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Original Research

Umbilical Cord Abnormalities and Stillbirth

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OBJECTIVE: Umbilical cord abnormalities are commonly cited as a cause of stillbirth, but details regarding these stillbirths are rare. Our objective was to characterize stillbirths associated with umbilical cord abnormalities using rigorous criteria and to examine associated risk factors.

METHODS: The Stillbirth Collaborative Research Network conducted a case-control study of stillbirth and live births from 2006 to 2008. We analyzed stillbirths that underwent complete fetal and placental evaluations and cause of death analysis using the INCODE (Initial Causes of Fetal Death) classification system. Umbilical cord abnormality was defined as cord entrapment (defined as nuchal, body, shoulder cord accompanied by evidence of cord occlusion on pathologic examination); knots, torsions, or strictures with thrombi, or other obstruction by pathologic examination; cord prolapse; vasa previa; and compromised fetal microcirculation, which is defined as a histopathologic finding that represents objective evidence of vascular obstruction and can be used to indirectly confirm umbilical cord abnormalities when suspected as a cause for stillbirth. We compared demographic and clinical factors between women with stillbirths associated with umbilical cord abnormalities and those associated with other causes, as well as with live births. Secondarily, we analyzed the subset of pregnancies with a low umbilical cord index.

RESULTS: Of 496 stillbirths with complete cause of death analysis by INCODE, 94 (19%, 95% CI 16–23%) were associated with umbilical cord abnormality. Forty-five (48%) had compromised fetal microcirculation, 27 (29%) had cord entrapment, 26 (27%) knots, torsions, or stricture, and five (5%) had cord prolapse. No cases of vasa previa occurred. With few exceptions, maternal characteristics were similar between umbilical cord abnormality stillbirths and non–umbilical cord abnormality stillbirths and between umbilical cord abnormality stillbirths and live births, including among a subanalysis of those with hypo-coiled umbilical cords.

CONCLUSION: Umbilical cord abnormalities are an important risk factor for stillbirth, accounting for 19% of cases, even when using rigorous criteria. Few specific maternal and clinical characteristics were associated with risk.

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Stillbirth, defined as fetal death occurring at or beyond 20 weeks of gestation, occurs in 6 of 1,000 pregnancies in the United States.[1] Since 2003, the number of stillbirths has been stable at approximately 24,000 each year.[1] Commonly referred to as a "cord accident," stillbirth due to umbilical cord abnormality occurs when blood flow through the cord is compromised sufficiently to cause death.[2,3] Umbilical cord abnormalities can be acute or chronic, as well as intermittent or persistent. Any of these can lead to inadequate delivery of oxygen and nutrients and clearance of metabolic waste. The reported rates of umbilical cord abnormalities associated with stillbirth is reported to be 2.5%–30%.[4–7] However, the diagnostic criteria used to define umbilical cord abnormalities in the setting of stillbirth have not been clearly defined, and confirmation of cord abnormalities as a cause of stillbirth using autopsy and placental pathology is rare.

Understanding the contribution of umbilical cord abnormalities to stillbirth is important. Stillbirths are commonly attributed to "cord accidents" without high quality data on which to base such clinical impressions. Without such data, stillbirths may be inappropriately attributed to umbilical cord abnormalities, leading to incorrect counseling, inadequate evaluation, and suboptimal care in subsequent pregnancies. Thus, our purpose was to thoroughly characterize stillbirths associated with umbilical cord abnormalities in the SCRN (Stillbirth Collaborative Research Network) study and to explore maternal and clinical factors associated with these stillbirths.

METHODS

This study is a secondary analysis of both stillbirths and live births enrolled in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development SCRN case-control study. The overall design, methods, and recruitment of the study have been previously reported.[8] This study was approved by each collaborating site institutional review board. Women were enrolled at delivery between March 2006 and September 2008. The five catchment areas were defined by state and county boundaries, including Rhode Island and portions of Massachusetts, Georgia, Texas, and Utah. Any residents of the five catchment areas who were at least 13 years of age and nonincarcerated were potentially eligible for the study. All eligible women whose delivery resulted in one or more stillborn fetuses were approached for consent, as well as a representative sample of live births, with oversampling of live births for preterm birth and non-Hispanic black race. Stillbirth was defined by Apgar scores of 0 at 1 and 5 minutes and no signs of life by direct observation. Terminations of pregnancy with a live fetus were excluded from the study.

Gestational age was determined by the best clinical estimate using multiple sources, including information from assisted reproduction, last menstrual period, and obstetric ultrasonograms.[8] Fetal deaths at 18 or 19 weeks of gestation without good dating were also included so that stillbirths beyond 20 weeks of gestation but with incorrect dating parameters could be enrolled. The protocol included an in-hospital interview, medical record abstraction, placental and umbilical cord gross and histopathology examination, and biospecimen collection for cases and controls. For stillbirths, a standardized postmortem examination was also performed.[9–11] All participating pathologists had training in perinatal pathology, and underwent centralized workshop training to perform standardized evaluations across sites.

Our analysis included all stillbirths that underwent complete fetal autopsy and placental histopathologic evaluations, including cause of death analysis using the INCODE (Initial Causes of Fetal Death) classification system. Stillbirths with missing cause of death data were not included. The INCODE system is a hierarchical division of potential causes of fetal death into probable, possible and present categories. Details have been previously published.[12] A probable cause carries a high likelihood of causing the fetal death. A possible cause is one for which there is reasonable certainty that the condition is on the pathophysiologic pathway leading to death. A present cause is a condition that is documented but in remission, controlled with medications, or not deemed to be involved in the etiology of the fetal death. To determine the INCODE cause of death, the results of a standardized examination of the fetus, umbilical cord, and placenta, as well as chart abstraction and test results were obtained as a part of a recommended work-up.[9–11]

Umbilical cord abnormality was defined as cord entrapment (nuchal, body, or shoulder cord accompanied by evidence of cord occlusion by histopathologic exam); knots; torsions or strictures with histopathologic evidence of thrombi or other obstruction; and evidence of fetal hypoxia, cord prolapse, vasa previa, or compromised fetal microcirculation (defined as thromboembolism of the umbilical vein, large fetal vessels, or thromboembolism of villous fetal capillaries and avascular villi with evidence of obstruction).[12,13] This expands the original INCODE criteria for umbilical cord abnormalities, which included only cord entrapment, knots, torsions, or strictures, cord prolapse, and vasa previa. The definition was expanded for this analysis

owing to subsequent recognition of umbilical vein thrombosis as an important finding in umbilical cord abnormality-associated stillbirth.[14] Only cases wherein umbilical cord abnormality was considered a probable or possible cause of death based on INCODE were considered umbilical cord abnormality stillbirths.

Demographic and clinical variables, including sociodemographic, medical, psychosocial, and reproductive history variables, were selected for analysis based on their potential associations with stillbirth. These variables were compared between women with stillbirths attributable to umbilical cord abnormality (umbilical cord abnormality stillbirths) and women with stillbirths associated with other causes (non–umbilical cord abnormality stillbirths), as well as with women with live births with adequate placental examination. A subanalysis was performed according to umbilical cord index (in coils per cm of cord length), which was categorized as high (umbilical cord index 0.3 coils/cm or higher), intermediate (0.07–0.3 coils/cm), or low (umbilical cord index 0.07coils/cm or lower), because umbilical cord index has been associated with stillbirth.[15]

This analysis was performed using SAS 9.4, and the unit of analysis was the pregnancy. Categorical variables were compared using Fisher exact and χ^2 analyses and continuous variables were assessed using *t* test. No corrections for multiple comparisons were made. *P*-values were considered significant if less than 0.05. Data were weighted for this analysis to account for study design of over- and under-sampling of racial or ethnic groups and gestational age at delivery. Use of analytical weights yields live-birth estimates that more closely approximate the general population of live births in the five geographic catchment areas during SCRN enrollment. The methods for calculation of weighted data have been described previously.[8]

RESULTS

A total of 496 pregnancies complicated by stillbirth and 1,447 women with pregnancy ending in live birth met study inclusion criteria for the primary analysis (Fig. 1). Of stillbirths, 94 (19%, 95% CI 16–23%) were attributed to umbilical cord abnormalities. Of these, 45 (48%) had compromised fetal microcirculation, 27 (29%) had cord entrapment, 26 (27%) had knots, torsions, or stricture, and 5 (5%) had a cord prolapse. No cases of vasa previa were identified (Table 1). Just more than half of umbilical cord abnormality stillbirths occurred after 32 weeks of gestation (Fig. 2).

There were no differences in demographic or socioeconomic factors in women with umbilical cord

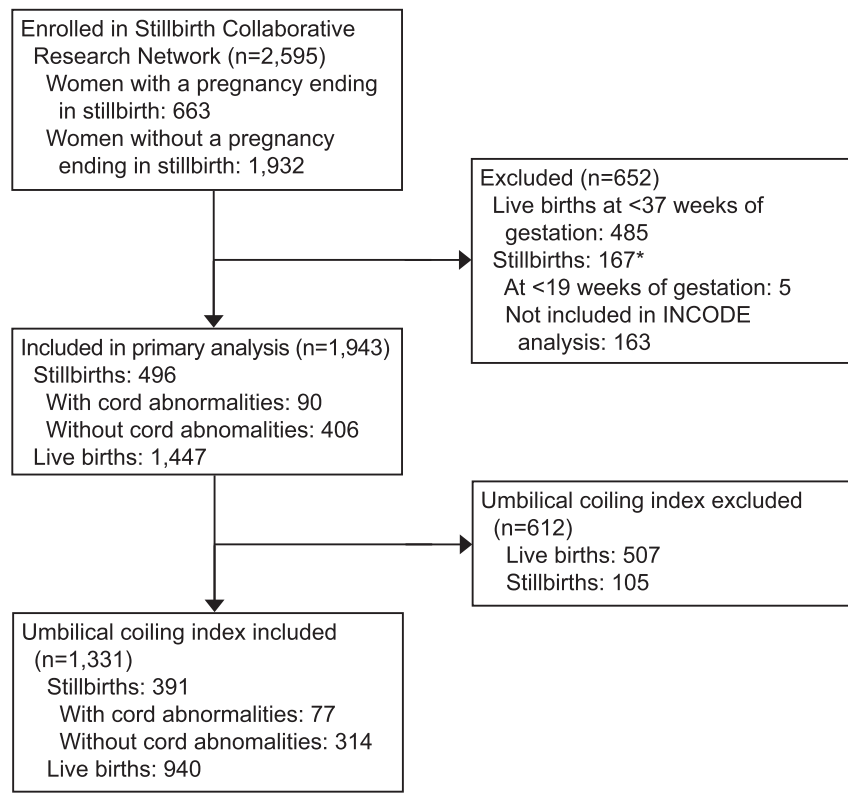

Fig. 1. Eligibility flow diagram. *Items not mutually exclusive.

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Table 1. Umbilical Cord Abnormality Subtypes Among Stillbirths According to Likelihood of Umbilical Cord Abnormality as a Cause of Death by INCODE

Umbilical Cord Abnormality Subtype	Overall (N=94)*	Subset	
		Probable (n=60)	Possible (n=34)
Compromised fetal microcirculation	45 (48)	22 (36)	24 (69)
Cord entrapment	27 (29)	17 (30)	10 (31)
Knots, torsions, strictures	26 (27)	26 (43)	0
Cord prolapse	5 (5)	5 (8)	0
Vasa previa	0	0	0

* Owing to overlap between compromised fetal microcirculation and other causes, percentages do not add up to 100.

abnormality stillbirths compared with women with non–umbilical cord abnormality stillbirths (Table 2). Compared with women with live births, women with umbilical cord abnormality stillbirths were more often obese (Table 2).

Medical and obstetric characteristics of umbilical cord abnormality and non–umbilical cord abnormality stillbirths are depicted in Table 3. Compared with non–umbilical cord abnormality stillbirths, umbilical cord abnormality stillbirths occurred an average of 3.2 weeks later in pregnancy. Otherwise, no differences were identified between umbilical cord abnormality and non–umbilical cord abnormality stillbirth cases. Compared with women with live births, women with umbilical cord abnormality stillbirths were less likely to have thyroid-stimulating hormone levels of 2.5 micro-international units/mL or higher. Although a clinical history of hypertension, diabetes, and multifetal pregnancy was marginally associated with umbilical cord abnormality stillbirth, no other significant differences were identified, including alcohol or drug exposure, and hypertensive disorders of pregnancy (Table 3).

Among the subset of 1,331 women included in analysis of umbilical cord index, there were a total of 357 deliveries with a high umbilical cord index, 709 with intermediate, and 168 with low umbilical cord index. Neither high umbilical cord index (present in 30% of stillbirths and 28% of live births, P=.609) nor intermediate umbilical cord index (present in 53% of stillbirths and 59% of live births, P=.061) were associated with stillbirth, overall. Low umbilical cord index was significantly associated with stillbirth overall (17% of stillbirths vs 12% of live births; odds ratio 1.4, 95% CI 1.02–2.01). To assess the robustness of the association between low umbilical cord index and stillbirth, we estimated an adjusted logistic regression model of stillbirth weighted for sampling design. Covariates considered for inclusion were factors with differences between groups in Table 3, with the final model including low umbilical cord index, parity and hypertension. After adjusting for parity and hypertension, low umbilical cord index remained significantly associated with stillbirth (adjusted odds ratio 1.5, 95% CI 1.1–2.1). In the subcohort of pregnancies with low umbilical cord index, women with umbilical cord abnormality stillbirths were more educated, had higher body mass indexes (BMIs, calculated as weight in kilograms divided by height in meters squared), and delivered later compared with non–umbilical cord abnormality stillbirths. Stillbirths differed from live births in that women with pregnancies ending in stillbirth had higher average BMI (Table 4). Among pregnancies with low umbilical cord index, the only factors that distinguished umbilical cord abnormality stillbirths from both live births and non–umbilical cord abnormality stillbirths was BMI.

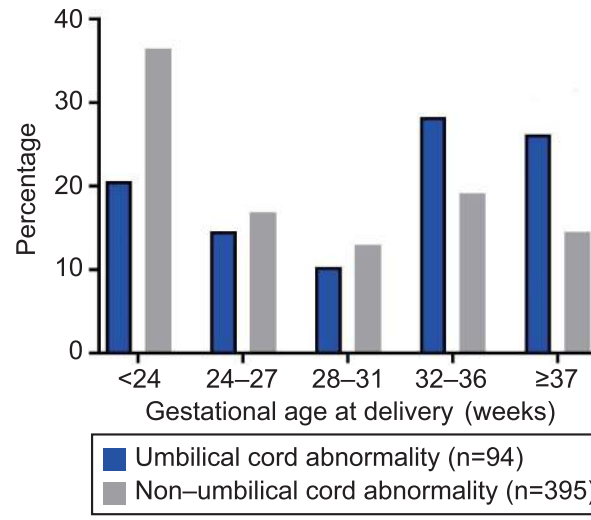

Fig. 2. Timing of stillbirth by cause of death. Overall P=.004 for umbilical abnormality vs non–umbilical cord abnormality stillbirth distributions across gestational periods.

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Table 2. Demographic Characteristics

Characteristic	Stillbirths		*P*, UCA vs Non-UCA	Live Births (n=1,285)	*P*, UCA Stillbirths vs Live Births
	UCA n=94	Non-UCA n=395			
Maternal age at delivery (y)	27.0±7.4	27.6±6.6	.519	27.5±5.7	.591
Maternal race–ethnicity			.093		.098
White non-Hispanic	32 (34)	136 (34)		603 (47)	
Black, non-Hispanic	14 (15)	103 (26)		144 (11)	
Hispanic	41 (44)	130 (33)		438 (34)	
Other	7 (7)	26 (7)		101 (8)	
Born in the United States			.434		.899
Yes	71 (81)	290 (77)		983 (80)	
No	17 (19)	87 (23)		242 (20)	
Insurance or method of payment			.925		.327
No insurance	6 (7)	24 (6)		45 (3)	
Any public or private	47 (50)	205 (52)		600 (47)	
Veterans Affairs	41 (43)	164 (42)		638 (50)	
Maternal education (y)	13.3±2.8	13.0±2.9	.300	13.5±2.9	.534
Maternal education, grade categorized			.746		.812
0–11 (none or primary)	17 (19)	82 (22)		219 (18)	
12 (completed secondary)	23 (27)	109 (29)		299 (24)	
13 or more (college)	47 (54)	185 (49)		702 (58)	
Family income past 12 mo			.852		.426
Only public or private	9 (10)	31 (8.4)		69 (6)	
Assistance and personal income	29 (33)	133 (36)		442 (36)	
Only personal income	48 (56)	209 (56)		704 (58)	
Relationship status			.240		.181
Not married or cohabitating	18 (21)	102 (27)		180 (15)	
Cohabitating or married	69 (79)	275 (73)		1,045 (85)	
Parity			.730		.062
Nulliparous	44 (47)	176 (45)		461 (36)	
Multiparous	50 (53)	219 (55)		816 (64)	
Maternal BMI (kg/m^2)	28.4±7.3	27.3±6.8	.179	26.3±6.4	.009
Maternal BMI categorized			.208		.026
Less than 30	59 (65)	278 (72)		964 (77)	
30 or greater (obese)	32 (35)	107 (28)		285 (23)	

UCA, umbilical cord abnormalities; BMI, body mass index.
Data are mean±SD or n (%) unless otherwise specified.
Column totals reflect weighted adjustment for over- and under-representation of population groups. Unweighted column totals: 90 UCA, 406 non-UCA, 1,447 live births.
P-values reported from Wald χ^2 for categorical variables or two-sample *t*-test for continuous variables.

We also evaluated umbilical cord index on a continuum; there were significant differences across all deciles in stillbirth, however, not in a manner indicative of a pattern of increasing or decreasing trend. The highest percentages of stillbirth occurred in the first, fourth, fifth and 10th deciles. Of note, when comparing an umbilical cord index of zero to any higher umbilical cord index, umbilical cord indexes of zero were twice more frequently seen among stillbirths compared with live births (10% vs 5%, *P*=.002).

The above results did not change when we compared women with missing umbilical cord index data with women with umbilical cord index available (Appendices 1 and 2, available online at http://links.lww.com/AOG/B725).

DISCUSSION

In a prospective study with high-quality data and rigorous cause of death analysis, we found that 19% of all stillbirths and 28% of stillbirths at or beyond 32 weeks of gestation were associated with umbilical cord abnormalities. Umbilical cord abnormality included five conditions or pathways: cord entrapment, knots, torsions, or strictures, cord prolapse, vasa previa, and compromised fetal microcirculation. Cord entrapment, which includes nuchal, body, or shoulder cord, is a common finding at birth, and, although even multiple nuchal loops are not associated with stillbirth, cord entrapment is associated with adverse intrapartum events.[16–19] Umbilical cord knots, torsions or strictures are reported to occur in 0.3–2.1%

Table 3. Clinical Characteristics

Characteristic	Stillbirths				
	UCA (n=94)	Non-UCA (n=395)	*P*, UCA vs Non-UCA	Live Births (n=1,285)	*P*, UCA Stillbirths vs Live Births
No prenatal care	4 (4)	39 (10)	.023	37 (3)	.690
Chronic hypertension	11 (11)	39 (10)	.695	69 (5)	.096
Asthma	9 (10)	37 (10)	.976	93 (8)	.525
Seizures	2 (2)	11 (3)	.779	21 (2)	.709
Pregestational diabetes	5 (6)	22 (5)	.972	15 (1)	.113
Thyroid disorder	3 (3)	15 (4)	.796	54 (4)	.562
Kidney disease	1 (2)	6 (2)	.953	7 (1)	.528
Sickle cell disease	0	0	—	0	—
Autoimmune disorder	1 (1)	0	—	13 (1)	.796
Mental illness	8 (9)	27 (7)	.569	85 (7)	.484
UTI during pregnancy	11 (12)	56 (15)	.506	188 (15)	.382
TSH (micro-international units/mL)					
2.5 or greater	19 (23)	93 (26)	.543	437 (41)	<.001
0.1 or less	1 (1)	5 (1)	.741	3 (0)	.480
Assisted reproductive technology	3 (3)	18 (4)	.466	50 (4)	.623
Umbilical cord cotinine (ng/mL)	11 (13)	64 (18)	.257	94 (9)	.293
Alcohol use during pregnancy	1 (1)	12 (3)	.150	19 (2)	.661
Tobacco use during pregnancy	11 (12)	49 (13)	.776	90 (7)	.219
Drug use during pregnancy	2 (2)	12 (3)	.694	31 (2)	.945
Abuse (physical, sexual, or emotional)	2 (3)	5 (1)	.517	28 (2)	.826
Multifetal pregnancy	6 (6)	27 (7)	.785	15 (1)	.053
Presenting symptom—vaginal bleeding	2 (3)	33 (9)	.024	10 (1)	.332
Preeclampsia	8 (9)	44 (12)	.435	91 (7)	.658
GA of stillbirth (wk)	30.6±7.6	27.4±6.9	<.001		
Male	41 (47)	198 (54)	.222	631 (50)	.624
Female	47 (53)	166 (46)		639 (50)	
LBW less than 2,500 g	31 (37)	68 (19)	.003	1,213 (98)	<.001
Stillbirth timing			.006		
Intrapartum	9 (9)	79 (20)			
Antepartum	85 (91)	316 (80)			

UCA, umbilical cord abnormalities; UTI, urinary tract infection; TSH, thyroid-stimulating hormone; LBW, low birth weight.
Column totals reflect weighted adjustment for over- and under-representation of population groups. Unweighted column totals: 90 UCA, 406 non-UCA, 1,447 live births.
P-values reported from Wald χ^2 for categorical variables or two-sample *t*-test for continuous variables. *P*-values are not reported where cell counts are 0.

of pregnancies with a stillbirth rate of 8–11%.[20–23] In the absence of histopathologic confirmation of umbilical cord abnormality as a cause of death, these studies are difficult to interpret, especially because nuchal cords and true knots are common findings that result in healthy live births in a majority of cases.[16–19,24] Cord prolapse usually occurs after preterm prelabor rupture of membranes and is associated with a high rate of perinatal mortality.[25] Although mortality is high if cord prolapse occurs, it accounted for only 9% of umbilical cord abnormality stillbirths and 1% of stillbirths overall in our study. Vasa previa occurs when the fetal vessels traverse the membranes overlying the internal cervical os. This occurs rarely and when diagnosed prenatally, has a low perinatal mortality.[26–28] Finally, compromised fetal microcirculation is a histopathologic finding that represents objective evidence of vascular obstruction and can be used to indirectly confirm umbilical cord abnormality when it is suspected as a cause for stillbirth. In this cohort, compromised fetal microcirculation was coded as a "possible" cause of death when it was present without clinical evidence of cord obstruction and as a "probable" cause when both the histopathologic criteria were met and clinical evidence of obstruction was present. With that being said, there is always the possibility of an overlap in conditions and pathways leading to fetal stillbirth.

Abnormal umbilical cord index is associated with adverse perinatal outcomes such as fetal heart rate decelerations, operative vaginal delivery, preterm birth, and stillbirth.[29–31] In our cohort, high umbilical cord index was not associated with stillbirth, whereas low umbilical cord index was. This adds to a body of

Table 4. Clinical Characteristics Among Pregnancies With Low Umbilical Cord Index (0.07 or Less)

Characteristic	Stillbirths		*P*-Value, UCA vs Non-UCA	Live Births (n=104)	*P*, UCA Stillbirths vs Live Births
	UCA (n=14)	Non-UCA (n=50)			
Maternal age at delivery (y)	30.6±8.0	26.4±6.0	0.083	27.1±5.4	0.126
Maternal education (y)	14.9±3.6	12.3±3.2	0.037	13.6±3.1	0.265
Nulliparous	3 (25)	22 (43)	0.188	35 (33)	0.516
Maternal BMI (kg/m^2)	31.0±7.0	26.1±5.3	0.022	26.1±5.3	0.014
Maternal BMI 30 or higher	7 (48)	9 (19)	0.066	25 (24)	0.111
Chronic hypertension	2 (15)	4 (8)	0.511	2 (2)	0.201
Asthma	0	6 (13)	—	5 (5)	—
Seizures	0	1 (2)	—	2 (2)	—
Pregestational diabetes	0	3 (7)	—	1 (1)	—
Thyroid disorder	2 (12)	1 (2)	0.215	1 (1)	0.196
Kidney disease	0	1 (2)	—	0	—
Sickle cell disease	0	1 (3)	—	0	—
Autoimmune disorder	1 (5)	0	—	0 (0)	0.354
Mental illness	3 (26)	5 (11)	0.308	7 (7)	0.195
UTI during pregnancy	1 (10)	7 (16)	0.589	13 (13)	0.797
TSH (micro-international units/mL)					
2.5 or greater	5 (38)	11 (34)	0.371	34 (40)	0.928
0.1 or less	0	0	—	0	—
Assisted reproductive technology	1 (5)	0	—	8 (8)	0.677
Alcohol use during pregnancy	0	1 (2)	—	1 (1)	—
Tobacco use during pregnancy	1 (8)	5 (10)	0.907	6 (6)	0.722
Drug use during pregnancy	0	2 (3)	—	2 (2)	—
Abuse (physical, sexual, or emotional)	0	0	—	1 (1)	—
Presenting symptom—vaginal bleeding	0	6 (12)	—	1 (1)	—
Preeclampsia	2 (18)	8 (17)	0.984	10 (10)	0.544
GA of stillbirth (wk)	32.5±7.6	27.6±7.1	0.029	—	—
Male	7 (51)	25 (51)	0.997	50 (48)	0.817
Female	7 (49)	24 (49)		54 (52)	
LBW less than 2,500 g	7 (50)	9 (19)	0.052	102 (98)	0.004
Stillbirth timing			0.030	—	
Intrapartum	1 (5)	13 (26)			
Antepartum	13 (95)	37 (74)			

UCA, umbilical cord abnormalities; BMI, body mass index; UTI, urinary tract infection; TSH, thyroid-stimulating hormone; LBW, low birth weight.

Column totals reflect weighted adjustment for over- and under-representation of population groups. Unweighted column totals: 13 UCA, 106 non-UCA, 233 live births. All comparisons include sampling weights.

P-values reported from Wald χ^2 for categorical variables or two-sample *t*-test for continuous variables. *P*-value not reported in presence of 0 cells.

literature reporting mixed results regarding high umbilical cord index[15,29–32] but consistent associations of low umbilical cord index with adverse events.[15,29,31,33] Several studies tested the association between prenatally assessed umbilical cord index and adverse outcomes with mixed results.[32,33] Mittal et al[33] prospectively assessed 200 pregnancies for umbilical cord index using ultrasonography between 20 and 24 weeks of gestation and found a low umbilical cord index to be associated with preterm contractions, oligohydramnios, intrapartum fetal heart rate abnormalities, operative vaginal delivery, and low birth weight. Ma'ayeh et al[32] prospectively assessed 72 women for high umbilical cord index using ultrasonography in the second trimester but did not identify associations with adverse outcomes. Taken together, the clinical significance of umbilical cord index, whether identified prenatally or after an adverse event such as stillbirth, remains uncertain.

Previous studies were comprised primarily of retrospectively reviewed case series and case-control studies, such that the reported contribution of umbilical cord abnormalities to stillbirth varies widely, from 8% to 65%.[34–38] Given the high frequency of nuchal cords and true knots in uncomplicated live births, there has been understandable skepticism when stillbirths are attributed to the umbilical cord abnormality. A previous analysis of SCRN data reported that

approximately 10% of stillbirths were associated with umbilical cord abnormality.[13] The rate of umbilical cord abnormality-associated stillbirth is higher in this analysis owing to our inclusion of umbilical vein thrombosis in the definition of umbilical cord abnormality based on data supporting its role in umbilical cord abnormality-associated stillbirth.[14] Our data establish an important baseline rate of umbilical cord abnormality stillbirths and confirm cord abnormalities as a substantial contributor to stillbirths in the United States.

Although we identified minor differences between umbilical cord abnormality stillbirths and live births, these factors were not different between umbilical cord abnormality stillbirths and non–umbilical cord abnormality stillbirths, such that they do not lend themselves to practical use for risk stratification. Among pregnancies with low umbilical cord index, maternal BMI was higher and among umbilical cord abnormality stillbirths than both non–umbilical cord abnormality stillbirths and live births. Of note, although this was statistically important finding, the actual BMI distribution are not different, which means that the finding was not clinically helpful. The relevance of these differences is unclear as there is not an apparent biologically plausible explanation.

A previous analysis of the SCRN cohort found that a higher proportion of stillbirth was associated with umbilical cord abnormality in non-Hispanic white women compared with other groups.[13] However, race and ethnicity were not associated with umbilical cord abnormality stillbirth in this analysis. Differences between the two analyses include the definition of umbilical cord abnormality and the incorporation of sampling weights to account for oversampling and ensure population-level representation for comparisons between stillbirths and live births. Because the rate of umbilical cord abnormality stillbirths is relatively low in all racial or ethnic groups, race and ethnicity are unlikely to be a useful predictor of umbilical cord abnormality stillbirth, whether or not the proportion of umbilical cord abnormality-attributable stillbirths truly varies across race and ethnicity.

Our study has multiple strengths. The prospective data collection, standardized evaluation protocols and unbiased recruitment strategy maximize data quality. The centralized training of perinatal pathologists, development and use of the INCODE system and confirmation of umbilical cord abnormality with placental and fetal histopathology also contributed to high data quality. In addition, we had a relatively large number of well-characterized stillbirths in a racially, ethnically and geographically diverse population. A limitation of our study was the lack of pathologist blinding to clinical circumstances. Also, our ability to subanalyze umbilical cord abnormality stillbirths by type was limited by sample size, despite having a large cohort of umbilical cord abnormality associated stillbirths. A final consideration is that because there is no gold standard for cause of death for stillbirth, INCODE is a useful assessment tool but not a definitive determination. Accordingly, we can report on stillbirths associated with umbilical cord abnormality but we cannot be certain that umbilical cord abnormality was the definitive "cause of death."

Our data underscore the need for further investigation into the prediction and prevention of stillbirths due to umbilical cord abnormality. This is especially important because most of these stillbirths occur relatively late in pregnancy in the setting of otherwise normal fetuses and pregnancies. Given a lack of clear risk factors, strategies should target the entire population. Studies are needed to characterize and evaluate systematic ultrasonographic evaluation of the umbilical cord. Based on our current state of knowledge of this condition, prevention efforts would potentially lead to excessive intervention that might cause more harm than good. For example, identification of nuchal cord alone is insufficient given its high incidence (up to 25%) and low specificity for stillbirth.[16] However, other ultrasonographic measurements may better predict umbilical cord abnormality and risk for stillbirth. Investigations into biomarkers indicating intermittent hypoxia may also be of value in identifying pregnancies with occult but clinically relevant umbilical cord abnormalities or occlusion.

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