International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

Retained Placenta in Third Stage of Labour: Epidemiology, Risk factors and Management

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Abstract:

Retained placenta is a significant obstetric complication characterized by failure of placental expulsion during the third stage of labor. It remains a major contributor to postpartum hemorrhage and maternal morbidity worldwide. The condition may result from failure of placental separation or incomplete expulsion after separation. Its incidence ranges from 0.1% to 3% of deliveries, with higher risk observed in cases of preterm delivery, prior uterine surgery, multiparity, and prolonged labor. The underlying mechanism is closely related to impaired retro-placental myometrial contraction, which is essential for placental detachment. Early recognition and appropriate management are critical to prevent severe complications such as hemorrhage and infection.

Keywords: Retained placenta, Third stage of labor, Postpartum hemorrhage, Manual removal, Risk factors, Myometrial contraction.

Introduction:

Retained placenta is a condition in which all or part of the placenta or membranes remain in the uterus during the third stage of labour. Retained placenta can be broadly divided into failed separation of the placenta from the uterine lining and placenta separated from the uterine lining but retained within the uterus. A retained placenta is commonly a cause of postpartum hemorrhage, both primary and secondary. It is generally defined as a placenta that has not undergone placental expulsion within 30 minutes of the baby's birth where the third stage of labor has been managed actively **(Granfors et al., 2020)**.

Epidemiology:

Estimates of retained placenta put the incidence at between 0.1% and 3%. Prospective investigations of retained placenta confirm these estimates, with one study of >45,000 patients showing that overall for all gestational ages, retained placenta happened in about 3% of deliveries, with gestational ages of <26 weeks and >37 weeks having a significantly increased risk of retained placenta requiring manual removal. Generally, incidence seems to be higher in developed countries where practices tend toward earlier manual removal of the placenta in the third stage of labor **(Endler et al., 2018)**.

Risk factors:

Established risk factors include prior retained placenta, preterm delivery, prior uterine surgery, previous pregnancy termination, miscarriage or curettage, grand multiparity (greater than five prior deliveries), and congenital uterine anomalies (often unrecognized prior to delivery) **(Luiza et al., 2015)**.

Prolonged oxytocin use could be a potentially modifiable risk factor for retained placenta, with one study reporting that oxytocin use for over 195 mins increased the odds ratio of the retained placenta by 2.0, and oxytocin use over 415 mins increased the odds ratio by 6.5. It is less clear whether oxytocin is directly involved in placental retention, or if the association is mediated by uterine atony or infection due to prolonged labor **(Aziz et al., 2016)**.

Importance of the retro-placental myometrium:

Retro-placental myometrial contraction is mandatory in order to produce shearing forces upon the interface between the placenta and myometrium and lead to its detachment. They divided the third stage into 4 phases according to the ultrasound appearances. In the latent phase, which immediately follows delivery of the fetus, all the myometrium contracts except for that behind the placenta which remains relaxed. In the contraction phase, the retro-placental myometrium contracts leading to the detachment phase where the placenta is sheared away from the decidua. In the expulsion phase, the placenta is expelled from the uterus by uterine contraction. Contractions occurring prior to delivery are insufficient to cause placental detachment as in the presence of the fetus, the myometrium is unable to achieve the necessary strain for detachment **(Deyer et al., 2000)**.

The blood flow through the arcuate and radial arteries is reduced during the latent phase and then ceases completely at the onset of the contraction phase. This occlusion occurs as a result of the myometrial 'physiological ligature'. The timing of this neat mechanism ensures that maternal blood flow to the placenta ceases prior to placental detachment. In this way, the only maternal blood lost is that from the intervillous spaces **(Krapp et al., 2000)**.

The duration of the third stage of labour is dependents on the length of the latent phase and a prolonged third stage is due to contractile failure in the retro-placental area. In the 5 cases of retained placenta in which they conducted serial ultrasonographic myometrial thickness measurements, they found a universal failure of retroplacental contraction. In these women, blood flow continues through the myometrium to the placenta irrespective of whether the cause is placenta accreta or prolongation of the latent phase. This provides a scientific explanation for the increased rates of hemorrhage during manual removal of placenta when compared with spontaneous delivery (**Krapp et al., 2000)**.

The placenta has been known for many years to be an important determinant of the onset of labour and it is likely that this occurs as a result of the loss of an inhibitory factor of placental origin. The association of retained placenta with both preterm delivery and the need for induction, suggests that it may be the same factor which is responsible for both. The role of the feto-placental unit in the regulation of uterine contractility is complex with a finely controlled balance between stimulatory and inhibitory factors **(Weeks, 2001)**.

This balance can be likened to a set of scales with inhibitory and stimulatory factors on either side. Loss of inhibition may result in the onset of labour (as with the administration of antiprogesterones) as may more in the stimulatory factors (as with the administration of exogenous oxytocin or prostaglandins). It could be hypothesized that if the pro-contractile stimuli were strong enough, then successful labour could occur even in the presence of persisting, localized placental inhibition. In this situation there would be a high risk of retained placenta due to the strong persistent placental inhibition of retro-placental myometrial contractility **(Hofmeyr and Gulmezoglu, 2000)**.

There are a number of candidates for the identity of this localized inhibitor. The placenta has a role in inhibiting myometrial contractions through the production of progesterone and possibly nitric oxide (NO). Progesterone is an important inhibitor of myometrial contractility in many animals, but the situation in humans is yet to be fully clarified. The anti-progesterone mifepristone is a powerful sensitizer of the myometrium to exogenous prostaglandins, and it is effective for induction of human labour in all trimesters of pregnancy. Attempts to identify the mechanism for this, however, have so far been unsuccessful as, unlike in animal models, a reduction in serum progesterone is not seen prior to labour **(Hofmeyr and Gulmezoglu, 2000)**.

Nitric oxide is also a powerful smooth muscle relaxant which is produced in large quantities by nitric oxide synthase (NOS) in the placenta. As it is rapidly oxidized following its production, its effect is very localized **(Ledingham et al., 2000)**.

The final implication of the discovery that the persistent latent phase is a cause of retained placenta is that contraction of this area would resolve the problem of dysfunctional labour and retained placenta. This could be either achieved through removing the inhibitor (e.g. by treatment with an anti-progesterone) or by stimulation

with oxytocics. Umbilical vein oxytocin has been suggested as a way of delivering a localized stimulus to the retro-placental myometrium **(Weeks, 2001)**.

Diagnosis:

Risks of retained placenta include hemorrhage and infection. After the placenta is delivered, the uterus should contract down to close off all the blood vessels inside the uterus. If the placenta only partially separates, the uterus cannot contract properly, so the blood vessels inside will continue to bleed. A retained placenta thereby leads to hemorrhage **(Duffy, 2014)**.

Retained placenta is clinically diagnosed when the placenta fails to spontaneously separate during the third stage of labor, with or without active management, or in the setting of severe bleeding in the absence of placental delivery. The first diagnostic criterion requires a time cutoff, though there is no uniform consensus as to timing for diagnosis of retained placenta in the third stage in the absence of postpartum hemorrhage. Selection of a clinical time definition can be based either on a population curve of observed spontaneous placental delivery times or on a time at which morbidity significantly increases. Thirty minutes have been used as a loose guideline, which comes by **Combs and Laros (1991)** who found that the third stage had a log-normal distribution, with a mean length of 6.8 minutes, with only 3.3% of deliveries having greater than 30 minutes third stage.

This timing has been supported by other studies as well. Interestingly, the authors calculated that the incidence of PPH, transfusion, and dilation and curettage remained constant during this period, increasing only after 30 minutes and plateauing at 75 minutes for both manually and spontaneously delivered placentas. Because PPH incidence did not increase until after 30 minutes **(Chibueze et al., 2015)**.

However, this guidance is not uniformly supported. In a subsequent study by **Deneux-Tharaux**, surveys from 14 European countries exhibited wide variations in wait time prior to manual placental removal, largely by country but also by the hospital. In countries such as Finland and Denmark, obstetricians tended to wait 60 minutes or more prior to manual removal of the placenta, versus in countries such as Spain and France, where providers removed the placenta after 30 minutes. Practices also varied considerably depending on whether or not the patient in question had prior epidural anesthesia. National and worldwide guidelines similarly have no consensus on when to intervene on an undelivered placenta. For instance, the National Institute for Health and Clinical Excellence suggests a wait time of 30 minutes in the United Kingdom prior to manual removal of the placenta, while the World Health Organization guidelines propose a wait time of 60 minutes **(Deneux-Tharaux et al., 2009)**.

The most significant risk of waiting a prolonged amount of time before removing the placenta is postpartum hemorrhage. In 2005, Magann and colleagues undertook a prospective observational study in which all women delivering vaginally were assessed for PPH. Using receiver operating characteristic curves, the authors showed that 95% of normal placental delivery occurs within 18 minutes, and that a third stage of labor longer than 18 minutes was associated with a significant risk of PPH **(Magann et al., 2012)**.

At times the bulk of the placenta will deliver spontaneously or manually, but small portions or an accessory lobe may be retained. This may be suspected when the placenta appears fragmented after delivery or when there is ongoing heavy uterine bleeding. In this situation, the uterine cavity may be evaluated with manual exploration or with ultrasound. The utility of ultrasound in this situation has yet to be established, with a focal endometrial mass, particularly with Doppler flow, being the findings of interest **(Practice, 2017)**.

In one study of routine ultrasound immediately after vaginal delivery, the sensitivity for diagnosing retained placental fragments was only 44% with a positive predictive value (PPV) of 58% **(Carlan et al., 1997)**. **Durfee et al. (2005)** showed a 75–80% sensitivity of postpartum ultrasound, though the mean time for evaluation was 21 days postpartum, when less blood and decidua are expected to be seen. While immediate ultrasound's PPV will be higher when there is clinical suspicion of retained POCs, a negative ultrasound should not deter manual or suction curettage when there is a strong clinical suspicion, especially in the setting of hemorrhage.

Management of retained placenta:

After delivery of the infant and prior to diagnosis of retained placenta, active management is recommended to facilitate spontaneous placental separation, including oxytocin, controlled cord traction, and uterine massage. Drugs, such as intraumbilical or intravenous oxytocin, are often used in the management of placental retention. It is useful ensuring the bladder is empty. Controlled cord traction has been recommended as a second alternative after more than 30 minutes have passed after stimulation of uterine contractions, provided the uterus is contracted. These maneuvers have been shown to decrease the risk of postpartum hemorrhage, though it has not been shown that active management will prevent retained placenta **(Duffy, 2014)**.

Once diagnosed, the placenta is usually manually extracted from the uterus. Because this procedure is painful, adequate analgesia should be achieved via epidural, conscious sedation, or general anesthesia prior to an attempt at extraction **(Lee, 2019)**.

Once the patient is comfortable, she should be appropriately positioned in lithotomy. A conical drape, preferably one that is graduated and marked to allow for quantitative blood loss, should be placed under the patient's buttocks. The operator should make every attempt to wear gown and gloves and maintain sterilization, both for personal and for patient protection. The patient's bladder should be drained. The provider should then use one hand to follow the umbilical cord through the vagina and cervix until the placenta is palpated. If the placenta is separated but not expelled, such as in the case of uterine atony, the tissue can be firmly grasped and brought through the cervix. Uterotonic medications, such as oxytocin, methylergonovine, carboprost, or other prostaglandins, should be given to facilitate contraction once the placenta is removed **(Hamerlynck et al., 2016)**.

Nitroglycerine (NTG) has been used to facilitate manual extraction by relaxing uterine smooth muscle. This may be particularly helpful when the placenta is trapped behind a partially closed cervix, though the use of NTG alone does not appear to facilitate spontaneous placental expulsion. It can be given as a 1 mg sublingual dose, or as sequential 50 mcg intravenous boluses, up to a total dose of 200 mcg. The medication can produce hypotension and tachycardia, which can confound assessments of maternal stability. Once the placenta is delivered, uterotonics should be promptly given to restore uterine tone and avoid significant atony **(Bjurström et al., 2018)**.

If the placenta remains attached to the uterine decidua, an attempt should be made to separate it manually. Using one hand to provide counter pressure on the fundus through the maternal abdomen, the provider should then use the internal hand to manually create a cleavage plane between the placenta with the attached decidua and the myometrium. Once separated, the placenta can be removed as described above. If a separation plane cannot be created behind all or part of the placenta, the provider should suspect a morbidly adherent placenta (MAP) and prepare for potential hemorrhage **(Carusi, 2018)**.

If placental removal is refractory or only partially successful (ie the placenta or parts of the placenta remain in the uterus), or if bleeding persists despite placental delivery, often the next step is surgical management with curettage **(Kongwattanakul et al., 2020)**.

This may be best achieved in an operating room, with optimal access to surgical equipment, analgesia, and patient resuscitation aids, if needed. Suction curettage is generally used, though a sharp curette may be needed to facilitate a separation plane. Access to uterine tamponade supplies with either a large intrauterine balloon or surgical packs should be immediately accessed in the event of hemorrhage. Cross-matched blood products should be made imminently available if placental separation is difficult or blood loss exceeds 1 L, and the care team should attend to uterotonic administration and attention to coagulopathy as the extraction is performed **(Roeca et al., 2017)**.

Due to the risk of endometritis, routine antibiotics are generally administered just before or shortly after manual removal of the placenta. Prophylaxis can parallel cesarean prophylaxis with a first-generation cephalosporin. Patients who are febrile at the time of extraction should be fully treated for chorioamnionitis with broad-spectrum antibiotics. **(Cahill et al., 2018)**.

Chibueze et al. (2015) attempted to summarize the literature on the efficacy of antibiotics for preventing adverse maternal outcomes related to manual placenta removal following vaginal birth. The authors reported on three retrospective cohort studies examining endometritis and puerperal fever after manual extraction for retained placenta. None of the three studies found evidence to suggest beneficial effects for routine antibiotic use in women undergoing intervention for retained placenta. The authors concluded that further research is required to adequately answer this question. Due to mixed data regarding prophylaxis, as well as the increasing risk of postpartum hemorrhage with prolonged third stage of labor, administration of antibiotics should not delay manual removal of retained placenta.

Occasionally, a portion of placental tissue may remain in the uterus, either knowingly or unbeknownst to the providers. This can present as abnormal bleeding days to weeks after delivery and should be suspected in the setting of a delayed postpartum hemorrhage. Recently, studies have examined the usefulness of hysteroscopic morcellation devices in aiding with retained placenta left in situ postpartum. In a series of case reports, Lee and colleagues reported a higher risk of complications with blind curettage compared to hysteroscopic morcellation. They additionally reported complete resection in 90% of hysteroscopic cases and reduction of both perforation and intrauterine adhesion risk **(Lee, 2019)**.

In another randomized control trial by **Hamerlynck et al. (2016)**, the authors randomized patients to undergo hysteroscopic resection of retained placenta with either hysteroscopic morcellation versus loop resection with rigid bipolar resectoscopes. These authors in comparison found that when comparing the two modalities, complete resection was comparatively high in both groups, and intrauterine adhesions were comparatively low. The one significant difference between the two groups was that the hysteroscopic group had significantly faster operative times. The ability to perform hysteroscopic removal depends on the amount of active bleeding, with suction curettage often needed when bleeding is heavy.

Ronsmans and Graham (2006) have examined alternative, nonsurgical, management for retained placenta, none of which have been successful. In 2006, 99 women in a large teaching hospital in the Netherlands with retained placenta (>60 mins after delivery) were given either 800 mcg misoprostol or placebo orally. The author's primary outcomes were number of manual removals of retained placenta and blood loss. The authors found that oral misoprostol reduced neither the need for manual removal nor the overall amount of blood loss. Both groups were observed for additional 45 mins after administration of misoprostol or placebo. While the authors found that 50% of remaining placentas at 60 mins delivered in the intervening 45 mins, it came at the expense of additional significant blood loss.

For a time, umbilical vein oxytocin was thought to be a promising alternative or adjunct to manual extraction of the placenta. A 2011 Cochrane Review summarized available data on the subject to assess the use of umbilical vein oxytocin either alone or in conjunction with intravenous oxytocin to reduce the need for manual removal of retained placenta. While inexpensive and easy to do, the authors found that all well-designed randomized control trials showed no significant effect of umbilical vein oxytocin on retained placenta **(Nardin et al., 2011)**.

Prevention:

Sulprostone is a potent stimulator of uterine smooth muscle contractions with high abortifacient activity. It is not licensed in the UK but has been shown to reduce the need for the manual removal of the placenta by 49% **(van Beekhuizen et al., 2006)**.

Complications:

- Retained placenta is, in itself, life-threatening because of its association with postpartum hemorrhage.
- Manual removal carries the risk of damage to the genital tract and of puerperal infection. It also increases the likelihood of bacterial contamination in the uterine cavity.**(Chongsomchai et al., 2006)**

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