



Association of Placental Umbilical Cord Insertion Site with Maternal and Fetal Outcomes: A Prospective Study

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Abstract

Introduction Adequate fetal growth during pregnancy depends upon the normal development and insertion of the umbilical cord. Central/paracentral placental cord insertion is considered normal, while marginal/velamentous cord insertion is considered abnormal. Although the location of placental umbilical cord insertion can be determined by ultrasound (US), it is not included in the routine protocol of a targeted anomaly scan. Through this study, we determined different placental umbilical cord insertion sites by US and categorized them as normal and abnormal, identified the risk factors involved, and evaluated the outcome of pregnancies using standard protocols. The rationale of this study was to identify pregnancies that require frequent monitoring and surveillance for an optimal perinatal outcome.

Methods A prospective cohort study was conducted in a tertiary care hospital for 18 months. A total of 345 pregnant women who attended the antenatal outpatient department between 18 and 22 weeks for targeted imaging for fetal anomalies scan were included in the study after informed consent. Detailed history followed by US documentation of the cord insertion site on the placenta was done and women were followed up throughout pregnancy to look for development of complications including hypertensive disorders, antepartum hemorrhage (APH), and fetal growth restriction (FGR). Intrapartum adverse events like fetal distress and intrapartum hemorrhage were assessed. Confirmation of US findings was done by macroscopic examination of the placenta and measuring the distance between the placental cord insertion and the edge of the placenta. The weight of the placenta was also documented. Newborns were evaluated for adverse outcomes like preterm birth, low birth weight, need for resuscitation, and neonatal intensive care unit (NICU) admission. Follow up of neonates and mothers was done till discharge.

Results Placental cord insertion was accurately determined at the anomaly scan with 100% sensitivity and specificity. The study showed 44 abnormal placental cord insertions (ACIs)—42 had marginal and 2 had velamentous cord insertions. There

Keywords

- ▶ marginal umbilical cord insertion
- ▶ maternal outcome
- ▶ fetal outcome
- ▶ fetal growth restriction
- ▶ baby weight

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was a high incidence of ACI noted in women aged more than 28 years, with body mass index of more than 26.38, multiparity, previous history of myomectomy, first trimester miscarriage, and conceived by assisted reproductive technology. Women with ACI had an increased risk of small for gestational age/FGR and APH and had an average baby weight of 2.7 kg, which was 200 g less than babies with normal cord insertion. They also had lower mean Apgar scores at 5 minutes and required resuscitation and NICU admission.

Conclusion Our study concluded that it will be a good practice to document the placental cord insertion during the mid trimester anomaly scan so that we can identify the subset of pregnant women who are prone to develop complications, thereby providing adequate surveillance for an optimal perinatal outcome.

Introduction

The umbilical cord (UC) or funiculus is a conduit between the developing embryo or fetus and the placenta which is formed by the third week of gestation.¹ Adequate fetal growth during pregnancy depends on the normal development and insertion of the UC. The developing fetus derives its nutrition and oxygen requirements from this connection.^{1,2}

The UC insertion site can be subdivided into four categories: central, paracentral, marginal/battledore, and velamentous/membranous. The placental end of the UC normally inserts into the central portion of the placenta, well away from the placental edge and this is termed as central cord insertion (CI). CI is considered paracentral when it is more than 2 cm away from the edge of the placenta, and marginal (MCI) is when it is located at the edge or within 2 cm of the edge of the placental disc. CI is termed velamentous (VCI) when the UC vessels are inserted into the chorioamniotic membranes.³ The central/paracentral category is considered normal CI, while marginal/velamentous insertion is considered abnormal. Images of different types of CI in gross specimens are shown in ►Fig. 1A–D.

Central and paracentral CIs represent more than 90% of placental CIs, while abnormal MCI in singletons ranges from 6.3 to 7% and VCI ranges from 0.5 to 1.69%.^{4–6}

Three theories have been proposed in the literature for the etiology of abnormal placental cord insertion (ACI):

1. Blastocyst polarity theory: Aberrant insertion site results from mispositioning of the blastocyst during implantation, with consequent defective placental disk orientation.

2. Abnormal placental development because of decreased chorionic vessel branching theory: Noncentral insertion results from abnormal vasculogenesis in the placenta.
3. Trophotropism/placental migration theory: It was considered significant earlier but has now been excluded due to the early appearance of abnormal CI during pregnancy, even before placental migration.⁷

Abnormal CI seems to be associated with impaired development and function of the placenta, and thus influences fetal growth and birth weight and has been linked to pregnancy induced hypertension.⁸ Other complications of abnormal CI include antepartum hemorrhage (APH) from placental abruption and placenta previa, increased risk of cesarean section (CS), poor Apgar score, and increased neonatal intensive care unit (NICU) admissions.¹ Risk factors for MCI are advanced maternal age (> 35 years), chronic maternal disease, female fetus, and MCI in the previous pregnancy.⁹ CI can be imaged from the first trimester onwards.¹⁰

Although the location of placental UC insertion can be determined by the ultrasound (US), it is not included in the routine protocol of a mid trimester anomaly scan. We have evaluated the association between the placental UC insertion site and maternal and perinatal outcomes using standard protocols. Through this study, we determined placental UC insertion sites and categorized them as normal and abnormal. The rationale of prenatal determination and stratification was to identify pregnancies that require frequent monitoring and surveillance. The association of abnormal CI with maternal, fetal, and neonatal complications was

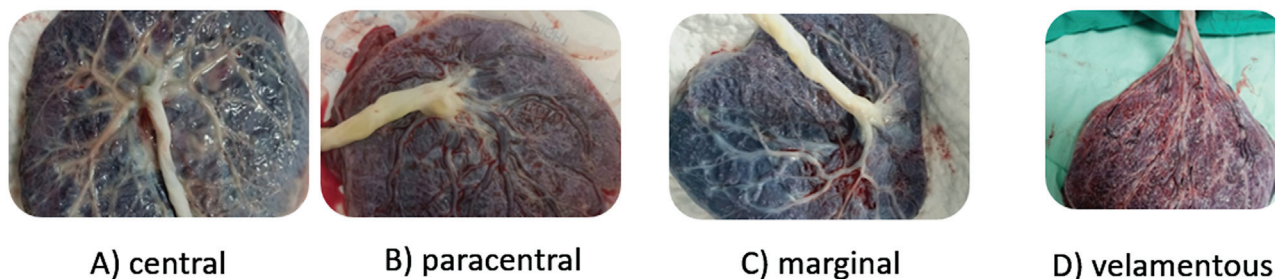


Fig. 1 (A–D) Gross images of different types of placental umbilical cord insertion site.

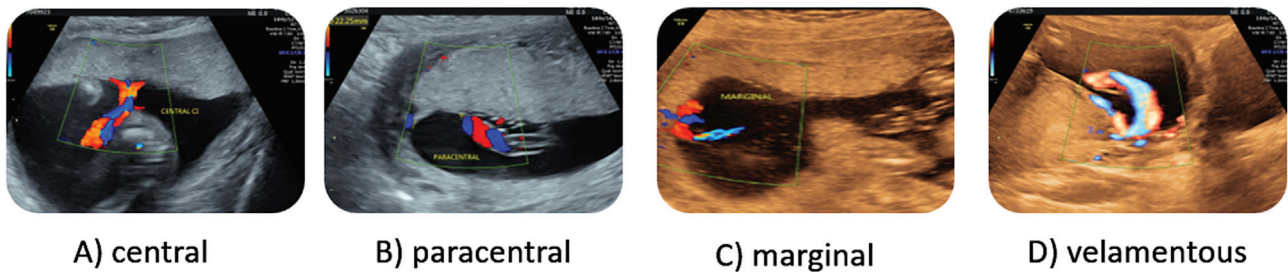


Fig. 2 (A–D) Ultrasound images of different types of placental umbilical cord insertion site.

studied. Different types of CI noted by US are shown in ►**Fig. 2A–D**.

Material and Methods

This was a prospective study conducted in a tertiary care center, in south Kerala for 18 months from January 1, 2020 to June 30, 2022. A total of 345 pregnant women who attended the antenatal outpatient department (OPD) for a mid trimester anomaly scan were included in the study after informed consent. Abnormal and normal placental UC insertion was taken at a ratio of 1:3. Census sampling of all pregnant women with ACI during the study period was taken as case, and women with normal CI were taken as controls. Only singleton pregnancies were included, and multiple gestations and fetuses with major structural abnormalities were not included in the study.

In our hospital, during the mid trimester anomaly scan, after determining the placental location, the placental UC insertion site was identified by a single fetal medicine specialist using a GE Voluson E8 C1-5D curved transabdominal transducer. In each case, the placental CI site was initially identified by two dimensional imaging by checking the entry of the umbilical vessels into the fetal surface of the placenta and noting the continuity of the cord with the chorionic plate. This was repeated in different planes by rotating the transducer to avoid errors. Color Doppler imaging was then used to assist the diagnosis. Care was also taken not to confuse a loop of the cord entering the fetal surface with the loop of the cord overlying the fetal surface of the placenta. The nearest placental edge was identified and the distance between the CI site and the edge was measured.

The following criteria were used:

- (1) Normal placental UC insertion site: All central CIs and paracentral CIs > 2 cm from the placental margin.
- (2) Abnormal placental UC insertion site:
 - (i) Marginal placental CI site: UC inserted within 2 cm from the placental margin.
 - (ii) VCI: Cord vessels get inserted into the chorioamniotic membranes before reaching the placenta. When VCI was diagnosed, the presence of vasa previa was looked for.

Detailed history followed by US documentation of the CI site on the placenta was done and women were followed up

throughout pregnancy to look for development of complications like hypertensive disorders, APH, and fetal growth restriction (FGR). Intrapartum adverse events like fetal distress and intrapartum hemorrhage (IPH) were assessed. Confirmation of US findings was done by macroscopic examination of the placenta and measuring the distance between the placental CI and the edge of the placenta using a measuring scale/tape. The weight of the placenta was also documented. Newborns were evaluated for adverse outcomes like preterm birth, low birth weight, need for resuscitation, and NICU admission. Follow up of neonates and mothers were done till discharge. A total of 44 ACIs were required for the study. A total of 25 ACIs documented from the anomaly scan were followed up till delivery. The required sample size could not be obtained due to the following limitations: US was done by a single fetal medicine specialist, limited time frame, and a low prevalence of ACI. To meet the study requirement, retrospective data from 19 placentas with ACI, which were identified postnatally, were also included in the study. To avoid selection bias, the placenta after delivery of the baby was examined and inclusion in the study was done based on random sampling.

All the data collected were entered on a preestablished and pretested questionnaire, which included the maternal age, parity, gestational age at delivery, any medical illness complicating pregnancy, and CI documented from the US. All data were entered into MS Excel and analyzed using the statistical software SPSS version 16.0. Descriptive statistics were summarized using means with standard deviations or median with interquartile ranges for continuous variables and percentiles and rates for categorical variables.

Results

A total of 345 pregnant women who attended the antenatal OPD for a mid trimester anomaly scan were included in the study after meeting the inclusion criteria and informed consent. The proportion of central/paracentral CI was noted in 320 (87.9%), 23 (6.3%) had MCI and 2 (0.5%) had VCI.

A total of 364 (345 + 19) gross placentas were examined, of which 44 had ACI in the placenta, 42 had MCI and 2 had VCI. The proportion of normal CI noted in the placenta as seen after delivery was 88%, MCI 11.5%, and 0.5% had VCI. US scanning had a sensitivity of 100% and a specificity of 100% in detecting correctly the site of CI ($N = 25$).

Mothers with higher mean age were associated with ACI and this association was statistically significant (p -value < 0.05), while the weight and body mass index (BMI) of the mother had no association with the CI site. Among different medical illnesses noted in the study population, diabetes mellitus, hypertension, anemia, hypothyroidism, and post-coronavirus disease 2019 (COVID-19) infection account for the majority. It was observed that out of the total ACI cases, 3.5% had gestational diabetes mellitus (GDM), 0.5% had gestational hypertension (GHTN), and 1.6% each had anemia and a history of COVID during pregnancy. A significant association of ACI with medical illness could not be noted as the study was conducted with a small number of participants. The maternal variables associated with abnormal CI are shown in ►Table 1.

Women with ACI had a higher chance of APH (odds ratio [OR]: 23.63, 95% confidence interval: 7.83–71.32) and IPH (OR: 31.9, 95% confidence interval: 3.47–292.49) and this association was statistically significant. APH is defined as bleeding from or into the genital tract, occurring from 24 weeks of pregnancy and prior to the birth of the baby. Excessive bleeding at the time of labor after the delivery of the baby but before the expulsion of the placenta is defined as IPH. However, the nuchal cord (OR: 6.43, 95% confidence interval: 2.65–15.58) was noted more in normal CI and this association was statistically significant.

In our study, 62.9% of women underwent vaginal delivery, preterm vaginal delivery was seen in 0.1%, and vacuum delivery in 0.1%, while 18.1% of women underwent elective

lower segment CS (LSCS) and 16.8% underwent emergency LSCS. Both normal (18.4%) and ACI (15.9%) had almost similar numbers of elective LSCS, while 15.4% of normal CI and 17.3% of the ACI had emergency LSCS.

There was a higher incidence of small for gestational age (SGA) with ACI. A total of 15.9% of ACI had SGA when compared with 5.6% in normal CI. Among the small fetuses noted in ACI 5 had FGR and 2 were SGA. Three pregnant women with FGR had intrapartum fetal distress for which emergency LSCS was done. The antepartum/intrapartum complications and mode of delivery details associated with abnormal CI are shown in ►Table 2.

The CI site had no statistical influence on the gestation age of delivery or the weight of the placenta. Women with ACI had an average baby weight of 2.7 kg when compared with normal CI the baby had an average weight of 2.9 kg. Sixteen (4.4%) babies required NICU admission, while 348 (95.6%) babies did not require NICU admission. Fourteen (3.8%) babies required resuscitation and 350 (96.2%) babies were stable at birth. The gender of the baby had no association with the CI site. The newborn details associated with abnormal CI are shown in ►Table 3.

Discussion

In our study, women with higher mean age were associated with ACI and this association was statistically significant (p -value < 0.05), similar to the findings in other studies.^{9,10} The BMI of our study population belonged to the obese group,

Table 1 Maternal variables associated with ACI

		Cord insertion site in the placenta		p -Value	Odds ratio (95% CI)
		Normal cord insertion, n (%)	Abnormal cord insertion, n (%)		
Age of mother in years	Mean (SD)	28.76 (3.99)	30.14 (3.645)	0.031	–
Weight in kg	Mean (SD)	67.764 (11.54)	71.23 (11.84)	0.063	–
BMI	Mean (SD)	26.38 (4.39)	26.95 (5.80)	0.447	–
Parity	Primipara	165 (89.7)	19 (10.3)	0.297	1.401 (0.742–2.65)
	Multipara	155 (86.1)	25 (13.9)		
Mode of conception	Spontaneous	279 (88.3)	37 (11.7)	0.569	1.287 (0.538–3.079)
	Artificial reproductive technology	41 (85.4)	7 (14.6)		
History of miscarriage	No	277 (88.5)	36 (11.5)	0.395	1.432 (0.624–3.28)
	Yes	43 (84.3)	8 (15.7)		
Uterine anomaly	No	317 (87.8)	44 (12.2)	0.519	0.878 (0.845–0.913)
	Yes	3 (100)	0		
Myomectomy	No	319 (89.4)	38 (10.6)	< 0.0001	50.368 (5.9–429.63)
	Yes	1 (14.3)	6 (85.7)		
Suction evacuation	No	293 (88.3)	39 (11.7)	0.475	1.45 (0.524–3.98)
	Yes	26 (83.9)	5 (16.1)		

Abbreviations: ACI, abnormal placental cord insertion; CI, confidence interval; SD, standard deviation.

Note: The values are boldfaced because they are statistically significant.

Table 2 Antepartum/intrapartum complications/mode of delivery details associated with ACI

		Cord insertion site in the placenta		p-Value	Odds ratio (95% CI)
		Normal cord insertion, n (%)	ACI, n (%)		
APH	No	315 (90.8)	32 (9.2)	< 0.0001	23.63 (7.83–71.32)
	Yes	5 (29.4)	12 (70.6)		
IPH	No	319 (88.9)	40 (11.1)	< 0.0001	31.9 (3.47–292.49)
	Yes	1 (20)	4 (80)		
Nuchal cord	No	306 (90)	34 (10)	< 0.0001	6.43 (2.65–15.58)
	Yes	14 (58.3)	10 (41.7)		
SGA/FGR	Yes	5.6	15.9	0.014	–
	No	94.4	84.1		
Mode of delivery					
Vaginal delivery		212 (66.2)	212 (66.2)	0.138	–
Elective LSCS		59 (18.4)	7 (15.9)	0.12	–
Emergency LSCS		49 (15.4)	13 (17.3)	0.89	–

Abbreviations: ACI, abnormal placental cord insertion; APH, antepartum hemorrhage; CI, confidence interval; FGR, fetal growth restriction; IPH, intrapartum hemorrhage; LSCS, lower segment cesarean section; SGA, small for gestational age.

Note: The values are boldfaced because they are statistically significant.

Table 3 Newborn details associated with ACI

		Cord insertion site in the placenta		p-Value	Odds ratio (95% CI)
		Normal cord insertion	ACI		
GA at delivery in weeks, mean (SD)		38.075 (0.965)	37.44 (2.271)	0.074	–
Weight of placenta in grams, mean (SD)		516.82 (42.34)	511 (40.24)	0.391	–
Weight of baby in kg, mean (SD)		2.99 (0.36)	2.7 (0.712)	0.175	–
Apgar at 1 min, mean (SD)		7.953 (0.355)	7.0 (0.957)	0.079	–
Apgar at 5 min, mean (SD)		8.97 (0.25)	8.7 (0.701)	0.018	–
Resuscitation, n (%)	No	312 (89.1)	38 (10.9)	< 0.0001	6.16 (2.03–18.7)
	Yes	8 (57.1)	6 (42.9)		
NICU admission, n (%)	No	312 (89.1)	36 (10.3)	< 0.0001	8.67 (3.07–24.49)
	Yes	8 (50)	8 (50)		
Gender, n (%)	Female	151 (88.3)	20 (11.4)	0.79	–
	Male	169 (87.6)	24 (12.4)		

Abbreviations: ACI, abnormal placental cord insertion; CI, confidence interval; GA, gestational age; NICU, neonatal intensive care unit; SD, standard deviation.

Note: The values are boldfaced because they are statistically significant.

according to the International Obesity Task Force for the Asian population.¹¹ The weight and BMI of the mother had no association with CI in our study. The study conducted by Brouillet et al also noted that there was no association between abnormal CI with BMI.³ Multipara (OR: 1.401, 95% confidence interval: 0.742–2.65) had a higher incidence of ACI, but this association was not found to be statistically significant. These findings were in contrast to the cross-sectional study conducted by Aragie et al¹⁰ in 2021, where they reported that primigravida were 3.87 times more likely to have ACI, and Räisänen et al study, which found an association of nulliparity with ACI. Pregnant women who

had conceived by assisted reproductive technology (ART) (OR: 1.287, 95% confidence interval: 0.538–3.079) had a higher incidence of ACI, but it was not statistically significant. A higher incidence of miscarriage was noted with ACI (OR: 1.432, 95% confidence interval: 0.624–3.28), but this association was not found to be statistically significant. Brouillet et al³ also noted the same. Women who had a history of myomectomy (OR: 50.368, 95% confidence interval: 5.9–429.63) had a higher chance of MCI, and this association was statistically significant. Many studies investigated the risk factors for ACI but none had looked into the previous history of myomectomy.

The overall incidence of MCI in singleton pregnancies ranges from 6.3 to 7%.³⁻⁵ In our study, abnormal: normal placental UC insertion is taken in the ratio 1:3. A total of 44 ACIs were taken for the study, hence, the proportion of ACI was 11.5%. Women with ACI had a higher chance of APH (OR: 23.63, 95% confidence interval: 7.83–71.32) and IPH (OR: 31.9, 95% confidence interval: 3.47–292.49) (p -value < 0.05). Many other studies also showed a higher incidence of APH with ACI.^{10,12} The nuchal cord (OR: 6.43, 95% confidence interval: 2.65–15.58) was noted more in normal CI and this association was statistically significant. Among the small fetuses noted in ACI, 5 had FGR and 2 were SGA. Three pregnant women with FGR had intrapartum fetal distress and emergency LSCS was done. A significant association of ACI with FGR was noted in many studies.^{3,9,13}

In our study, US detection of the placental CI site had a sensitivity of 100% and a specificity of 100% in detecting the site of CI accurately. Nomiyama et al (1998) inferred that 100% sensitivity and 99.8% specificity were found in US diagnosis of ACI.¹⁴ In the prospective study by Di Salvo et al, they concluded that US had an overall sensitivity of 69%, specificity of 100%, and accuracy of 91% for detecting ACI.¹³ Another prospective study conducted by Sepulveda et al observed that a confident identification of the placental CI site was achieved in 99% of cases.¹⁵ The reason for this accuracy they stated was that all US scans were performed by a single experienced fetal medicine specialist. In our study, the placental CI was documented by a single experienced fetal medicine specialist, which might have improved the sensitivity and specificity.

As per our study, CI had no statistical influence on gestation age of delivery, gender of the baby, and weight of the placenta, which was similar to the findings of Nkwabong et al.⁹ Regarding the mode of delivery, both groups had an almost similar number of vaginal deliveries and LSCS. Emergency LSCS was performed in 15.4% of normal CIs and 17.3% of ACI. The main indication noted for emergency LSCS was fetal distress. The results of our study were similar to the studies before.^{12,15,16} The average weight of baby born with normal CI was 2.99 ± 0.36 , and ACI was 2.7 ± 0.612 . Babies with ACI were 200 g smaller when compared with normal CI, which was similar to findings from other studies.^{3,9}

Strengths and Limitations of the Study

The placental UC insertion site is not well studied or reported in literature, possibly due to the lack of standardized definition and the lack of awareness of antenatal diagnosis. The strength of our study is its prospective nature which proved that placental UC insertion could be located with good sensitivity and accuracy. However, the main limitation is that the required sample size could not be obtained due to the reasons explained in the methodology section and thus retrospective data from 19 placentas with ACI had to be included in the study. Other limitations are that our study was conducted with a small study population and over a short period. More multicenter studies with larger sample sizes should be performed to assess the effect of abnormal CI sites on maternal, fetal, and neonatal outcomes.

Conclusion

This study concludes that US detection of the placental CI site has a sensitivity of 100% and a specificity of 100% in detecting the site of CI accurately. There is a high incidence of ACI noted in women aged more than 28 years, with BMI more than 26.38, multiparity, previous history of myomectomy, first trimester miscarriage, and those conceived by ART. There was also an increased risk of SGA/FGR, APH, low Apgar score at 5 minutes, and NICU admission in the ACI group. Neonates with ACI were 200 g smaller than their counterparts with normal CI. However, no statistical association could be drawn between ACI and gestation age at delivery, mode of delivery, and weight of the placenta and nuchal cord. Our study failed to show any association with comorbidities like GHTN, GDM, anemia, and COVID-19 infection in the ACI group.

Implications in Clinical Practice

It is not a routine practice to look for placental CI in singleton pregnancies in a mid trimester anomaly scan. However, from our study, we conclude that placental CI can be identified with confidence and accuracy in the anomaly scan. We recommend that it is good practice to document placental CI so that we can identify those pregnant women who are prone to develop complications, thereby instituting adequate surveillance for an optimal perinatal outcome.

Conflict of Interest

None declared.

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