




Umbilical Cord Hypercoiling with Stricture and Intrauterine Fetal Death: Association with Maternal Factors and Implications for Pathogenesis

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ABSTRACT

Introduction: Hypercoiling of umbilical cord with stricture (HCS) is one of the most common etiologies of intrauterine fetal death (IUFD). Whether Wharton's Jelly close to fetal abdomen plays roles in pathogenesis is controversial. **Methods:** Fetal autopsies were reviewed between 2015 and 2022 and HCS with maternal and fetal factors were examined to determine if these factors were relevant to HCS and IUFD. **Results:** Totally 389 fetal autopsies were reviewed and 75 cases of HCS were identified. HCS was found more frequently in older (maternal age ≥ 35) multiparous women with longer cords and increased umbilical coiling index (UCI) (both $p < 0.01$). There was no significant difference in maternal race/ethnicity, BMI, fetal sex, genetics, seasonality, multiple pregnancies or anomalies in HCS. **Conclusions:** HCS appeared related to maternal characteristics and it occurred more frequently in older multiparous women associated with longer cords. Lack or poorly developed Wharton's jelly close to fetal abdomen plays important role in IUFD.

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Introduction

Intrauterine fetal death (IUFD) is one of the most catastrophic events in life affecting the family and society [1–3]. The etiology of IUFD is multifactorial, and placental examination during fetal postmortem examination or separately is critical to determine the causes for many cases [1,2,4,5]. There are many classifications of IUFD, and placental cause of IUFD is not always incorporated into or emphasized in the classification regimens [6–10]. Placental etiology of IUFD includes placental bed pathology, placental developmental/parenchymal abnormalities, umbilical cord abnormalities, or not otherwise specified [7,11]. Hypercoiling of umbilical cord with stricture (HCS) is one of the most common etiologies of IUFD in second and third trimesters [2,3]. Hypercoiling, in conjunction with other umbilical cord abnormalities (e.g. knots, vascular abnormalities, thrombosis), is often categorized as a 'cord abnormality' leading to IUFD [4]. The risk factors of hypercoiling of umbilical cord include excessively long umbilical cord which may have genetic predisposition [12]. The factors influencing

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umbilical cord coiling and methods to prevent such events remain poorly understood [13]. It also has been debated that lack of or poorly developed Wharton's Jelly close to the fetal abdominal wall plays an important role in development of stricture of hypercoiled cord, but this view of Wharton's jelly is controversial [14]. Some investigators believed that the Wharton's jelly was squeezed secondary to the coiling of the cord, and hypercoiling of cord with stricture in this location is secondary to postmortem changes, rather than the primary cause of IUFD [15,16]. However, this view cannot explain the etiology of IUFD with focal stricture of umbilical cord close to the fetal abdominal wall with normal coils or even hypocoiled cord. Wharton's jelly consists of mucoid stromal tissue that protects the umbilical vessels from compression. Development of Wharton's jelly and factors influencing the developmental process are poorly understood. It is known that focal absence of Wharton's jelly due to mechanical forces such as true tight knots of umbilical cord leads to fetal vascular malperfusion or IUFD [16,17]. Little is known what factors affect the development of Wharton's jelly at this particular area [18]. To investigate maternal, fetal, and placental factors in development of IUFD, we reviewed a series of cases of IUFD and HCS in regarding these factors, and we have found that maternal factors are important in pathogenesis of hypercoiled umbilical cord with strictures [13,18].

Methods

This retrospective study is exempt from institutional review board approval according to section 46.101(b) of 45CFR 46, which states that research involving the study of existing pathologic and diagnostic specimens in such a manner that subjects cannot be identified is exempt from the Department of Health and Human Services Protection of Human Research Subjects. Fetal autopsy reports, placental reports, genetic (chromosomal microarray) reports between 2015 and 2022 were reviewed including the gross photographs. All IUFD cases were classified by using TULIP classification as described including categories of congenital, placental, prematurity/infection, other and unknown [7]. We combined the categories of prematurity and infection in TULIP classification as a single category because fetal infection and maternal/placental infection cannot be readily separated in most of the cases. Placental examination and sampling were performed by following the Amsterdam guideline [19]. Fetal autopsy and stillbirth workup were performed by following the existing guidelines [20]. Umbilical coiling index (UCI) was calculated based on the coil numbers per 10 cm umbilical cord in length recorded in the medical record, and the total length of the cord [2,19]. UCI less than 0.1 was defined hypocoiled, and UCI was 0.3 or over hypercoiled. UCI between 0.1 and 0.3 was classified as normal. Stricture of umbilical cord was defined as an area of the cord less than or equal to 50% of the cord diameter. Hypercoiling of umbilical cord with stricture and all other umbilical cord abnormalities were classified as placental abnormalities as described in TULIP classification previously [7]. Placental abnormalities as one group were not further subclassified in TULIP classification (placental bed pathology, placental pathology including developmental, parenchymal and localization pathology) as previously described for the purpose of current study of umbilical cord [2,7]. Umbilical cord length less than 10 cm was recorded as a category of missing data (no coiling data). Maternal, fetal, placental and genetic

information were recorded in Excel spreadsheet (Microsoft Corp). The patients' racial/ethnic data were retrieved from the electronic medical record (Cerner System) according to the Center for Medicare and Medicaid Services (CMS) criteria as Asian, non-Hispanic Black, Hispanic, and non-Hispanic White. The racial/ethnic data also included "unknown", "others", or "declined" as one group without further information [21]. Fetal gender (sex) was retrieved from the medical record as female and male, and maternal marital status were defined as Married, Single, and Divorced/separated. Patients who declined to answer the marital status questions were recorded as "Other" including "decline," "others" and "unknown." The patients' age, body mass index (BMI), para, gravida were retrieved from the medical record and recorded as previously described [21,22]. Spring of the season was defined as from March to May, Summer from June to August, Fall from September to November, and winter from December to February. Statistical analyses were performed by using baseline characteristics table, Student t-test, and multivariate ANOVA test in R-package. $p < 0.05$ is considered statistically significant.

Results

A total 389 fetal autopsy cases with placental reports and gross photographs were reviewed between 2015 and 2022, and the TULIP classification was used for all the cases (Table 1). There were 59 cases of congenital/syndromic anomalies (15.2%), 89 cases of placental abnormalities (22.9%), 101 cases of prematurity including maternal/placental/fetal infections (26%), 11 cases of others including maternal diabetes, pre-eclampsia, lupus and other maternal diseases (2.8%), and 129 cases of unknown etiology (33.2%) (Table 1). These results in TULIP classification were similar to those published previously [2]. The category of unknown etiology in our data appeared higher than some previous studies but similar to other published results [2,7]. The most significant differences among the various categories of TULIP classification were related to umbilical cord including umbilical cord length, UCI, gestational age and umbilical vascular abnormality (two vessel cord) and recurrent IUFD were more common in the category of congenital abnormalities (Table 1). The umbilical coiling index was significantly higher in placental category than other categories as expected, since the umbilical cord abnormalities were classified as placental category in TULIP classification ($p < 0.001$, Fig. 1). This result is also consistent with those published previously [2]. The umbilical cord length was moderately correlated with gestational age with Pearson correlation coefficient of 0.58 (Fig. 2). All IUFD cases were categorized as hypercoiling, hypocoiling and normal coiling by using umbilical coiling index, and umbilical coiling abnormalities were statistically significantly associated with fetal weight, gestational age, umbilical cord length and placental weight (Table 2). There were 95 cases classified as hypercoiling (UCI 0.3 or over), 29 cases as hypocoiling (UCI less than 0.1), and 143 cases as normal (UCI between 0.1 and 0.3). There were 122 cases with incomplete data and unknown UCI (Table 2). A total 75 cases of hypercoiled umbilical cord with stricture as cause of IUFD were found to be associated with fetal, maternal and placental characteristics (Fig. 3). Totally 50 of these 75 (67%) cases were categorized as hypercoiled by using UCI, 9 of the 75 cases were normal coiled by using UCI, and 2 cases were hypocoiled ($p < 0.01$, Table 2).

Table 1. Tulip classification of intrauterine fetal death.

Tulip groups	Congenital	Other	Placenta	Prematurity	Unknown	p-value
Hypercoiled group	(N = 59)(15.2%) 11 (18.64%)	(N = 11)(2.8%) 1 (9.09%)	(N = 89)(22.9%) 53 (59.55%)	(N = 101)(26.0%) 3 (2.97%)	(N = 129)(33.2%) 7 (5.43%)	<0.01 0.32
Sex						
Female	30 (50.85%)	4 (36.36%)	37 (41.57%)	50 (49.50%)	55 (42.64%)	
Male	29 (49.15%)	7 (63.64%)	50 (56.18%)	51 (50.50%)	74 (57.36%)	
Fetal weight (gram)	373.00 [105.50;1007.50]	2216.00 [115.00;3465.00]	207.00 [68.00;980.00]	193.00 [102.00;318.00]	135.00 [50.00;628.00]	0.06
Gestation (week)	22.00 [18.00;28.00]	32.00 [17.00;36.50]	22.50 [19.00;30.00]	19.00 [17.00;21.00]	18.00 [15.00;29.50]	<0.01
Placental weight	107.00 [77.00;217.00]	327.00 [99.00;426.00]	118.00 [65.00;230.00]	102.00 [76.00;140.00]	88.00 [58.00;263.00]	0.15
Cord length (cm)	25.50 [18.00;30.00]	24.00 [21.00;32.00]	31.00 [22.00;42.00]	24.00 [18.00;31.00]	25.00 [17.00;39.00]	<0.01
Umbilical coiling index (UCI)	0.20 [0.10;0.25]	0.15 [0.05;0.25]	0.30 [0.20;0.60]	0.20 [0.10;0.20]	0.20 [0.10;0.30]	<0.01
Cord coiling by UCI						
No data	20 (33.90%)	3 (27.27%)	17 (19.10%)	29 (28.71%)	53 (41.09%)	<0.01
Hypercoiled	10 (16.95%)	2 (18.18%)	45 (50.56%)	12 (11.88%)	26 (20.16%)	
Hypo-coiled	5 (8.47%)	2 (18.18%)	5 (5.62%)	7 (6.93%)	10 (7.75%)	
Normal	24 (40.68%)	4 (36.36%)	22 (24.72%)	53 (52.48%)	40 (31.01%)	
Maternal age	29.08 ± 6.16	29.09 ± 5.70	31.02 ± 5.89	30.78 ± 5.80	29.85 ± 5.63	0.22
Gravida	3.00 [1.50;4.00]	3.00 [1.50;3.00]	3.00 [2.00;4.00]	2.00 [2.00;4.50]	3.00 [2.00;4.00]	0.45
Para	1.00 [0.00;2.00]	1.00 [0.00;1.50]	1.00 [0.00;3.00]	1.00 [0.00;2.00]	1.00 [0.00;2.00]	0.13
BMI	29.00 [25.50;33.50]	26.00 [23.00;30.00]	30.00 [27.00;36.00]	30.00 [25.00;34.00]	29.00 [25.00;34.50]	0.23
Multiple pregnancies	0 (0.0%)	0 (0.0%)	13 (14.61%)	10 (9.90%)	12 (9.52%)	0.03
Two vessel cord	5 (8.47%)	0 (0.0%)	3 (3.37%)	0 (0.0%)	3 (2.38%)	0.04
Recurrence	5 (8.47%)	0 (0.0%)	2 (2.25%)	12 (11.88%)	5 (3.97%)	0.04
IVF	1 (1.69%)	0 (0.0%)	3 (3.37%)	2 (1.98%)	2 (1.59%)	0.88

BMI: body mass index; IVF: in vitro fertilization.

Data presented as mean/average with percentage of the total or 95% confidence intervals. *p* <0.05 is considered significant and bolded.

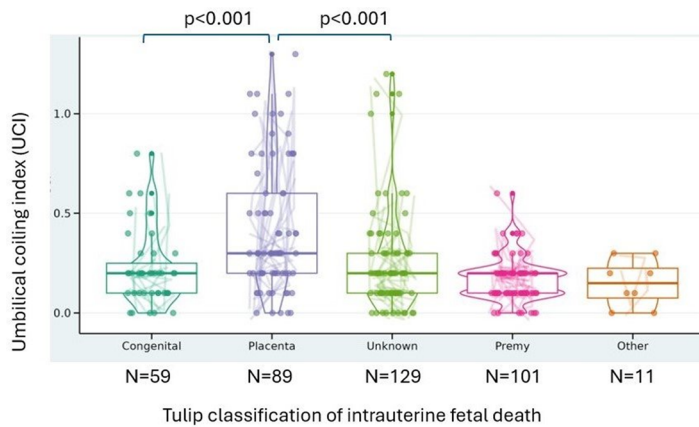


Figure 1. TULIP classification of IUFD and umbilical coiling index (UCI). Statistically significant differences of UCI in various categories of etiologies in TULIP classification of IUFD.

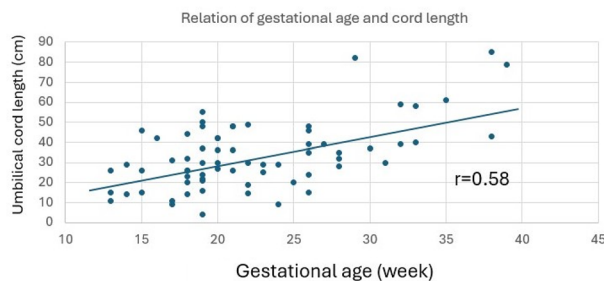


Figure 2. Correlation of gestational age and fetal umbilical cord length with Pearson correlation coefficient of 0.58. Pearson correlation coefficient was calculated in Microsoft Excel spreadsheet.

Hypercoiled cord with stricture was not only seen significantly more common in hypercoiling category, but also seen in hypocoiling and normal categories (Table 2). Hypercoiled umbilical cord with stricture was significantly more frequent in older multiparous women ($p=0.04$ and $p<0.01$, Table 3). Hypercoiled umbilical cord with stricture was statistically significantly associated with lower birth weight ($p=0.01$, Table 4). Hypercoiled umbilical cord with stricture was statistically significantly associated with longer umbilical cords ($p<0.01$), increased number of coils per 10 cm in length ($p<0.01$) and UCI ($p<0.01$) as previously reported (Table 5) (Fig. 4). There appeared to be more married women than singles with hypercoiled umbilical cord with stricture, but statistical significance was not reached (Table 3). It affected female and male fetuses equally (Table 4). There were no significant differences in multiple pregnancies, fetal umbilical vessels, and fetal genetics (Table 4). There was no significant difference in maternal race/ethnicity, BMI, gestational age, seasonal variation, or fetal anomalies in hypercoiled umbilical cord with stricture (Tables 3 and 6).

Discussion

Measuring umbilical cord coiling accurately has been a challenge for pathologists and obstetricians, as significant variations can occur in measurement of the cord length

Table 2. Hypercoiling and hypocoiling and intrauterine fetal death.

Cord coiling by UCI	No coiling data (N=122)(31.4%)	Hypercoiling (N=95)(24.4%)	Hypocoiling (N=29)(7.5%)	Normal (N=143)(36.8%)	p-value
Hypercoiled with stricture	14 (11.48%)	50 (52.63%)	2 (6.90%)	9 (6.29%)	<0.01
Sex					0.10
Female	48 (39.34%)	40 (42.11%)	14 (48.28%)	74 (51.75%)	
Male	74 (60.66%)	53 (55.79%)	15 (51.72%)	69 (48.25%)	
Unknown	0 (0.0%)	2 (2.11%)	0 (0.0%)	0 (0.0%)	
Fetal weight (gram)	84.50 [35.00;243.00]	270.00 [103.00;1342.00]	156.00 [71.00;188.00]	317.00 [132.00;955.00]	<0.01
Gestation (week)	17.00 [15.00;20.00]	22.00 [19.00;32.00]	18.00 [16.00;19.00]	21.00 [17.50;28.00]	<0.01
Placental weight (gram)	79.50 [55.50;154.00]	108.00 [76.00;252.00]	76.00 [59.00;107.00]	114.50 [78.00;222.00]	<0.01
Tulip classification					<0.01
Congenital	20 (16.39%)	10 (10.53%)	5 (17.24%)	24 (16.78%)	
Placenta	17 (13.93%)	45 (47.37%)	5 (17.24%)	22 (15.38%)	
Prematurity	29 (23.77%)	12 (12.63%)	7 (24.14%)	53 (37.06%)	
Other	3 (2.46%)	2 (2.11%)	2 (6.90%)	4 (2.80%)	
Unknown	53 (43.44%)	26 (27.37%)	10 (34.48%)	40 (27.97%)	
Cord length (cm)	17.00 [13.00;23.00]	33.00 [25.00;46.00]	18.50 [14.00;25.00]	26.00 [21.00;33.50]	<0.01
Umbilical coiling index (UCI)	–	0.40 [0.30;0.60]	0.00 [0.00;0.00]	0.20 [0.10;0.20]	<0.01
Maternal age (year)	31.18 ± 5.86	30.28 ± 5.59	28.72 ± 5.04	29.67 ± 6.03	0.09
Gravida	3.00 [2.00;5.00]	3.00 [2.00;4.50]	3.00 [2.00;4.00]	2.00 [2.00;3.00]	
Para	1.00 [0.00;2.00]	1.00 [0.00;2.50]	1.00 [0.00;2.00]	1.00 [0.00;1.00]	
BMI	30.00 [25.00;36.00]	30.00 [25.00;36.00]	29.50 [25.50;33.00]	29.00 [25.00;33.00]	0.61
Multiple pregnancies	13 (10.74%)	6 (6.38%)	2 (7.14%)	14 (9.79%)	0.69

BMI: body mass index; IVF: in vitro fertilization.

Data presented as mean/average with percentage of the total or 95% confidence intervals. $p < 0.05$ is considered significant and bolded.

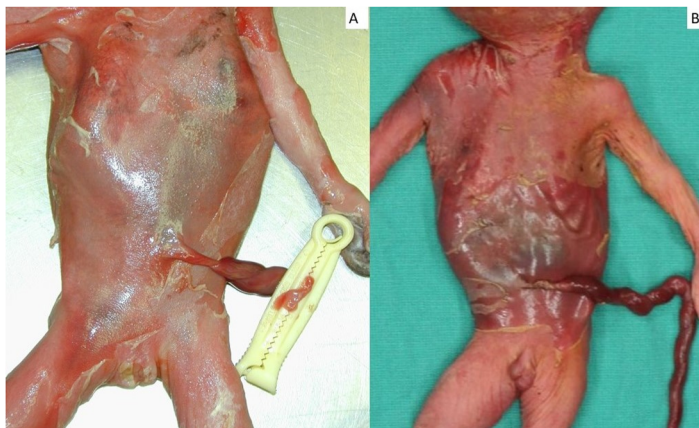


Figure 3. Hypercoiled umbilical cord with stricture close to the fetal abdominal wall as a cause of intrauterine fetal death.

and number of coils, resulting in large variations of the collected data [23]. The practice in labor and delivery room in regard to how long the cord should be attached to the baby also varies. Current guideline from College of American Pathologists recommends count the coil number per 10 cm umbilical cord in length, and 3 coils per 10 cm or less is considered normal, and more than 3 coils per 10 cm is considered

Table 3. Hypercoiled cord with stricture and maternal characteristics.

Hypercoiled with stricture	Absent	Present	Total	<i>p</i> -value
	(<i>N</i> = 314)(80.7%)	(<i>N</i> = 75)(19.3%)	(<i>N</i> = 389)	
Maternal age (year)	29.0 [26.0;34.0]	32.0 [27.5;36.0]	30.0 [26.0;35.0]	0.01
Gestational age (week)	20.0 [17.0;27.0]	20.0 [18.0;26.0]	20.0 [17.0;27.0]	0.56
Maternal age group				0.04
Group 1 (<20 years)	9 (2.9%)	0 (0.0%)	9 (2.3%)	
Group 2 (20 to 34)	227 (72.3%)	47 (62.7%)	274 (70.4%)	
Group 3 (35 or older)	78 (24.8%)	28 (37.3%)	106 (27.2%)	
Gravida	2.0 [2.0; 4.0]	4.0 [2.0; 5.0]	3.0 [2.0; 4.0]	<0.01
Para	1.0 [0.0; 2.0]	2.0 [0.0; 3.0]	1.0 [0.0; 2.0]	<0.01
Race /ethnicity				0.48
Asian	38 (12.1%)	11 (14.7%)	49 (12.6%)	
Black	39 (12.4%)	7 (9.3%)	46 (11.8%)	
Hispanic	135 (43.0%)	26 (34.7%)	161 (41.4%)	
Other	31 (9.9%)	8 (10.7%)	39 (10.0%)	
White	71 (22.6%)	23 (30.7%)	94 (24.2%)	
Marital status				0.05
Divorced	9 (2.9%)	0 (0.0%)	9 (2.3%)	
Married	170 (54.1%)	46 (61.3%)	216 (55.5%)	
Other/Unknown/ Declined	1 (0.3%)	2 (2.7%)	3 (0.8%)	
Single	134 (42.7%)	27 (36.0%)	161 (41.4%)	
Body Mass Index (BMI)	29.5 [25.0;34.0]	30.0 [26.0;34.5]	30.0 [25.0;34.0]	0.28

BMI: body mass index.

Data presented as mean/average with percentage of the total or 95% confidence intervals. $p < 0.05$ is considered significant and bolded.

Table 4. Hypercoiled cord with stricture and fetal characteristics.

Hypercoiled with stricture	Absent	Present	Total	<i>p</i> -value
	(<i>N</i> = 314)	(<i>N</i> = 75)	(<i>N</i> = 389)	
Fetal sex				
Female	142 (45.2%)	34 (45.3%)	176 (45.2%)	
Male	172 (54.8%)	39 (52.0%)	211 (54.2%)	
Unknown	0 (0.0%)	2 (2.7%)	2 (0.5%)	
Fetal weight (gram)	199.0 [80.0;605.0]	108.0 [47.0;533.5]	180.0 [70.0;590.0]	0.01
Twin/triplet	28 (9.0%)	7 (9.3%)		1.00
Two vessel cord	8 (2.6%)	3 (4.0%)	11 (2.8%)	0.78
Genetics (any)	24 (16.3%)	8 (17.0%)	32 (16.5%)	1.00

Data presented as mean/average with percentage of the total or 95% confidence intervals. $p < 0.05$ is considered significant and bolded.

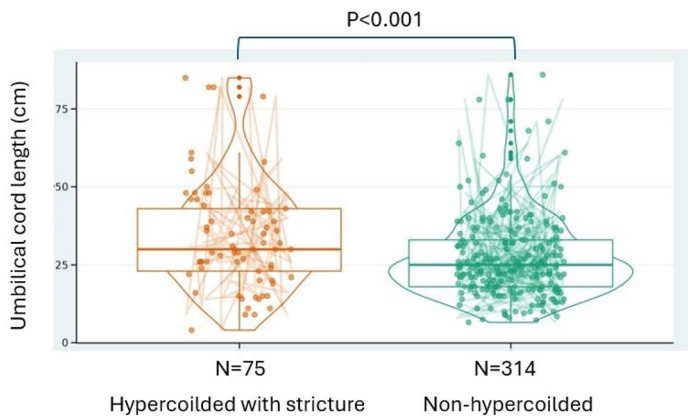
hypercoiling [19]. In cases of IUFD in second and third trimesters, the fetus, placenta and umbilical cord are usually delivered together with less variation, and umbilical cord length and coils can be measured more accurately. In our experience, it is important to take a closer look at the umbilical cord close to the fetal abdominal wall when the fetus was examined, and it is suboptimal when the placenta is examined alone separately and the fetus is not present.

Our data showed that hypercoiled umbilical cord with stricture is a significantly common etiology of IUFD, representing 19.3% of all IUFD cases in our data. This result is similar to those previously published [2]. Our data also revealed statistically significant association of hypercoiled cord with stricture with multiparous mothers with advanced maternal age (maternal age ≥ 35). Hypercoiled cord with stricture was also associated with long hypercoiled umbilical cord and significantly lower fetal

Table 5. Hypercoiled cord with stricture and placental characteristics.

Hypercoiled with stricture	Absent (N = 314)	Present (N = 75)	Total (N = 389)	p-value
Placental weight (gram)	105.0 [70.0;209.0]	84.0 [59.0;158.0]	104.0 [66.0;202.0]	0.06
Placental infarct	16 (5.3%)	6 (8.0%)	22 (5.9%)	0.54
Intervillous thrombi	16 (5.3%)	4 (5.3%)	20 (5.3%)	1.00
Chorioamnionitis (infectious)	104 (34.6%)	7 (9.3%)	111 (29.5%)	<0.01
Umbilical cord length (cm)	25.0 [18.0;33.0]	30.0 [23.0;43.0]	26.0 [18.0;36.0]	<0.01
Cord coils per 10 cm	2.0 [1.0; 2.0]	5.0 [3.0; 8.0]	2.0 [1.0; 3.0]	<0.01
Umbilical coiling index (UCI)	0.20 [0.10;0.20]	0.50 [0.30;0.80]	0.20 [0.10;0.30]	<0.01

Data presented as mean/average with percentage of the total or 95% confidence intervals. $p < 0.05$ is considered significant and bolded.

**Figure 4.** Statistically significant differences of umbilical cord length in cases of hypercoiled cord with stricture and non-hypercoiled cord ($p < 0.001$).

weight, similar to those described previously [2]. In addition, our data showed that hypercoiled cord with stricture can occur in cases with hypocoiling or normal coiling cord, and this finding indicated that focal hypercoiling close to the fetal abdominal wall without overall hypercoiling of umbilical cord or increased overall UCI is an important etiology of IUFD, and focal hypercoiling may relate to poorly developed Wharton's jelly at this particular area without hypercoiling of the entire umbilical cord as defined by UCI. This result supports the view that poorly developed Wharton's jelly close to the fetal abdominal wall plays an important role in umbilical cord stricture and IUFD, and argues against the view of umbilical cord hypercoiling with stricture being secondary to postmortem changes. This finding also implies that both hypercoiling of umbilical cord and poorly developed Wharton's jelly are necessary primary factors for development of IUFD, and neither hypercoiling of umbilical cord nor poorly developed Wharton's jelly alone is sufficient to result in IUFD. The unique and heterogeneity of mechanical features of Wharton's jelly at fetal end and placental ends in recent study seem to support our results that the Wharton's jelly at fetal end of umbilical cord is important in protecting the umbilical vessels from compression or occlusion [24]. Reduction of Wharton's jelly close to fetal abdominal wall can be

Table 6. Hypercoiled cord with stricture and other factors.

Hypercoiled with stricture	Absent (N=314)	Present (N=75)	Total (N=389)	p-value
Season				0.91
Spring	88 (28.0%)	21 (28.0%)	109 (28.0%)	
Summer	87 (27.7%)	18 (24.0%)	105 (27.0%)	
Autumn	75 (23.9%)	20 (26.7%)	95 (24.4%)	
Winter	64 (20.4%)	16 (21.3%)	80 (20.6%)	
Recurrence	21 (6.8%)	3 (4.0%)	24 (6.2%)	0.54
<i>In vitro</i> fertilization (IVF)	6 (1.9%)	2 (2.7%)	8 (2.1%)	1.00

Data presented as mean/average with percentage of the total. $p < 0.05$ is considered significant.

visualized by ultrasound, and the reduced Wharton's jelly was associated with reduced blood flow in the umbilical vein in female fetuses regardless the umbilical cord coiling [25,26]. Cross sectional area of Wharton's jelly was significantly associated with fetal growth [27]. Careful monitoring of Wharton's jelly close to fetal abdominal wall in early second to third trimesters by ultrasonography may help identify the patients at risk of focal stricture of umbilical cord with hypercoiling and IUFD.

We have not found any significant association between seasons of the year and hypercoiling of umbilical cord, although seasonal change in Southern California is mild, and study in a different geographic location with significant changes of weather pattern and seasons might yield different results. Association of seasonality with mental health is well established, and seasonal affective disorder (SAD) is a known type of depression related to the change of season [28–30]. Maternal depression during pregnancy can alter placental DNA through methylation [31], and it will be interesting and useful to examine the seasonal factors affecting maternal emotions during pregnancy on the fetal and placental pathology.

Limitation

The study is retrospective with a number limitations. Our data were collected from fetal autopsy cases without ultrasound data for evaluation of the umbilical cord when the fetuses were alive. As stated previously that the umbilical cord lengths in these cases were measured with both placentas and fetuses, making the cord length more accurate than measuring these for placentas and or fetuses alone. Some of the placentas were fixed with formalin and it is known that formalin fixation of umbilical cord reduced cord length [32]. Furthermore, there were 129 cases (33.2%) with unknown cause of death or missing data. Although it is similar to those published previously, this data with missing umbilical cord information may have skewed the results with impact on the study conclusion. Examination of both placenta and fetus by the same perinatal pathologist may help improve the outcome in reducing the missing case information and in determining the cause of IUFD.

Conclusion

Hypercoiling of the umbilical cord with stricture as the cause of IUFD appeared related to maternal characteristics, and it occurred more frequently in older multiparous

women associated with longer cords. Both hypercoiling and stricture, likely due to the poor development or absence of Wharton's Jelly, appear necessary for IUFD in these cases.

Author contributions

CRedit: **Aidan Clement**: Data curation, Investigation, Methodology, Visualization, Writing – review & editing; **Art Mendoza**: Conceptualization, Investigation, Methodology, Visualization, Writing – review & editing; **Chris Wixom**: Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization; **Peilin Zhang**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing.

Disclosure statement

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References

- [1] de Laat MWM, Franx A, van Alderen ED, Nikkels PGJ, Visser GHA. The umbilical coiling index, a review of the literature. *J Matern Fetal Neonatal Med.* 2005;17(2):93–100. doi:10.1080/14767050400028899.
- [2] Dutman AC, Nikkels PG. Umbilical hypercoiling in 2nd- and 3rd-trimester intrauterine fetal death. *Pediatr Dev Pathol.* 2015;18(1):10–6. doi:10.2350/13-10-1390-OA.1.
- [3] Peng HQ, Levitin-Smith M, Rochelson B, Kahn E. Umbilical cord stricture and overcoiling are common causes of fetal demise. *Pediatr Dev Pathol.* 2006;9(1):14–9. doi:10.2350/05-05-0051.1.
- [4] Hammad IA, Blue NR, Allshouse AA, Silver RM, Gibbins KJ, Page JM, Goldenberg RL, Reddy UM, Saade GR, Dudley DJ, et al. Umbilical cord abnormalities and stillbirth. *Obstet Gynecol.* 2020;135(3):644–52. doi:10.1097/AOG.0000000000003676.
- [5] Horn L-C, Faber R, Stepan H, Simon E, Robel R, Wittekind C. Umbilical cord hypercoiling and thinning: a rare cause of intrauterine death in the second trimester of pregnancy. *Pediatr Dev Pathol.* 2006;9(1):20–4. doi:10.2350/08-05-0095.1.
- [6] Reddy UM, Goldenberg R, Silver R, Smith GCS, Pauli RM, Wapner RJ, Gardosi J, Pinar H, Grafe M, Kupfermanc M, et al. Stillbirth classification—developing an international consensus for research: executive summary of a National Institute of Child Health and Human Development workshop. *Obstet Gynecol.* 2009;114(4):901–14. doi:10.1097/AOG.0b013e3181b8f6e4.
- [7] Korteweg FJ, Gordijn SJ, Timmer A, Erwich JJHM, Bergman KA, Bouman K, Ravise JM, Heringa MP, Holm JP. The Tulip classification of perinatal mortality: introduction and multidisciplinary inter-rater agreement. *BJOG.* 2006;113(4):393–401. doi:10.1111/j.1471-0528.2006.00881.x.

- [8] Reis AP, Rocha A, Lebre A, Ramos U, Cunha A. Perinatal mortality classification: an analysis of 112 cases of stillbirth. *J Obstet Gynaecol.* 2017;37(7):835–9. doi:10.1080/01443615.2017.1323854.
- [9] Vergani P, Cozzolino S, Pozzi E, Cuttin MS, Greco M, Ornaghi S, Lucchini V. Identifying the causes of stillbirth: a comparison of four classification systems. *Am J Obstet Gynecol.* 2008;199(3):319.e1–4–319.e4. doi:10.1016/j.ajog.2008.06.098.
- [10] Lupariello F, Di Vella G, Botta G. Stillbirth diagnosis and classification: comparison of ReCoDe and ICD-PM systems. *J Perinat Med.* 2022;50(6):713–21. doi:10.1515/jpm-2022-0014.
- [11] Korteweg FJ, Gordijn SJ, Timmer A, Holm JP, Ravisé JM, Erwich JJHM. A placental cause of intra-uterine fetal death depends on the perinatal mortality classification system used. *Placenta.* 2008;29(1):71–80. doi:10.1016/j.placenta.2007.07.003.
- [12] Linde LE, Rasmussen S, Kessler J, Ebbing C. Extreme umbilical cord lengths, cord knot and entanglement: risk factors and risk of adverse outcomes, a population-based study. *PLoS One.* 2018;13(3):e0194814. doi:10.1371/journal.pone.0194814.
- [13] Ezimokhai M, Rizk DE, Thomas L. Maternal risk factors for abnormal vascular coiling of the umbilical cord. *Am J Perinatol.* 2000;17(8):441–5. doi:10.1055/s-2000-13452.
- [14] Botezatu R, et al. Absence of Wharton's Jelly at the abdominal site of the umbilical cord insertion. Rare case report and review of the literature. *Medicina (Kaunas).* 2021;57(11):1268.
- [15] Bendon RW. Articles on umbilical cord torsion and fetal death. *Pediatr Dev Pathol.* 2007;10(2):165–6. doi:10.2350/06-09-0161.1.
- [16] Benirschke K. Obstetrically important lesions of the umbilical cord. *J Reprod Med.* 1994;39(4):262–72.
- [17] Baergen RN. Cord abnormalities, structural lesions, and cord “accidents”. *Semin Diagn Pathol.* 2007;24(1):23–32. doi:10.1053/j.semmp.2007.02.004.
- [18] Kalluru PKR, Kalluru HR, Allagadda TR, Talur M, Gonepogu MC, Gupta S. Abnormal umbilical cord coiling and association with pregnancy factors. *J Turk Ger Gynecol Assoc.* 2024;25(1):44–52. doi:10.4274/jtgga.galenos.2023.2023-3-3.
- [19] Khong TY, Mooney EE, Ariel I, Balmus NCM, Boyd TK, Brundler M-A, Derricott H, Evans MJ, Faye-Petersen OM, Gillan JE, et al. Sampling and definitions of placental lesions: Amsterdam Placental Workshop Group Consensus Statement. *Arch Pathol Lab Med.* 2016;140(7):698–713. doi:10.5858/arpa.2015-0225-CC.
- [20] Korteweg FJ, Erwich JJHM, Timmer A, van der Meer J, Ravisé JM, Veeger NJGM, Holm JP. Evaluation of 1025 fetal deaths: proposed diagnostic workup. *Am J Obstet Gynecol.* 2012;206(1):53.e1–53.e12. doi:10.1016/j.ajog.2011.10.026.
- [21] Zhang P, Dygulski S, Al-Sayyed F, Dygulska B, Lederman S. Differences in prevalence of pregnancy complications and placental pathology by race and ethnicity in a New York Community Hospital. *JAMA Netw Open.* 2022;5(5):e2210719. doi:10.1001/jamanetworkopen.2022.10719.
- [22] Zhang P, Haymar T, Al-Sayyed F, Dygulski S, Dygulska B, Devi A, Lederman S, Salafia C, Baergen R. Placental pathology associated with maternal age and maternal obesity in singleton pregnancy. *J Matern Fetal Neonatal Med.* 2022;35(25):9517–26.
- [23] Khong TY. Evidence-based pathology: umbilical cord coiling. *Pathology.* 2010;42(7):618–22. doi:10.3109/00313025.2010.520309.
- [24] Gervaso F, Boschetti F, Pennati G. Evaluation of the Wharton's jelly poroelastic parameters through compressive tests on placental and foetal ends of human umbilical cords. *J Mech Behav Biomed Mater.* 2014;35:51–8. doi:10.1016/j.jmbbm.2014.03.016.
- [25] Skulstad SM, Ulriksen M, Rasmussen S, Kiserud T. Effect of umbilical ring constriction on Wharton's jelly. *Ultrasound Obstet Gynecol.* 2006;28(5):692–8. doi:10.1002/uog.3814.
- [26] Di Naro E, Ghezzi F, Raio L, Franchi M, D'Addario V, Lanzillotti G, Schneider H. Umbilical vein blood flow in fetuses with normal and lean umbilical cord. *Ultrasound Obstet Gynecol.* 2001;17(3):224–8. doi:10.1046/j.1469-0705.2001.00309.x.
- [27] Togni FA, Araujo Júnior E, Vasques FAP, Moron AF, Torloni MR, Nardoza LMM. The cross-sectional area of umbilical cord components in normal pregnancy. *Int J Gynaecol Obstet.* 2007;96(3):156–61. doi:10.1016/j.ijgo.2006.10.003.

- [28] Partonen T, Lönqvist J. Seasonal affective disorder. *Lancet*. 1998;352(9137):1369–74. doi:[10.1016/S0140-6736\(98\)01015-0](https://doi.org/10.1016/S0140-6736(98)01015-0).
- [29] Galima SV, Vogel SR, Kowalski AW. Seasonal affective disorder: common questions and answers. *Am Fam Physician*. 2020;102(11):668–72.
- [30] Nevarez-Flores AG, Bostock ECS, Neil AL. The underexplored presence of seasonal affective disorder in the southern hemisphere: a narrative review of the Australian literature. *J Psychiatr Res*. 2023;162:170–9. doi:[10.1016/j.jpsychires.2023.05.003](https://doi.org/10.1016/j.jpsychires.2023.05.003).
- [31] Martinez CA, Marteinsdottir I, Josefsson A, Sydsjö G, Theodorsson E, Rodriguez-Martinez H. Epigenetic modifications appear in the human placenta following anxiety and depression during pregnancy. *Placenta*. 2023;140:72–9. doi:[10.1016/j.placenta.2023.07.298](https://doi.org/10.1016/j.placenta.2023.07.298).
- [32] Downey A, Hore K, McAuliffe FM, Mooney EE. Umbilical cord shortening: quantification postdelivery and postfixation. *Pediatr Dev Pathol*. 2014;17(5):327–9. doi:[10.2350/14-02-1437-OA.1](https://doi.org/10.2350/14-02-1437-OA.1).