ABSTRACT

Introduction: True knot of the umbilical cord is characterized by a cord loop with increased tension and hence higher risk for obstetric and neonatal outcome intervention. It is a finding observed in 1-2% of births.

Aim: Review the etiology, physiopathogeny, diagnosis and prognosis of true knot of the umbilical cord.

Methodology: We carried out a review searching for scientific articles present in the electronic database PubMed, using the descriptors “true knot”, “umbilical cord”, “Doppler sonography” and “prenatal diagnosis”. Articles published until 2013 were included in the review.

Discussion: True knot of the umbilical cord is a relatively common finding at birth. However, its diagnosis in uterus is still quite rare. Several factors have been related to its etiology, including the size of the umbilical cord. Its appearance occurs mostly between 9 and 28 weeks of gestation, in the fetal period of greater mobility. The major part of the true knot of the umbilical cord is not associated to an increased risk of obstetric intervention and neonatal outcomes because most are loose. However, the true knots can tighten during pregnancy due to fetal movement or during labor, leading to reduced blood flow and consequent fetal asphyxia and death. As a result, the close monitoring of pregnancy in cases of true knot of umbilical cord is required. The prenatal diagnosis of a true knot of the umbilical cord can be a challenge. Sonographic complementary techniques, including color Doppler and Dopplervelocimetry can improve the detection rate and help to differentiate true from false knots. And this has important implications for the management and prognosis of pregnancy, besides consequences for the fetus and newborn.

Keywords: Umbilical Cord; Fetus; Ultrasonography, Prenatal; Prenatal Care; Prognosis.

Abbreviations: Not applicable.
1. INTRODUCTION

The true knot of the umbilical cord is characterized by a cord loop with increased tension and hence higher risk for obstetric and neonatal outcome intervention. It is a frequent finding at delivery, being described worldwide in 1-2% of births. However, the diagnosis of true knot of the umbilical cord usually remains undiscovered during the prenatal period [1-6]. The main concern, however, is the possibility of the knot tightening during fetal movements or descent of the neonate through the pelvis in vaginal delivery, resulting in decreased umbilical blood flow, fetal asphyxia and perinatal death. As a result, cautious and careful monitoring of pregnancy with true knot of the umbilical cord is mandatory [6,7]. Recently, the diagnosis of a true knot cord can be performed in the intrauterine phase due to the improvement of ultrasonographic methods [8,9]. Nevertheless, in most cases, the identification of the true knot of the umbilical cord is not seen due to various reasons. The main limitations include the difficulty in examining the entire length of the umbilical cord in the womb, the spatial configuration of the umbilical cord in the amniotic cavity and the visualization of the characteristics of the knot in two dimensions [10].

The aim of this study was to review the etiology, pathogenesis and diagnosis of true knot of the umbilical cord, including features that aid in its identification by prenatal ultrasound, and their consequences for the fetus and newborn. For this purpose, we conducted a review in the PubMed, SciELO and LILACS databases, using descriptors like "true knot", "umbilical cord", "Doppler sonography" and "prenatal diagnosis". In this review, articles published in the databases up to 2013 were included. No studies developed in Brazil related to true knot of the umbilical cord were found. Throughout Latin America, only 3 studies were found, all of them developed in Chile.

2. CLASSIFICATION AND EPIDEMIOLOGY

Umbilical cord knots in general can be classified as true or loose. The true knots are identified with increased tension and thus with a higher risk for obstetric and neonatal outcome intervention. The loose knots can tighten during pregnancy due to fetal movements, or during labor, leading to decreased flow in the cord blood [11]. The true knot of the umbilical cord has a relatively high incidence at birth [6,12]. It has been usually observed worldwide in 1 to 2% of all births [2]. In turn, their incidence in prenatal care is small, but is growing due to its greater identification [13]. The true knot of the umbilical cord represents approximately 4% of all
complications of the umbilical cord, but, in contrast to other conditions as nuchal coils and cords around the body, it is directly related to fetal death [2].

3. ETIOLOGY

True knots of the umbilical cord arise from rotating movement of the fetus in uterus, mostly in the 1st and 2nd trimester of pregnancy (especially between the ninth and twenty-eighth weeks of gestation). This hypothesis is supported by the observation that the frequency of the knot cord in aborted fetuses is equal to that seen at birth [2,3,14]. Moreover, the length of the cord does not increase significantly after 28 weeks of pregnancy [15]. According Hyrtl, the period of formation of a knot cord could be calculated by its location. However, this assumption has never been proven [16]. There is evidence that the true cord knot is associated with some maternal conditions, such as multiparity. Nevertheless, there are not many studies that support this theory [2,3,7]. Other maternal factors associated to true knot of the umbilical cord include: advanced maternal age, history of miscarriages, obesity, anemia and chronic hypertension, gestational diabetes mellitus, prolonged pregnancy and polyhydramnios [2,5,6,21] (Table 1).

Regarding fetal characteristics, umbilical cord knots are more observed in male than female fetuses [3,7], but this is probably due to the fact that the cords are longer in the first [15]. In addition, other studies have shown that the true knot of umbilical cord is associated to longer strands [2,7,15,17,18]. In newborns at term, the mean length of the cord is 55 cm, and umbilical cords greater than 60-80 cm are considered longer [19,20]. Other factors associated to true knot of umbilical cord include fetal size (small fetus), polyhydramnios and monoamniotic twin pregnancy [2,3,5,6,21-23](Table 1). Blickstein et al. (1987) suggest that the location of the true knot of umbilical cord has no correlation with other variables, and that their occurrence near the middle cord suggests that it is formed by random [7].

4. PATHOPHYSIOLOGY

The pathophysiology of the formation of true knot of umbilical cord remains somewhat unclear [7]. Usually the true knot of umbilical cord is presented as an unexpected discovery at delivery and there is no increased risk to obstetric intervention or worsening in neonatal outcomes because most of them are loose [12]. On the other hand, the loose knot can tighten during pregnancy due to fetal movements or during delivery, leading to
decreased blood flow through umbilical cord and consequent fetal distress, asphyxia and death [5-7,11]. This would happen especially after rigorous fetal movements.

According to Feldman (1920), blood pressure in the cord ranges from 39.3 to 83.7 mmHg, while venous pressure is approximately 16 mmHg. When tight, the true knot of umbilical cord can block both venous and arterial flows. On the other hand, possibly the loose knot is of minor importance as long as they remain loose [24].

Hemodynamic alterations of true knot of umbilical cord do not affect primarily placental unit. As known, there is a progressive pattern of hemodynamic changes: the first phase is characterized by an abnormal Doppler of uterine artery with normal umbilical arteries and cerebral circulation, in an adjustment phase to hypoxemia. In the second phase, we found abnormal waves in fetal arterial networks with absent diastolic flow and, in the last step, reversed diastolic flow in many fetal arterial vessels [12]. Maher and Conti (1996) noted in their study that the presence of true knot of the umbilical cord does not alter the incidence of acidemia in umbilical artery or in umbilical cord blood gas analysis [25]. True knot of the umbilical cord has different pathological findings, which may include: 1) compression, 2) loss of Wharton’s jelly, or 3) persistence of structural changes after untied [26]. When tight, true knot of umbilical cord can also demonstrate vascular congestion and edema distal to the knot site [2].

In cords with a knot, the cord diameter and tension may be of importance to determine the size and fetal well-being [27,28]. However, since the diameter of the cord is not accurate (due to large variations in the Wharton’s jelly), this assumption should be further confirmed in experimental models [7].

5. PRENATAL DIAGNOSIS

Prenatal diagnosis of true knot of the umbilical cord is infrequently reported and is often an incidental finding [8,9,11,29]. Its prenatal characteristics may not be apparent. The visualization of the knot is easily lost in screening through prenatal ultrasound in the second and third trimesters [10]. Although early observations suggest that the knot of umbilical cord is formed during early pregnancy, when the fetus is very mobile and there is enough amniotic fluid surrounding him. Recent observations claim that the majority of true knot of umbilical cord is formed during delivery [7,30]. Failure to diagnose can be explained by several factors. The
interpretation by two-dimensional ultrasound images of a complex three-dimensional object, such as a knot of the umbilical cord, is extremely difficult [10] (Fig. 1).

Moreover, the interposition of fetal parts and reduction of amniotic fluid could make the diagnosis a challenge. For this reason, the true knot of umbilical cord is an obstetric complication with usually postnatal diagnosis. The complementary sonographic techniques, including color Doppler, Doppler velocimetry, and four-dimensional ultrasound may improve the detection rate of true knot and differentiate it from false or loose knot [6,11] (Fig. 2).
Three-dimensional ultrasound is also used as a complementary method to better anatomical and functional characterization, allowing the diagnosis to be performed with greater confidence. Thus, this method is considered most sensitive.

Many studies propose guidelines for ultrasound identification of true knot of cord, in order to recognize them early [13,31]. Sonographic characteristics, such as the “four leaf clover” and “hanging noose” (patterns resulting from umbilical cord torsion leading respectively to a knot with aspect of a four leaf clover or hanging noose) [8,9,11] or an unusual pattern seen on color flow [4] are strongly related to the presence of true knot of umbilical cord [3,10]. The persistence of the standard image of “four leaf clover” is useful to establish a definitive diagnosis [10,32].

Doppler ultrasound shows a hemodynamic pattern characterized by a change in the profile of the wave form in the fetal venous network with normal values for flow in uterine and umbilical arteries impedance. This normal profile of the umbilical arteries tends to remain unchanged until the last stage of hemodynamic decompensation, whereas the profile of the uterine arteries remained normal until delivery. Thus, it is important to be careful in the evaluation of fetal umbilical cord when this hemodynamic pattern is observed [15].
Some true knot of umbilical cord can be demonstrated indirectly through fetal supraventricular tachycardia and a standard cardiotocography associated to true knot of umbilical cord. The presence of a true knot of umbilical cord should always be suspected in the presence of intrauterine growth restriction, when the fetal venous network show changes before the arterial network, and after exclusion of other possible reasons for the growth restriction [9,33-35] (Fig. 3).

**Fig. 3.**

*Postnatal aspect of a true knot of the umbilical cord verified soon after birth.*

If it was possible to early diagnose the true knot of umbilical cord and follow its clinical course, we would better understand how to monitor a pregnancy in which this occurs. Thus, the potential complications could be early prevented or recognized with monitoring by ultrasound techniques. Therefore, close monitoring of the pregnancy is mandatory in cases of true knot of umbilical cord, mainly through the Doppler velocimetry of the umbilical artery. Continuous cardiotocography during labor is also recommended. Four-dimensional ultrasound can help in the differential diagnosis of a suspected true knot of
umbilical cord. Besides, Doppler flowmetry is a useful tool to diagnosis an umbilical cord knot that can tighten with active fetal movements during the course of pregnancy [11].

6. CONSEQUENCES FOR THE FETUS AND NEWBORN

Baudelocque (1789) noted that newborns were healthy despite the presence of two to three umbilical cord knots [36]. Gardien (1813) also found that very long umbilical cords do not sufficiently interfere with the fetal circulation even if they have true knots [37]. The true knot of umbilical cord rarely causes problems before the birth. However, it can cause problems during delivery, and even lead to fetal death. This happens because the loose knot may tighten during labor, leading to decreased umbilical blood flow and consequent fetal distress and asphyxia [38].

The importance of true knot of the umbilical cord is considered by many authors as being insignificant [36,39,40], or even beneficial, i.e., some studies show that survival rates found in babies with true knot of umbilical cord were higher than in those without it [2,41]. However, in most of these series, the real frequency of true knot of umbilical cord is poorly documented [42]. Although the majority of true knot of the umbilical cord does not present clinical significance, mainly because it is loose, there is an association between this finding and fetal intrauterine death [2]. It is known that the true knot of the umbilical cord is associated to a four to ten times higher risk of fetal death [5,6,12,43]. In addition, 5% of all stillbirths are associated to true knot of umbilical cord [4]. It can lead to serious complications for the fetus due to possible changes in intrauterine fetal circulation with subsequent intrauterine growth restriction or fetal death [15]. The risk of fetal distress is 7%. Prenatal diagnosis of true knot of umbilical cord is also associated to serious perinatal complications such as meconium-stained amniotic fluid [5].

Therefore, a true knot of umbilical cord is a potential risk for the fetus. According to Spellacy et al. (1966), thirteen true knots of umbilical cord were found among 967 births studied (1.4%). Eight of them presented no clinical importance. Four patients showed signs of fetal distress during labor, necessitating cesarean. In addition, one intrauterine fetal death occurred at 19 weeks gestation due to a true knot of umbilical cord [2].

Studies by Browne (1925) revealed that even a loose knot could compromise the perfusion of the umbilical vein [27]. Moreover, Chasnoff and Fletcher (1977) contradicted Browne's results and observed that a loose knot did not affect the venous perfusion. However, in the presence of a tight knot, if the diameter of the cord
is smaller, greater is the pressure required to overcome the knot, because more pressure is needed to perfuse through a specific obstruction [28]. It is important to note that this study was performed in artificial normal cord knots and, as Benirschke said, the cord in vivo would behave differently. Another factor not considered by these investigators was the length of the umbilical cord and the location of the knot [44]. Previous studies showed no effect of true knot of the umbilical cord on the Apgar score. Maher and Conti (1996) found that the fetus umbilical vein's pH at birth was normal in cases of true knot of umbilical cord [25]. Neonates with true knot of umbilical cord probably have temporary distress during delivery, and usually recover from this injury soon after birth. The probable cause for the transitional distress would be the knot tight in the second stage of labor.

As mentioned in the etiology section, some authors have shown a significant difference in the frequency of true knot of the umbilical cord between the genders, which are more common in male fetuses. It is noteworthy that female fetus with a true knot of umbilical cord would have a higher risk of suffering. However, the reason for this is not clear yet [7].

7. CONCLUSIONS

Intrauterine diagnosis of true knot of umbilical cord can be a challenge. Although the true knot cord is relatively common at birth, the report of its prenatal diagnosis is infrequent. The presence of true knot of umbilical cord should always be suspected in the presence of intrauterine growth restriction, especially of unknown etiology. Sonographic findings such "four leaf clover" and "hanging noose" signals, or an unusual pattern seen on Doppler color flow, may assist in its identification.

Knots of the umbilical cord usually are not associated to an increased risk of obstetric intervention and neonatal outcomes because most of them are loose. However, the loose knot may tighten during pregnancy due to fetal movements or during labor, leading to decreased umbilical blood flow and consequent fetal distress, asphyxia and death. As a result, cautious and careful monitoring of pregnancy cases of true knot of umbilical cord is recommended. Monitoring of the pregnancy through Doppler velocimetry, especially of the umbilical artery, is mandatory and it is considered the main evaluation form. It may help to identify umbilical cord knots that may tight during the
course of pregnancy, leading do hypoperfusion and hypoxemia. During the labour, continuous 
cardiotocography is indicated.
Thus, the monitoring is essential for the proper management and, consequently, success in the course of 
pregnancy and labour.

8. CONSENT
Not applicable.

9. ETHICAL APPROVAL
Not applicable.

10. COMPETING INTERESTS
Authors have declared that no competing interests exist.

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