

Research Article

Curettage is a risk factor for marginal umbilical cord insertion

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Submitted: 10 December 2019

Approved: 01 July 2020

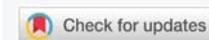
Published: 02 July 2020

How to cite this article: Nkwabong E, Mbeleck SJM, Tumasang F. Curettage is a risk factor for marginal umbilical cord insertion. Clin J Obstet Gynecol. 2020; 3: 081-084.

DOI: 10.29328/journal.cjog.1001054

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Keywords: Marginal umbilical cord insertion; Risk factors; Dilatation and curettage; Fetal female sex; Manual vacuum aspiration



Abstract

Objective: To identify the risk factors for marginal cord insertion (MCI).

Material and Methods: This case-control study was carried out between 1st February and 30th June 2019. Singletons with and without MCI at delivery were recruited. Main variables analyzed included maternal age, parity, number of previous dilatation and curettage (D&C) or manual vacuum aspiration (MVA), time interval between each procedure and conception, cord insertion. Fisher's exact test, t-test and logistic regression were used to compare data from both groups.

Results: We found 60 cases of MCI (4.1%). The significant ($p < 0.05$) risk factors for MCI were past-history of D&C (aOR 5.97, 95% CI 1.95-18.25) particularly when conception occurred < 5 months after D&C (OR 10.5, 95% CI 1.36-81.05), fetal female sex (aOR 3.82, 95% CI 1.41-10.32), parity ≥ 4 (aOR 2.63, 95% CI 1.05-12.71) and past-history of MVA (aOR 2.06, 95% CI 1.23-8.76).

Conclusion: Women should be advised to conceive at least five months after D&C.

Introduction

Marginal cord insertion (MCI) is defined as the insertion of the umbilical cord within a distance of < 3 cm from the placental margins [1]. For others, the cord is said to be marginally inserted when the distance between the external margin of the umbilical cord and that of the placenta is less than 2 cm [2,3]. The prevalence of MCI varies between 6.3% and 7% in singleton pregnancies [1,4,5].

The umbilical cord insertion site to the placenta can be central, lateral, marginal or velamentous. Central and lateral umbilical cord insertions, categorized as normal, represent more than 90% of cord insertions of term placentas [1]. Velamentous and marginal cord insertions are categorized as abnormal.

The pathogenesis of MCI is not well known. It is thought to result from abnormal primary implantation or 'polarity theory' [5]. Another theory is the 'trophotropism theory'

which postulates that the placenta grows in areas with good blood supply and atrophies in areas where blood supply is poor [5]. The last theory is the 'abnormal placental development because of decreased chorionic vessel branching theory'. According to this theory, MCI results from abnormal vasculogenesis in the placenta.

MCI can be diagnosed ultrasonographically as from the 18th week of gestation [6]. MCI is associated with adverse maternal and especially perinatal outcomes. There is a strong association between MCI and intrauterine growth retardation (IUGR), preeclampsia, nuchal cord entanglement, antepartum hemorrhage from placenta abruption or placenta praevia, increased risk of cesarean section (CS), low birth weight (LBW), poor Apgar score and transfer of newborn to neonatal intensive care unit (NICU) [1,4,7,8].

There is scarcity of papers on risk factors for MCI in the literature. Known risk factors for MCI are advanced

maternal age (≥ 35 years), chronic maternal diseases (chronic hypertension, asthma and diabetes), female fetus, assisted reproductive technology and previous CS [4].

The effect of various endometrial insults on the pathogenesis of MCI has not yet been evaluated. Some other risk factors might exist. Knowing the risk factors for MCI might help in the prevention or in the diagnosis of some cases. To the best of our knowledge, no study has evaluated the risk factors for MCI in a developing country. Hence this study which aimed at identifying these risk factors.

Methods

This case-control study was carried out between 1st February and 30th June 2019 in two University Teaching Hospitals. All singletons with MCI at delivery (≥ 28 complete weeks) were recruited as cases. For each case, the three singletons delivered immediately after the case without MCI were recruited as controls. A written informed consent was obtained from each woman or from their relatives. This study was approved by the institutional ethics committee.

The variables recorded on a pre-established questionnaire included maternal age at delivery, parity, tobacco or alcohol consumption, number of previous dilatation and curettage (D&C) or manual vacuum aspiration (MVA), time interval between D&C or MVA and conception, past history of CS, chronic hypertension (blood pressure $\geq 140/90$ mmHg before pregnancy or before 20 weeks' gestation or both), overt diabetes (fasting blood sugar > 125 mg/dl), gestational age at delivery (confirmed by an ultrasound scan performed before 20 weeks of gestation), mode of delivery, cord insertion (MCI was defined in this survey as the insertion of the umbilical cord with its external margin at less than 2 cm from that of the placenta [2,3]).

The necessary minimum sample size was calculated as needing at least 50 cases of MCI, using the following formula:

$N=2 \times (Z\alpha + Z\beta / P_0 - P_1)^2 \times P \times (1-P)$, where $Z\alpha = 1.96$ corresponds to a type I error of 2.5%, $Z\beta = 1.96$ corresponds to a type II error of 2.5% or a power of 97.5%, P_0 the prevalence of placenta abruption amongst women with MCI (29.6%)⁹, P_1 the prevalence of placenta abruption amongst women without MCI (1.2%)⁹ and P is $(P_0 + P_1) / 2$. To increase the power of our study, we decided to recruit three controls for each case.

Data were analyzed using SPSS 21.0 (IBM Corp., Armonk, NY, USA). Data of women whose newborns presented MCI were compared to those without MCI. Fisher's exact test was used to compare categorical variables and t-test to compare continuous variables. We used odds ratio (OR) with their 95% confidence intervals (CIs) to present the comparison between the two groups. Logistic regression was used to control for confounders. $p < 0.05$ was considered statistically significant.

Results

During the study period, we had a total of 60 cases of MCI out of 1470 singleton deliveries, given a prevalence of 4.1%. As controls, 180 newborns without MCI were recruited. Some sociodemographic and obstetrical variables of the study population are given in table 1.

Women of parity ≥ 4 were more found amongst cases than amongst controls (10 or 16.7% vs. 6 or 3.3%, OR 5.80, 95% CI 2.01-16.74, $p = 0.001$). Parity ≥ 4 remained a risk factor for MCI even after adjustment for confounding factor.

As concerns occupation, civil servant was also more found amongst cases than amongst controls at univariate analysis (19 or 31.7% vs. 31 or 17.2%, OR 2.22, 95% CI 1.14-4.32, $p = 0.015$), but it was not associated with MCI at multivariate analysis.

Mean gestational age at delivery was 38.8 ± 1.0 (36-42) in the MCI group vs. 38.9 ± 1.1 (33-42) in the control group ($p = 0.533$). Nevertheless, mean birth weight was lower in the

Table 1: Some sociodemographic characteristics of the population under study.

Variables	Pregnant women (n = 60) with MCI N (%)	Pregnant women (n = 180) without MCI N (%)	OR	95% CI	p - value
Maternal age (y)	27.8 \pm 3.6 (18-35)	26.1 \pm 4.6 (16-40)	-	-	0.009
Parity	1.8 \pm 0.9 (1-5)	1.9 \pm 1.4 (0-12)	-	-	0.604
Maternal age (y)	≥ 30	18 (30.0)	1.60	0.82-3.09	0.109
	< 30	42 (70.0)			
Number of MVA*	≥ 2	3/49 (6.1)	3.63	0.71-18.59	0.127
	≤ 1	46/49 (93.9)			
Number of D&C**	n = 2	9/47 (19.1)	5.24	1.83-14.97	0.002
	n ≤ 1	38/47 (80.9)			
Previous mode of delivery	CS	9 (15)	1.49	0.63-3.51	0.238
	VD	51 (85)			
Fetal sex	Female	44 (73.3)	2.30	1.20-4.37	0.007
	Male	16 (26.7)			
Birth weight (g)	< 3000	20 (33.3)	10.75	4.41-26.15	< 0.001
	≥ 3000	40 (66.7)			
Placenta weight	< 600	56 (93.3)	13.39	4.65-38.48	< 0.001
	≥ 600	4 (6.7)			

*Women with past history of D&C excluded, **Women with past history of MVA excluded.

MCI: Marginal Cord Insertion; OR: Odds Ratio; CI: Confidence Interval; MVA: Manual Vacuum Aspiration; D&C: Dilatation & Curettage

MCI group than in the control group: 2986.9 ± 161.0 g (2600-3560) vs. 3198.4 ± 219.3 g (2200-3850), $p < 0.0001$.

Mean placenta weight was also significantly lower in the MCI group (551.1 ± 52.6 g, range 480-700 vs. 614.9 ± 68.9 , range 360-800, $p < 0.0001$).

Newborns of women aged 30 to 34 were at risk of MCI (17 or 28.3% vs. 27 or 15%, OR 2.24, 95% CI 1.11-4.48, $p = 0.019$), but those of women aged between 20 and 24 were protected (5 or 8.4% vs. 55 or 30.4%, OR 0.20, 95% CI 0.08-0.54, $p = 0.0002$).

We found no association between previous mode of delivery and MCI. Also, no association was found between overt diabetes, chronic hypertension, placenta insertion, tobacco or alcohol consumptions and MCI (Table 2).

As concerns the 60 women of the MCI group, past history of D&C was found amongst 11 of them and past history of MVA amongst 13, as against 36 who had no past history of these two procedures. In the control group, amongst the 180 women, 10 had past history of D&C, 18 past history of MVA as against 152 with no past history of these two procedures.

Past history of D&C (amongst women with no past history of MVA) was a risk factor for MCI (11/47 or 23.4% vs. 10/162 or 6.1%, OR 4.64, 95% CI 1.83-11.77, $p = 0.001$). The risk of MCI increased with the number of D&C (Table 1). Past history of D&C was a risk factor for MCI even after adjustment for confounding factors (Table 3). Women whose current pregnancy occurred < 5 months after the last D&C were more found amongst cases (9/11 or 81.8% vs. 3/10 or 30%, OR 10.5, 95% CI 1.36-81.05, $p = 0.024$).

We also found that women with past history of MVA (amongst women with no past history of D&C) were at risk for MCI (13/49 or 26.5% vs. 18/170 or 10.6%, OR 3.05, 95% CI 1.36-6.79, $p = 0.007$). Contrarily to D&C, women who

conceived < 5 months after MVA were not more at risk than those who conceived ≥ 5 months after (9/13 or 69.2% vs. 12/18 or 66.7%, OR 1.12, 95% CI 0.24-5.20, $p = 0.597$).

Protective factors for MCI were maternal age between 20 and 24 years, nulliparity (5 or 7.7% vs. 60 or 31.4%, OR 0.18, 95% CI 0.07-0.47, $p < 0.0001$), absence of D&C (OR 0.21, 95% CI 0.08-0.54, $p = 0.001$), absence of MVA (OR 0.32, 95% CI 0.14-0.73, $p = 0.006$) and newborn of male sex (OR 0.43, 95% CI 0.22-0.82, $p = 0.007$).

Discussion

Our study found a prevalence of MCI of 4.1%. Risk factors for MCI were past history of D&C, conception < 5 months after D&C, fetal female sex, parity ≥ 4 and past history of MVA.

Our prevalence of MCI was lower than that of 7% and 7.2% observed respectively in USA and in our units previously [5,7].

We found no association between MCI and maternal age. Previous studies found maternal age ≥ 40 as a risk factor for MCI [4,9]. The absence of association between MCI and maternal age might be attributed to the absence of woman aged ≥ 40 in our study population. We also found also no association between MCI and overt diabetes, chronic hypertension, previous mode of delivery or placenta insertion.

Past history of intrauterine procedures (D&C or MVA) was a risk factor for MCI in our series, even after logistic regression. Various insults on the endometrium can lead to its subsequent poor regeneration [10]. In our study, D&C was riskier than MVA. Consequently, MVA should be preferred to D&C, as studies showed that MVA was efficient as D&C for diagnostic procedure in women with abnormal uterine bleeding [11]. Furthermore, D&C is more traumatizing than MVA [12]. Women with past history of two D&C were more at risk. This is in accordance with the findings of some authors who observed gradual endometrium thinning with repeated D&C [13].

Table 2: Distribution of some other variables amongst the study population.

Variables	Pregnant women with MCI (n = 60) N (%)	Pregnant women without MCI (n = 180) N (%)	OR	95% CI	p - value
Overt diabetes	2 (3.3)	4 (2.2)	1.51	0.27-8.49	0.467
Chronic hypertension	5 (8.3)	12 (6.7)	1.27	0.42-3.77	0.426
Placenta Praevia	2 (3.3)	5 (2.8)	1.20	0.22-6.38	0.557
Alcohol consumption	1 (1.7)	16 (8.9)	0.17	0.02-1.33	0.079
Tobacco consumption	0 (0)	4 (2.2)	-	-	0.314

MCI: Marginal Cord Insertion; OR: Odds Ratio; CI: Confidence Interval

Table 3: Independent risk factors for MCI.

Risk factors	OR	95% CI	p - value	aOR	95% CI	p - value
Past history of D&C	4.64	1.83-11.77	0.001	5.97	1.95-18.25	0.002
Female sex	2.30	1.20-4.37	0.007	3.82	1.41-10.32	0.008
Parity ≥ 4	5.80	2.00-16.74	0.001	2.63	1.05-12.71	0.029
Past history of MVA	3.05	1.36-6.79	0.007	2.06	1.23-8.76	0.039
Maternal age 30-34	2.24	1.11-4.48	0.019	2.28	0.87-5.98	0.092
Civil servant	2.22	1.14-4.34	0.015	1.69	0.65-4.33	0.274

MCI: Marginal Cord Insertion; OR: Odds Ratio; CI: Confidence Interval; aOR: adjusted OR; D&C: Dilatation & Curettage; MVA: Manual Vacuum Aspiration

During D&C, there might have been some foci of endometrial destruction. Thereafter, the endometrium might not have regenerated completely before the next conception, especially if the conception occurred within the four months that followed D&C. Some studies observed that the endometrium is only appropriate for normal reproductive function six months after D&C, the extent of the damage to endometrial function not found to be reflected by the endometrial thickness only [14].

In the cases of conception within the four months that followed D&C, some areas of the endometrium might not have been appropriate for placenta development. This might lead to asymmetrical placenta development from the point of cord insertion, the placenta being less developed where the endometrium is not well regenerated, leading to reduced placenta development. Indeed, the mean placenta weight was significantly low amongst cases. Histological examinations of the placentas were not done, giving that for cultural reasons many women took it back immediately to bury it. Examination might have visualized the suspected placental anomalies.

The risk of MCI was reduced amongst women who conceived at least five months after D&C. Therefore, women should be advised to conceive at least five months after this procedure.

Fetal female sex was a risk factor for MCI in our study even after adjustment for confounding factors, as observed by some authors [4]. The explanation is unknown. Studies should be carried out to explain this association.

Finally, fetuses of women with parity ≥ 4 were also at risk of MCI even after multivariate analysis. This might be attributed to successive deliveries of the placentas. There might exist some foci of endometrial injury during placental separation (perhaps due to foci of morbidly adherent placenta, for instance placenta accreta) and probably subsequent poor regeneration of the endometrium, with subsequent asymmetrical development of the placenta, as already explained above. More studies should be carried out to confirm these assertions.

The limitations of our study are our small sample size and the absence of women aged 40 in our series. Furthermore, we could not do histologic examination of the placentas. More studies with larger sample size should be carried out to confirm these risk factors and to look for others.

Conclusion

Risk factors for MCI in our series were past history of D&C, fetal female sex, parity ≥ 4 and past history of MVA. Therefore, MVA and especially D&C should be avoided as much as possible. MVA should substitute D&C for intra-uterine procedures. Moreover, if D&C is performed, women should be advised to conceive at least five months after the procedure. Lastly, 2nd trimester ultrasound scan should emphasize on

the umbilical cord insertion amongst women with the above-mentioned risk factors for MCI.

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