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Antenatal Umbilical Coiling Index as a Predictor of NICU Admission as Fetal Adverse Outcome Using Color Doppler in the third trimester-A Nested Case Control Study

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ABSTRACT

Background: The umbilical cord is extremely important for the developing foetus because it transports deoxygenated blood to the placenta through two umbilical arteries and supplies the foetus with oxygenated blood through the umbilical vein. Umbilical cord coiling increases the chord's flexibility and tensile strength, while also offering resistance to outside pressures that might interrupt the fetus's blood supply.

Objective: To determine the correlation between antenatal umbilical coiling index (UCI) and neonatal intensive care unit (NICU) admission as a fetal adverse outcome using color Doppler.

Methodology: This nested case-control study was conducted on pregnant women attending to Ain Shams University Maternity Hospital Outpatient Department Ultrasound Clinics for antenatal care during the period from May 2021 until December 2022.

Results: Regarding coiling index, it was statistically significantly higher among cases of NICU group compared to controls (0.53 ± 0.14 vs. 0.48 ± 0.11). There was a statistically significant higher frequency of hypercoiling in NICU group compared to non-NICU group. Regarding umbilical artery resistance index (URI), our study revealed that it was statistically significantly higher among cases of NICU group compared to control one (0.64 ± 0.08 vs. 0.60 ± 0.04). URI and UCI (< 75%) were unreliable in predicting NICU admission; AUC (area under the curve) was 71% for URI and 65% for UCI. On the other hand, URI was reliable in predicting hyper-coiling (as an indicator of adverse outcome) P<0.0001 and AUC was 77. The best cut-off value of URI was 0.61 with a sensitivity of 77%, specificity of 56%, PPV of 64% and NPV of 71% with a diagnostic accuracy of 66%. Women whose neonates have been admitted to NICU showed significantly higher rates of CS, low APGAR score and preterm labor when compared to women whose neonates have not (p<0.05).

Conclusion: Umbilical coiling index was positively correlated with umbilical artery resistance index, denoting that hyper-coiling correlates with increased resistance to blood flow in the umbilical cord, but there was no statistical evidence of using UCI as predictor of NICU admission in the current study. Umbilical cord coiling may be used as a simple method to detect placental insufficiency as it positively correlated with the umbilical artery RI even without using color Doppler.

Keywords: Umbilical coiling, Neonatal intensive care unit, Color Doppler.

INTRODUCTION

The umbilical cord is extremely important for the developing foetus because it transports deoxygenated blood to the placenta through two umbilical arteries and supplies the foetus with oxygenated blood through the umbilical vein. Umbilical cord coiling increases the chord's flexibility and tensile strength, while also offering resistance to outside pressures that might interrupt the fetus's blood supply. Berengarius was the first to report the coiling feature of umbilical cord in 1521, while Edmonds was the first to quantify in 1954 [(1)].

As early as 4 weeks, coiling develops after conception. Exact mechanism behind coiling remains still unclear, however some authors have suggested that fetal movements, embryo torsion, foetal hemodynamic stresses and various umbilical vascular development patterns may be the underlying processes [(2)].

Strong and his colleagues [(3)] in 1994 were the first to coin the phrase "umbilical cord coiling index," which is defined as "the number of coils in the cord divided by the length of the cord in centimeters".

Numerous studies have looked at the foetal umbilical cord's growth, anatomy, biomechanics, blood flow pattern, and usefulness of sonography in identifying aberrant blood flow and coiling in utero as a symptom of foetal compromise. According to these research, aberrant umbilical cord coiling is linked to worse neonatal outcomes. Only a few research have looked at Doppler ultrasonography blood flow parameters and their associations with the umbilical cord coiling index and neonatal outcome [(1,4,5)]. As a result, it is hypothesised that aberrant coiling index might be connected with abnormal cord blood flow patterns, and therefore worse perinatal outcomes. It is interesting to note that these investigations have revealed that both hypo-coiling and hyper-coiling are associated with unfavourable perinatal outcomes [(5)].

Preterm delivery, foetal development limitation, oligohydramnios, foetal heart rate abnormalities, instrumental deliveries, and low birth weight (LBW) are adverse perinatal outcomes linked to aberrant umbilical coiling index. On the other hand, it was not discovered that abnormal umbilical cord coiling was linked to any of the following negative outcomes: pregnancy-induced hypertension, antepartum haemorrhage, preterm rupture of membranes, meconium liquor staining, emergency

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Caesarean section, subpar APGAR scores, or NICU admissions [6]. Therefore, prenatal measurement of the coiling index and associated Doppler blood flow features would serve as a predictor of unfavourable perinatal outcomes, which can reduce perinatal morbidity and death [4].

This study aimed to determine the correlation between antenatal umbilical coiling index and NICU admission as a fetal adverse outcome using color Doppler.

METHODOLOGY

This nested case-control study was conducted on pregnant women attending to Ain Shams University Maternity Hospital Outpatient Department Ultrasound Clinics for antenatal care during the period from May 2021 until December 2022.

Study population: All pregnant women receiving prenatal care in the Outpatient Department Clinics were assessed for eligibility:

Inclusion criteria: Gestational age 28-40 weeks. Singleton live fetus.

Exclusion criteria: Fetal growth restriction. Pregnancy with medical disorders (chronic hypertension, diabetes, cardiac disease and hepatic and renal impairment). Obstetric complications (pre-eclampsia, antepartum hemorrhage, mal-presentations, and gross fetal anomalies). Multiple Pregnancies. Single umbilical artery.

Sample size calculation & justification: The sample size was determined using the online PASS option, with power set to 0.8 and type-1 error set to 0.05. Data from prior research by **Bhojwani *et al.*** [7] revealed that the incidence rate of aberrant coiling was 45% in mothers whose neonates were hospitalised to the NICU and 24% in women whose neonates were not admitted to the NICU. According to these numbers, a sample size of 61 women in each arm of the research is required.

As a nested case-control study, women were recruited and followed up till delivery, till neonates from 61 women were admitted to the NICU where recruitment was stopped. A matched group of 61 women were selected from women whose neonates had not been admitted to the NICU as a control. A total of 400 women were followed up till this sample size was reached.

Ethical considerations: Ain Shams Medical Ethics Committee of Ain Shams Faculty of Medicine gave its approval to this study. All participants gave written consents after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Confidentiality: Only the patient's initials were included in the case report, and when the patient's name appeared on any other document, the investigators stored it in a secure location. To allow record identification, the investigators kept a personal patient identification list (patient initials with associated patient names).

Concerning safety and efficacy: No evidence of harmful effects.

Study interventions and procedures:

a) **Complete history taking:** including age, previous obstetric history and number of previous Cesarian deliveries and its neonatal outcomes. Naegele's rule was used to estimate gestational age based on menstruation history, and medical comorbidities with pregnancy as hepatic, renal, endocrinal, psychosocial condition, cardiovascular, diabetes, chronic hypertension.

b) **Examination:** Including general examination as vital data assessment, abdominal examination (Leopold maneuvers" was used to determine the position, presentation, and engagement of the fetus in utero).

c) **Investigation:** All cases had their routine investigations as complete blood picture, liver and kidney function tests, coagulation profile ["prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR)"], viral hepatitis markers: hepatitis B and C viruses, blood group (ABO) and Rh.

d) **Antenatal ultrasound examination:**

- Classical fetal biometric parameters measurements that included bi-parietal diameter **(BPD)**, occipitofrontal diameter **(OFD)** head circumference **(HC)**, trans-abdominal diameter **(TAD**), abdominal circumference **(AC)**, humerus length **(HL)** and femur length **(FL).**
- **A fetal anatomical ultrasound survey** (grayscale and color Doppler) of the placenta and umbilical cord was performed once at 28-40 weeks of gestational age.
- Every patient had their umbilical cord coiling index measured and documented. It is determined by multiplying the reciprocal of the distance in centimeters between the outer edge of the following coil along the ipsilateral side of the umbilical cord and the inner edge of an artery or venous wall.
- Umbilical artery resistance index URI was also obtained for all the patients.

e) **Post-natal follow-up:** After delivery, patients whose neonates had not been admitted to NICU were considered as the control group **(Group A)**, while those whose neonates have been admitted to NICU were considered as the cases group **(Group**

B). Retrograde analysis of the ultrasound results of patients of both groups was used for statistical analysis and correlation with the fetal outcome.

f)

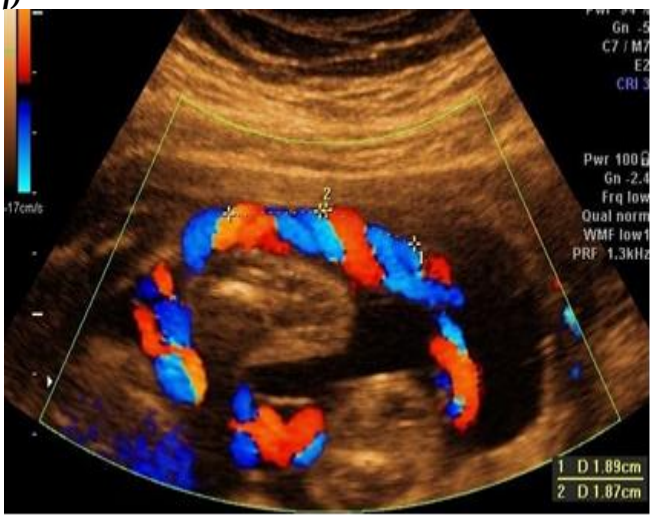


Figure (1): Colour Doppler US demonstrating assessment of the umbilical coiling index along the ipsilateral cord side from the inner border of an artery to the outside edge of the same artery at the adjacent twist. This location has an umbilical coiling index of 0.52 [8].

Statistical analysis

The numbers were input, evaluated, and statistically analysed using SPSS version 22.0 software. Data were presented as the mean ± SD, range or percentage of instances. The independent t-test and the 2 test were used to compare the proportions and means between the two groups. They determined the average URI and UCI. Based on the latter, they were categorised as follows: UCI scores in the normal-coiled group fall between the 10th and 90th percentiles of the mean UCI. A group that is hypo-coiled was one whose values are below the median. Having values higher than the 90th percentile of the mean was a hyper-coiled group. The hypo-coiled and hyper-coiled groups were compared to the normo-coiled group, this is in addition to the comparison between cases and control regarding UCI, URI, and other studied variables.

Comparison of cases and controls with relation to UCI, URI, and other examined factors was done using the Chi-Square test and the Fisher's exact test. The correlation coefficient (r), which expresses the degree and direction of the linear relationship between URI and UCI was used to measure correlation. ROC curve was used to show how well the URI can diagnose and forecast hyper-coiling. Statistical significance was defined as a P value ≤ 0.05.

RESULTS

We applied our study on 122 patients divided into two equal groups: Group (A) Non- NICU Group (n=61) and group (B) NICU group (n=61), with the same inclusion and exclusion criteria (Table 1).

Table (1): Descriptive Statistics

		N	Mean	SD	SD Error	95% Confidence Interval for Mean	Minimum	Maximum
UCI	Control A	61	0.48	0.11	0.01	0.45 0.50	0.16	0.73
	Cases B	61	0.53	0.14	0.02	0.50 0.57	0.16	0.74
URI	Control A	61	0.60	0.04	0.001	0.59 0.61	0.52	0.69
	Cases B	61	0.64	0.08	0.01	0.62 0.67	0.44	0.81
GA	Control A	61	37.9	1.52	0.20	37.51 38.29	34.0	40.0
	Cases B	61	36.03	2.56	0.33	35.38 36.39	29.0	40.00
Maternal age	Control A	61	30.46	6.50	0.83	28.79 32.12	19.0	42.00
	Cases B	61	30.05	6.36	0.81	28.42 31.68	19.0	44.00

		Percentiles						
		5	10	25	50	75	90	95
UCI	Control A	0.21	0.39	0.42	0.45	0.56	0.64	0.68
	Cases B	0.21	0.39	0.45	0.51	0.64	0.72	0.74
URI	Control A	0.52	0.55	0.57	0.60	0.63	0.65	0.65
	Cases B	0.45	0.52	0.60	0.65	0.70	0.74	0.78

OR: Odds ratio; C.I. Confidence Interval

Women whose neonates have been admitted to NICU showed statistically significant higher antenatal mean UCI and URI when compared to women whose neonates have not (p<0.05) (Table 2).

Table (2): Comparison between cases and control group according to mean URI and UCI

		N	Mean	SD	SD Error	95% Confidence Interval for Mean	Minimum	Maximum	P
UCI	Control A	61	0.48	0.11	0.01	0.45 0.50	0.16	0.73	0.01
	Cases B	61	0.53	0.14	0.02	0.50 0.57	0.16	0.74	
URI	Control A	61	0.60	0.04	0.001	0.59 0.61	0.52	0.69	<0.001
	Cases B	61	0.64	0.08	0.01	0.62 0.67	0.44	0.81	

Student's t test

Women whose neonates have been admitted to NICU showed significantly lower mean gestational age when compared to women whose neonates have not (P<0.001). However, there were no statistically significant differences between cases and controls as regards the mean maternal age and parity (P>0.05) (Table 3).

Table (3): Comparison between cases and control group according to mean GA, maternal age and parity

		N	Mean	SD	SD Error	95% Confidence Interval for Mean	Minimum	Maximum	P
Parity	Control A	61	1.85	0.36	0.05	1.76 1.94	1.00	2.00	0.80
	Cases B	61	1.87	0.34	0.04	1.78 1.96	1.00	2.00	
GA	Control A	61	37.9	1.52	0.20	37.51 38.29	34.00	40.00	<0.0001
	Cases B	61	36.03	2.56	0.33	35.38 36.39	29.00	40.00	
Maternal age	Control A	61	30.46	6.50	0.83	28.79 32.12	19.00	42.00	0.73
	Cases B	61	30.05	6.36	0.81	28.42 31.68	19.00	44.00	

Student's t test

Women whose neonates have been admitted to NICU showed significantly higher rates of CS, low APGAR score and preterm labor when compared to women whose neonates have not (p<0.05). On the other hand, there was no statistically significant difference between cases and controls as regards meconium staining (p>0.05). As mentioned before, UCI and URI were found to be significantly higher in cases when compared to controls. Hence, an association is suggested between abnormally high UCI and URI and these adverse outcomes (Cesarian delivery, low APGAR score and preterm delivery), but this association was not likely with meconium liquor staining.

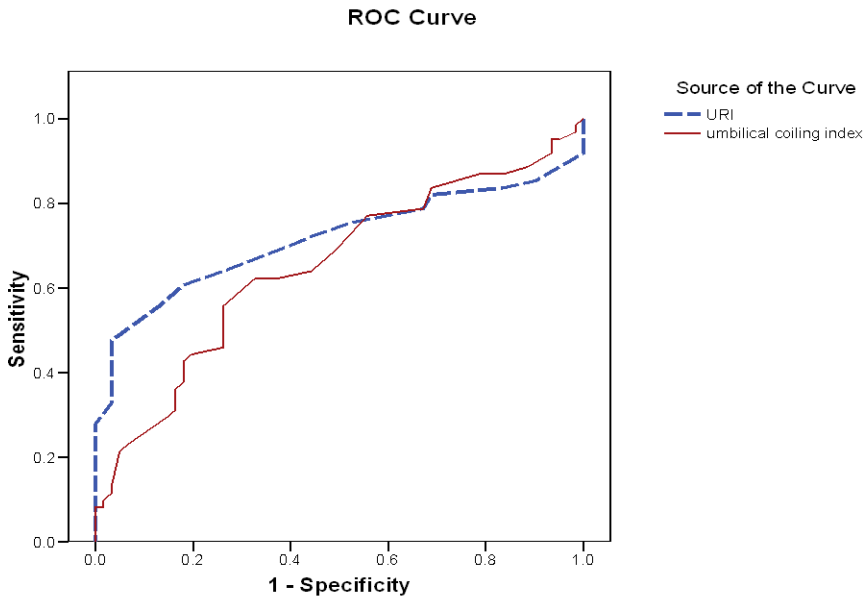
Table (4): Comparison between cases (61) and Controls (61) according to mode of delivery, APGAR score and preterm labor

	Mode of Delivery				OR	P
	C.S		S.V.D			
Control (A)	42	68.9%	19	31.1%	2.11(1.04-4.29)	0.03
Cases (B)	52	85.2%	9	14.8%		
	Apgar score				**OR**	**P**
	Normal		Low			
Control (A)	53	86.9%	8	13.1%	4.30(1.74-10.61)	0.001
Cases (B)	37	60.7%	24	39.3%		
	Preterm labor				**OR**	**P**
	Normal labor		Preterm labor			
Control (A)	49	80.3%	12	19.7%	3.25(1.49-7.09)	0.001
Cases (B)	31	50.8%	30	49.2%		

	Meconium Staining				OR	P
	Absent		Present			
Control (A)	54	88.5%	7	11.5%	1.75(0.54-5.67)	0.53
Cases (B)	57	93.4%	4	6.6%		

OR: odds ratio

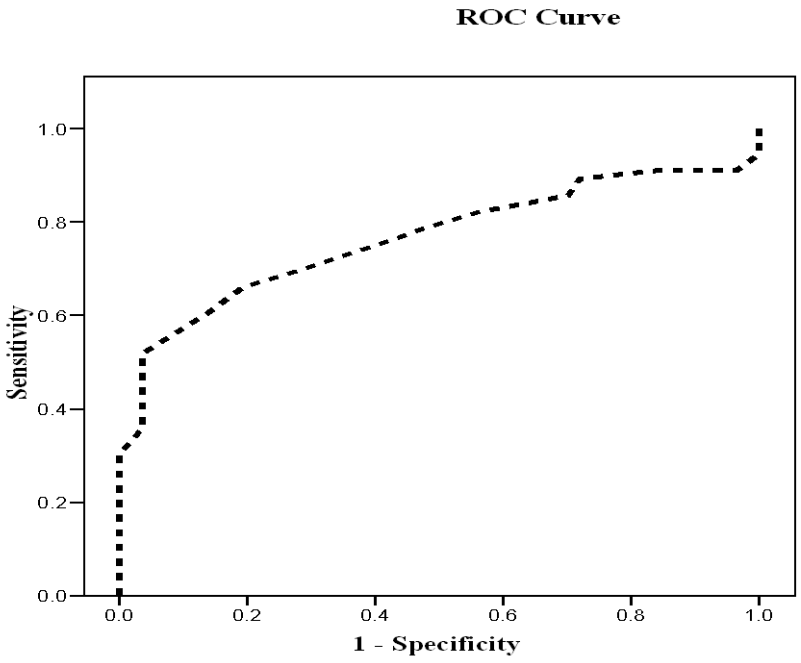
URI and UCI were **unreliable** (< 75%) to predict NICU admission as a fetal adverse outcome. AUC was 71% for URI and 65% for UCI (Figure 2).



	AUC	St error	P	95% CI
URI	0.71	0.05	<0.0001	**0.62-0.82**
UCI	0.65	0.07	0.004	**0.55-0.75**

Figure (2): ROC curve to define the best cut off for URI and UCI to predict NICU admission.

URI was **reliable** to predict hyper-coiling (P<0.0001) and AUC was 77 %. The best cut off value of URI was 0.61 with a sensitivity of 77%, specificity of 56%, PPV of 64% and NPV of 71% with a diagnostic accuracy of 66%. Cases with URI > 0.61 were more than 4 folds likely to be involved in adverse outcome than those with level < 0.61 (odd ratio = 4, 95%CI: 1.8 to 9.2) (Figure 3).



	AUC	St error	P	95% CI
URI	0.77	0.05	<0.0001	**0.67-0.86**

Figure (3): ROC curve to define the best cut off for URI to detect hyper-coiling.

DISCUSSION

To the best of our ability, there is paucity of studies in literature assessing our study outcomes and most of studies that disagree with our results were due to several causes as different study methodology, outcomes, sample size and different medical conditions and gestational ages of studied cases at time of enrollment. It is worthy to mention that we aimed mainly at this study to study the correlation between umbilical hyper-coiling and high umbilical resistance index and adverse neonatal outcomes, specifically NICU admission, and hence our study was designed.

In this study regarding the coiling index, it was statistically significantly higher among cases of NICU group compared to controls. There was statistically significant higher frequency of hyper coiling in NICU group compared to non-NICU group. Regarding URI, our study revealed that it was statistically significantly higher among cases of NICU group compared to control one.

URI and UCI (< 75%) were unreliable in predicting NICU admission; AUC was 71% for URI and 65% for UCI. On the other hand, URI was reliable in predicting hyper coiling (as an indicator of adverse outcome) (P<0.0001) and AUC was 77. The best cut-off value of URI was 0.61 with a sensitivity of 77%, specificity of 56%, PPV of 64% and NPV of 71% with a diagnostic accuracy of 66%. Cases with URI > 0.61 were more than 4 times more likely to be involved in adverse outcomes than those with level < 0.61.

Women whose neonates have been admitted to NICU showed significantly higher rate of CS, low APGAR score and preterm labor when compared to women whose neonates have not (p<0.05). On the other hand, there was no statistically significant difference between cases and controls as regards meconium staining (p>0.05). As mentioned, UCI and URI were found to be significantly higher in cases when compared to controls, hence, an association is suggested between abnormally high UCI and URI and these adverse outcomes (Cesarian delivery, low APGAR score and preterm delivery, but this association is not likely with meconium liquor staining. **Chitra and his colleagues** [8] measured umbilical coiling index (UCI) postnatally while we did it antenatally and studied the association of abnormal UCI to maternal and perinatal outcome. According to their findings, the mean umbilical coiling index was shown to be substantially related to NICU admission, which is consistent with the findings of our study. However, they also found links between aberrant UCI and foetal heart rate abnormalities, abruptio-placentae, premature labour, oligohydramnios, and hypertensive diseases. The presence of diabetes mellitus, polyhydramnios, Caesarean delivery, congenital abnormalities, and neonatal respiratory distress were all linked to hyper-coiling (> 0.36). **Jain and Mather** [9] and **Aanandini and his colleagues** [10] concluded that non-re-assuring fetal heart rate, which was not an outcome in our study, was significantly associated with abnormal coiling while **Mittal and his colleagues** [1] and **Pergialiotis and his colleagues** [11] reported no such significance.

Khan and his colleagues [12] and **Dijk and his colleagues** [13] concluded that the umbilical cord coiling index was not significantly correlated with the manner of delivery, and this is not in concordance with our study results. However, this can be attributed to different studies' designs where they studied directly the correlation between abnormal UCI and different adverse outcomes, this was done by addressing cases as "abnormal UCI" and controls as "normal UCI", and this greatly differs from ours. **Razak and his colleagues** [14] stated that hypo-coiled cords were associated with higher number of LBW babies while **Tripathy** [15] stated that hyper-coiled cords were associated with LBW. **Tahmasebi and his colleagues** [16] showed no significant association of abnormal UCI with birth weight. On the other hand, **Jo and his colleagues** [17], **Rana and her colleagues** [5], and **de Laat and his colleagues** [2] found that babies with low birth weight are much more likely to have an aberrant coiling index. Birth weight was not a measurable outcome in our study.

Razak and his colleagues [14] disagree in part with our study results, as they discovered that hyper-coiling was substantially correlated with alcohol stained with meconium. However, their sample size was smaller than ours, and they measured UCI at 18-24 weeks while we measured it at 28-40 weeks. This in addition to their different study design, where their cases were "abnormal cord" and their controls "normal cord", to study the correlation between different aspects of cord abnormalities and adverse outcomes. **de Laat and his colleagues** [2], **Bhojwani and his colleagues** [7], **Predanic and his colleagues** [18], **El Behery and her colleagues** [19], **Prathibha and his colleagues** [20] and **Rahi and his colleagues** [21] have shown a significant association between hyper-coiling and intrauterine growth restriction which was one of the exclusion criteria in our study. **Gaikwad and his colleagues** [22] and **Rohinidevi and his colleagues** [23] found that hypo-coiling of the umbilical cord was connected with low APGAR, but hyper-coiling group did not exhibit this connection, and this disagrees with our study results associating low APGAR with hypercoiling. On the contrary, as regards this association, our results match with that of **Sharma and his colleagues** [24], **Tahmasebi and Alighanbari** [16] and **Machin and his colleagues** [25] and we propose that the lower Wharton's jelly content and distinct segmental thinning of the umbilical cord arteries, which predispose an infant to a low Apgar score, are plausible explanations for this connection. Also, **de**

Laat and his colleagues [(2)] and **Rana and her colleagues** [(5)] agree with our findings, indicating that there was a substantial link between poor APGAR in newborns and an aberrant umbilical cord coiling index **(p-value <0.001).**

The strength points of this study:

- Using colour Doppler technology. It was the first study conducted at Ain Shams University Hospitals to examine the relationship between the index of prenatal umbilical cord coiling and perinatal outcome.
- All clinical assessment and evaluation of study outcomes were done by the same team.
- Study design guaranteed direct investigation between NICU admission and abnormal UCI and URI. This was done by addressing cases as patients whose neonates were NICU admitted, while controls were patients whose neonates were not. All outcomes, including abnormal UCI and URI and other adverse outcomes were measured and correlated directly to NICU admission.

The limitations of the study:

- Study design, which correlated directly and greatly the association of NICU admission as an outcome with abnormal UCI and URI as an exposure, instead of correlating abnormal UCI and URI to different adverse outcomes.
- Preterm babies were not excluded from the population under study; hence, results can be biased.
- All maternal ages were included in both study groups, which may affect vascularity.
- Larger numbers are needed for further assessment.
- Not being a multi-centric study.

CONCLUSION

Umbilical coiling index was positively correlated with umbilical artery resistance index, denoting that hyper-coiling correlates with increased resistance to blood flow in the umbilical cord, but there was no statistical evidence of using UCI as a predictor of NICU admission in the current study. Umbilical cord coiling may be used as a simple method to detect placental insufficiency as it positively correlated with the umbilical artery RI even without using color Doppler. Cases with umbilical artery resistance index of > 0.61 were 4 times more likely to be involved in adverse outcome than those with level < 0.61 as higher rate of Cesarean section, preterm labor and lower Apgar score. The best cut off value of umbilical artery resistance index was 0.61 to detect umbilical cord hyper-coiling with a sensitivity of 77%, specificity of 56%, PPV of 64% and NPV of 71% with a diagnostic accuracy of 66%.

- **Sponsoring financially:** Nil.
- **Competing interests:** Nil.

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