA or of macrosomia, which has been the focus previously.[2,14,34]

Despite the shortcomings, there are strengths to our analysis. There is a paucity of publications on SEFW among diabetic women and its association with CNM.[6] While others have focused on shoulder dystocia related to SEFW,[33] we explored other neonatal morbidity linked with SEFW. Our findings of increased likelihood of shoulder dystocia and of hypoglycemia have biological plausibility.

Conclusion

In summary, the CNM was significantly higher among diabetic women with SEFW > 90th percentile as compared with 10th to 90th percentile. Larger observational trials are needed to confirm the findings, as well as interventional trial to determine if early-term delivery among diabetic mitigates the morbidity[43] associated with SEFW > 90th percentile for GA.

Conflict of Interest
The authors report no conflict of interest.

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Condensation
Among diabetics, the composite neonatal morbidity was higher if sonographic estimated fetal weight was > 90th percentile for gestational age (28%) than at 10 to 90th percentile (13%; OR, 2.65; 95% CI, 1.07–6.59).

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