

# Umbilical cord constriction as a cause of intrauterine fetal death

## *Constricção de cordão umbilical como causa de morte fetal intrauterina*

Victor Antônio Kuiava<sup>1</sup>; Henrique M. Pasqual<sup>1</sup>; Ana Luiza S. Garcia<sup>1</sup>; Bianca L. Barbarioli<sup>1</sup>; Fernanda M. Carlotto<sup>1</sup>; Gabriel K. Costa<sup>1</sup>; Laurenlisiê L. H. Brittes<sup>1</sup>; Maiara Christine Macagnan<sup>1</sup>; Nathália Dal Prá Zucco<sup>1</sup>; Rubens Rodriguez<sup>1,2</sup>

1. Universidade de Passo Fundo, Passo Fundo, Rio Grande do Sul, Brazil. 2. Instituto de Patologia de Passo Fundo, Passo Fundo, Rio Grande do Sul, Brazil.

### ABSTRACT

The umbilical cord constriction (UCC) is an uncommon condition and an important etiology for stillborn fetuses. The main goal of this study was to verify the UCC occurrence as the cause of intrauterine fetal death, the associated etiology and its pathological characteristics. Therefore, a descriptive retrospective cross-sectional study was developed using the database from a Pathology Institute, in Brazil, from 1995 to 2017. The results presented a total of 1,359 embryo/fetus deaths – 69 (5.07%) due to UCC, 60.9% males and 39.1% females. The average age of pregnant women was 27.5 years  $\pm$  7.2 years of standard deviation (SD). The majority of deaths occurred during the second trimester (76.5%), followed by the first (14.7%) and third (8.8%) trimesters, respectively. One constriction alone was found in 87% of cases, 11% had two constrictions and only 1% had three or more. The presence of congenital malformations was detected in 20.2% of necropsies, the identification of chronic fetal distress was described in 71% of the technical reports and 17% of the cases had obstructive vasculopathy characteristics in microscopy analysis. Regarding the anatomopathological characteristics between the male and female sexes, no significant difference was found ( $p > 0.05$ ) correlating gestational age, weight or congenital malformations. UCC was a cause of fetal death found in 5% of the cases, and it was linked to congenital malformations, fetal distress and obliterative vasculopathy.

**Key words:** fetal death; fetal distress; umbilical cord.

### RESUMO

A constricção de cordão umbilical (CCU) é uma condição infrequente, não bem descrita na literatura, apesar de ser uma importante etiologia observada em fetos natimortos. O objetivo deste estudo foi verificar a ocorrência de CCU como causa de morte fetal e as características etiopatológicas associadas. Para tanto, um estudo retrospectivo transversal foi realizado a partir das informações do banco de dados do Instituto de Patologia de Passo Fundo, durante os anos de 1995 a 2017. Os resultados foram: 1.359 mortes de embriões/fetos, das quais 69 (5,07%) foram devidas a CCU; 60,9% eram do sexo masculino e 39,1%, do feminino. A média de idade das gestantes foi de 27,5 anos; desvio padrão (DP) de  $\pm$  7,2 anos. A maioria das mortes ocorreu no segundo trimestre (76,5%), seguido pelo primeiro (14,7%) e terceiro (8,8%). Entre o total de CCU observadas, 87% tiveram ocorrência de apenas uma constricção; 11%, de duas; e 1%, de três ou mais. A presença de malformações congênitas foi encontrada em 20,2% das necropsias; a identificação de sofrimento fetal crônico foi relatada em 71% dos laudos; e características de vasculopatia obstrutiva na análise da microscopia, em 17% dos casos. Em relação às características anatomopatológicas entre os sexos masculino e feminino, nenhuma diferença significativa ( $p > 0,05$ ) foi encontrada correlacionando idade gestacional dos fetos/embriões, peso ou malformações congênitas. A CCU é uma condição incomum de morte fetal associada a baixo peso fetal e restrição de crescimento. Nossa pesquisa sugere uma possível relação entre a CCU e a vasculopatia obliterativa.

**Unitermos:** morte fetal; sofrimento fetal; cordão umbilical.

## RESUMEN

*La constricción del cordón umbilical (CCU) es una condición infrecuente que no está bien descrita en la literatura, a pesar de ser una importante etiología observada en mortinatos. El objetivo de este estudio fue verificar la ocurrencia de CCU como causa de muerte fetal y las características patológicas asociadas. Para ello, se llevó a cabo un estudio retrospectivo transversal con informaciones de la base de datos de un Instituto de Patología, en Brasil, de 1995 hasta 2017. Los resultados fueron: 1.359 muertes de embriones/fetos, de las cuales 69 (5,07%) se debieron a CCU; 60,9% eran del sexo masculino y 39,1%, del femenino. El promedio de edad de las mujeres embarazadas fue de 27,5 años; desviación estándar de  $\pm 7,2$  años. La mayoría de las muertes ocurrió en el segundo trimestre (76,5%), seguido del primero (14,7%) y del tercero (8,8%). Entre el total de casos de CCU observados, 87% tuvieron sólo una constricción; 11%, dos; y 1%, tres o más. La presencia de malformaciones congénitas fue encontrada en 20,2% de las necropsias; la identificación de sufrimiento fetal crónico fue reportada en 71% de los informes; y características de vasculopatía obstructiva en el análisis de microscopía, en 17% de los casos. Con respecto a las características anatomopatológicas entre los sexos masculino y femenino, no se encontró ninguna diferencia significativa ( $p > 0,05$ ) correlacionando edad gestacional de los fetos/embriones, peso o malformaciones congénitas. La CCU es una condición rara de muerte fetal asociada a bajo peso fetal y restricción de crecimiento. Nuestra investigación sugiere una posible relación entre la CCU y la vasculopatía oclerativa.*

*Palabras clave: muerte fetal; sufrimiento fetal; cordón umbilical.*

## INTRODUCTION

The gestational process is associated with significant uterine and systemic hemodynamic changes, to cope with the metabolic demands of both mother and developing fetus. Although the female body keeps a dynamic balance by compensatory mechanisms, the boundaries between normality and disease are ill-defined, and their unbalance represents high risks of maternal-fetal morbidity and mortality<sup>(1-3)</sup>.

The umbilical cord allows the placenta-fetus communication, playing an important role in immunological surveillance and maternal tolerance to the fetus. In obstetrics, the umbilical cord provides valuable information about pregnancy evolution. Thus, any alteration could cause damage in fetal development, anomalies, perinatal complications or even intrauterine fetal death. For example, when umbilical cord constriction (UCC) occurs near the fetus abdominal wall it causes fetal death<sup>(4-7)</sup>.

The UCC is an infrequent and not well described condition and still has no formally accepted etiology in the literature. Nevertheless, its recognition is easy and based on macroscopic identification<sup>(1, 8-10)</sup>. Some studies have reported a prevalence of 10%-20% of fetal deaths related to UCC. Umbilical cord stenosis may also be present, but is generally associated with other anomalies such as torsion or excessive length of the cord<sup>(2, 8, 11)</sup>.

The UCC has as a pathological feature that decreases Wharton's jelly (a connective tissue matrix responsible for protecting the

umbilical vessels), what predisposes to torsions, edema, fibrosis and thrombosis. Therefore, there is a decrease in fetal blood flow leading to fetal distress and death<sup>(12, 13)</sup>.

This anomaly has traditionally been considered sporadic, which implied a very low risk of recurrence in subsequent pregnancies. However, some studies showed consecutive abortions due to umbilical stenosis, raising the question of the presence of a genetic component<sup>(14, 15-17)</sup>.

The present study aimed to verify the occurrence of UCC as a cause of fetal death and its etiopathological characteristics.

## METHODS

A retrospective cross-sectional study using the database of the Pathology Institute of Passo Fundo (IPPF). The IPPF is located in the north of the state of Rio Grande do Sul, Brazil. The database involved all the fetal death occurrences (1,359) from 1995 to 2017, from which only cases of umbilical cord constriction were elected, amounting to 69 cases (5.07%).

The variables analyzed in the study were maternal age, gestational age, placental and fetal/embryo weight, presence of a single umbilical artery, umbilical cord measurements, total fetal/embryo length, sex, presence or absence of chronic fetal distress, congenital malformations, circular cord and obstructive vasculopathy of villi vessels.

Statistical analysis was performed using GraphPad Prism 6 statistical software and Microsoft Excel 2010. Statistical comparisons between the years were made with the Student's *t* test for parametric variables and Mann-Whitney test for non-parametric variables. Values of *p* < 0.05 were considered significant.

The study was approved by the Research Ethics Committee of Universidade de Passo Fundo, under number 04477218.1.0000.5342.

## RESULTS

Among the total of 1,359 fetal deaths, only 69 cases were caused by UCC. The average maternal age was 27.5 years ± 7.2 years of standard deviation (SD). No multiple cases happened to the same woman. As regards the pregnancy period, most cases happened in the second trimester (76.5%), followed by first (14.7%) and third (8,8%) trimesters (**Figure**).

The placenta characteristics were: average weight of 116 g (SD ± 76), umbilical cord length of 20.9 cm (SD ± 10.9) and thickness of 0.87 cm (SD ± 0.37). The difference between normal cord thickness and the caliber in the stenosis area was 77%, decreased at the constriction surrounding. Only 7% of the cases presented a single umbilical artery. One constriction was found in 87%, two in 11%, and three or more constrictions in just 1% of all cases (**Table 1**).

The average embryo/fetus weight was 235 g [confidence interval (CI) 95%, 178-285], with total length of 19.65 cm (SD ± 6.5); 60.9% were males and 39.1% females. Presence of congenital malformations was described in 20.2% of necropsies; many of those

were synchronous in the same individual. The most prevalent malformation occurred in the lower limbs (8.6%): half of them affected the embryos feet. Other malformations included: single umbilical artery (7%), colonic rotation (4.3%), and renal agenesis (4.3%). Identification of chronic fetus distress was reported in 71% of cases, nuchal cord in 10%, and characteristics of obstructive vasculopathy in microscopy analysis in 17% (**Table 2**).

Concerning the anatomopathological characteristics between male and female fetuses, no significance was found correlating gestational age, birth weight or congenital malformations.

**TABLE 1** – Description of the anatomopathological characteristics of the placenta and umbilical cord

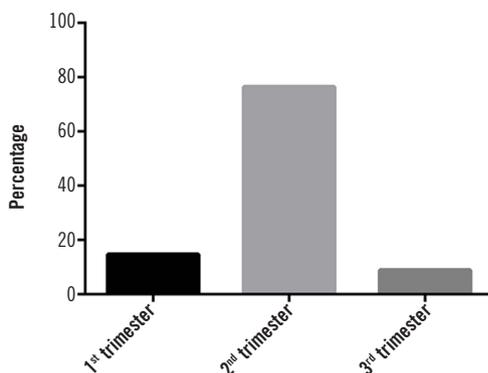
| Placenta                       |         | SD      |
|--------------------------------|---------|---------|
| Weight of placenta             | 116 g   | ± 76.01 |
| Umbilical cord length          | 20.9 cm | ± 10.9  |
| Thickness                      | 0.87 cm | ± 0.37  |
| <b>Single umbilical artery</b> |         |         |
| Yes                            | 7%      |         |
| No                             | 93%     |         |
| <b>Number of constrictions</b> |         |         |
| One                            | 87%     |         |
| Two                            | 11%     |         |
| Three                          | 1%      |         |

*SD: standard deviation.*

**TABLE 2** – Description of the anatomopathological characteristics of embryos/fetuses

| Embryo/fetus                             |          | SD    |
|--|----------|-------|
| Weight                                   | 235 g    | ± 23  |
| Length                                   | 19.65 cm | ± 6.5 |
| <b>Sex</b>                               |          |       |
| Male                                     | 60.9%    |       |
| Female                                   | 39.1%    |       |
| <b>Identified chronic fetal distress</b> | 71%      |       |
| <b>Congenital malformations</b>          |          |       |
| <b>Present</b>                           | 20.2%    |       |
| Malformations, lower limb                | 8.6%     |       |
| Single umbilical artery                  | 7%       |       |
| Renal agenesis                           | 4.3%     |       |
| Colonic rotation                         | 4.3%     |       |
| Others                                   | 17%      |       |
| <b>Absent</b>                            | 79.8%    |       |
| <b>Umbilical cord circular</b>           | 10%      |       |
| <b>Obstructive vasculopathy</b>          |          |       |
| <b>Present</b>                           | 17%      |       |
| <b>Absent</b>                            | 83%      |       |

*SD: standard deviation.*



**FIGURE** – Visual demonstration of the percentages of confirmed cases of umbilical cord constrictions during the trimesters of pregnancy

## DISCUSSION

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Maternal age is usually associated with several outcomes throughout pregnancy. However, as shown in the present study, there was no correlation between maternal age and UCC<sup>(9, 18, 19)</sup>.

Corroborating the literature, the study showed an increase in the probability of new stenosis in a subsequent gestation in cases of pregnancies previously diagnosed with UCC. Nevertheless, the absence of this recurrence is still questioned, bringing up doubts about the involvement of a genetic component that may allow recidivism<sup>(9, 12, 13, 15)</sup>. Many cases of UCC have been reported, but only few studies aimed to investigate the possibility of an associated genetic component increasing the risk of recurrence in further pregnancies. Amongst them, the largest accomplished study concluded that there is a minimal or null genetic component in UCC (1.5%) in pregnancies following previous malformation<sup>(9)</sup>.

Regarding the period of involvement in pregnancy, the highest rate of cord stenosis diagnosis occurs in the second trimester, followed by the first and third trimesters<sup>(20, 21)</sup>, matching the data of the present study.

According to the literature, the presence of a single umbilical artery is not related to an increase in fetal mortality<sup>(22)</sup>, confirming the findings of our study, since only 7% of the 69 cases presented such abnormality. Concerning placenta weight, umbilical cord length and number of constrictions, the shortage of data in the literature prevents comparison to the findings of this study. Nevertheless, this paper is the first to show significant data about placenta weight, umbilical cord length and number of constrictions, and allows further correlations to be investigated.

Low fetal weight and low total length observed in the anatomopathological reports of the present study may indicate UCC as one of the etiologies of intrauterine growth restriction (IUGR)<sup>(19, 20, 23)</sup>.

IUGR is identified when fetal weight is ranked below the 10<sup>th</sup> percentile for gestational age, being a common clinical problem associated with increased perinatal morbidity and mortality.

Another finding that corroborates this hypothesis is the chronic fetal distress, identified in 71% of sampled fetuses, a finding often associated with fetal-placental alterations in IUGR patients. Besides that, the presence of congenital malformations in 20.2% of samples validates IUGR as a possible etiology, since there is an association between fetal malformations and IUGR<sup>(23)</sup>.

Our study suggested a prevalence of cord constriction in males. This finding contradicts previous IUGR studies that indicated a higher prevalence in females<sup>(18)</sup>. However, it is important to highlight that there is no distinction concerning gender among the possible etiologies of growth restriction in the literature. This may have been the reason why cord stenosis prevalence had such discrepancies with previously existing data.

Another fact that may corroborate a possible association between the conditions is that fetuses with IUGR, specifically after the second trimester, could have their growth restricted by thrombophilia, although studies are still controversial<sup>(21, 24)</sup>. Furthermore, the presence of obliterative vasculopathy in 17% of the samples may indicate a possible association between pathologies as thrombophilia and UCC, since obstructive vasculopathy is a common finding in histopathological reports of patients with thrombophilia<sup>(24)</sup>. However, further studies are needed to elucidate the possible association between these factors.

## CONCLUSION

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UCC was a cause of fetal death in 5% of cases of the present study. A link with congenital malformations was established in 20% of the sample, fetal distress in 71%, and obliterative vasculopathy in 17%. The obliterative vasculopathy finding, reported in thrombophilia, suggests a possible correlation between these two conditions.

## CONFLICTS OF INTEREST

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All authors deny any conflict of interest.

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#### CORRESPONDING AUTHOR

Victor Antônio Kuiava  0000-0002-0332-4604  
e-mail: victorkuiava@gmail.com



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