MANAGEMENT OF UTERINE ATONY

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1,2,3MBChB DGO.

INTRODUCTION

It is estimated about 529,000 mothers die every year (World Health Organisation [WHO] 2005). Postpartum haemorrhage (PPH), a life-threatening condition, remains the major cause of maternal mortality worldwide (Pahlavan et al., 2001). Majority of these mortalities are from Asia (48%) and Africa (47.5%) with only the minority (less than 1%) from developed countries.(Ramanathan & Arulkumaran, 2006) In., the Confidential Enquiry into Maternal Deaths (CEMD) from 1991 to 2005 revealed that PPH attributed 13-27% of all reported deaths(Division of Family Health Development, Ministry of Health, 1994; Division of Family Health Development, Ministry of Health, 1996; Division of Family Health Development, Ministry of Health, 2000; Division of Family Health Development, Ministry of Health, 2005).

Although PPH is no longer the leading cause of maternal mortality in the developed countries, it still remains as one of the most important causes of maternal morbidity.

Recently, two reports from Canada and United States (Joseph et al. 2007; Callaghan, Kuklina & Berg 2010) reported a 23-26% increase in the rate of PPH. Despite reports of an increasing rate, maternal mortality in these two countries remained low indicating the effective management of PPH. Nevertheless, in developing countries, PPH related maternal mortality remains a serious concern due to limited health care facilities, underdeveloped management strategies and deprivation of trained health care personnel.

Disastrously massive PPH can lead to coagulopathy, pituitary ischaemia, cardiovascular insufficiency, and multi-organ failure. It is also associated with an increased need for blood and blood products transfusion, intensive care admission, peri-partum hysterectomy and its
related intra- or post-operative complications. Even in a milder form of haemorrhage, anaemia itself would interfere with bonding and care for the newborn (Devine, 2009).

Uterine atony is identified as the main cause of PPH accounting for about 90% in most reports associated mortality between 1994-2005 (Division of Family Health Development, Ministry of Health, 1994; Division of Family Health Development, Ministry of Health, 1996; Division of Family Health Development, Ministry of Health, 2000; Division of Family Health Development, Ministry of Health, 2005).

Many complications can occur in the postpartum period, the period that extends from delivery to the 42nd day after delivery. These complications include hemorrhage, infection, thromboembolic diseases, psychosis, hypertensive diseases and other anomalies as well. The worst complication is postpartum hemorrhage (PPH). PPH, defined as a vaginal bleeding of ≥500 ml after vaginal or cesarean delivery, is observed in 5.4% to 8.5% of deliveries. It is the major cause of maternal mortality worldwide given that hemorrhagic shock can rapidly lead to neurological, renal, cardiac or respiratory organ dysfunction. PPH is also responsible for the majority of cases of near-misses. The commonest cause of PPH is uterine atony (UA), defined as the inability of the uterus to retract after delivery despite usual uterotonics administration. It is observed in 4% to 7% of deliveries. UA represents up to 82% of cases of PPH. Since UA is not always predictable, active management of third stage of labor (AMTSL) is mandatory if we want to prevent PPH. AMTSL using intramuscular injection of 10 IU of oxytocin is practiced as routine in our maternities.

The risk factors (RFs) for UA are known only in 77% of cases. Known risk factors include prolonged labor, multiple gestations, placenta previa, exposure to general anesthesia, ≥2 prior cesarean deliveries, prolonged labor or second stage of labor, birth weight >4000g, preeclampsia, chorioamnionitis, induction or augmentation of labor, maternal anemia, hydramnios and UA in a previous delivery. Some other RFs might exist. Knowing the RFs might help in prevention or early diagnosis of some cases of UA. To the best of our knowledge, no study has evaluated the risk factors for UA in a sub-Saharan country. The aim of this study therefore was to evaluate such risk as a contribution to the reduction of maternal mortality.
DEFINITION

Postpartum haemorrhage

Postpartum hemorrhage (PPH) occurs in 5–15% of deliveries and the wide range reflects the different definitions used. It is the most common cause of maternal deaths worldwide, and its prominent role in developing countries has recently been highlighted in a WHO meta-analysis.\(^1\) In the UK it accounts for 10.6% of all direct maternal deaths and the most recent Confidential Enquiry into Maternal and Child Health (2003–2005) highlighted PPH as the third most common cause of maternal mortality. In this report, 14 direct deaths were due to obstetric hemorrhage and of them nine were due to PPH. In addition, two further deaths were due to genital tract trauma and one due to ruptured uterus\(^2\).

PPH is classified as primary which occurs within the first 24 hours after delivery, and secondary which occurs between 24 hours and 6–12 weeks postpartum.\(^4\) Over recent years there has been an increase in risk factors for PPH, both in the UK and USA. These include an increase in the mean maternal age at childbirth.\(^5,7\) In England and Wales the average age of mothers at childbirth has increased by three years since 1971, rising from 26.2 years to 29.1 years in 2000.\(^6\) Advanced maternal age,\(^7,8\) increasing number of multiple pregnancies\(^9\) due to assisted reproduction and increasing cesarean section rates\(^10\) are associated with increased incidence of placenta praevia and its sequelae.\(^11,12\)

Balloon tamponade of the uterus has been reported as a useful intervention in women with massive and intractable PPH. Placement of an intrauterine Sengstaken-Blakemore oesophageal catheter (SBOC) can be used as a ‘tamponade test’, enabling the obstetrician to identify which women will require surgical intervention.\(^13\) Case series using balloon tamponade have reported success rates in arresting PPH ranging between 60 and 100%.\(^3,13-21\)

An important limitation of retrospective studies is that they may be subject to inadequate reporting, selection bias and positive-outcome bias. The aim of this study was to prospectively evaluate the use of the SBOC as a prognostic and therapeutic measure in intractable PPH.
Algorithm using the mnemonic ‘HAEMOSTASIS’.[22]

Help
Assess (i.e hemodynamic status, blood loss)
Establish Etiology, Ecobolics, Ensure availability of blood
Establish Etiology: four T’s +Tone +Tissue +Trauma +Thrombin
Ecobolics (syntometrine, ergometrine, bolus syntocinon)
Ensure availability of blood and blood products
Massage the uterus
Oxytocin infusion/prostaglandins (iv/per rectal/intramuscular/intramyometrial)
Shift to theatre _ exclude retained products and trauma: bimanual compression
Tamponade (balloon) or uterine packing
Apply compression sutures
Systematic pelvic devascularisation
Interventional radiologist _ if appropriate, ‘uterine artery embolisation’
Subtotal or total abdominal hysterectomy

Uterine atony
Uterine atony is defined as failure of myometrium to contract and retract following delivery. Powerful and effective myometrial contractions are vital to arrest bleeding. Uterine atony in contrary, the uterus is soft and ‘boggy’ with presence of excessive bleeding from genital tract. A prompt recognition followed by uterine massage and administration of uterotonic agents often arrest the bleeding. However, in the presence of already well contracted uterus, any persistent bleeding should prompt exploration for other causes of postpartum haemorrhage such as retained placental fragments or genital tract injuries.

Risk factors for uterine atony
Identification of women at risk of uterine atony is of utmost importance to allow optimisation and preventive measures to be taken. Hence, a well-arranged delivery plan and appropriate referral to a well-equipped centre should be done. The recognised risk factors that are associated with uterine atony are listed in
Table 1: Risk factors for uterine atony. (Breathnach & Geary, 2006)

<table>
<thead>
<tr>
<th>Factors associated with uterine over distension</th>
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<tbody>
<tr>
<td>Multiple pregnancy</td>
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<tr>
<td>Polyhydramnios</td>
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<tr>
<td>Fetal macrosomia</td>
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<tr>
<td>Labour related factors</td>
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<tr>
<td>Induction of labour</td>
</tr>
<tr>
<td>Prolonged labour</td>
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<tr>
<td>Precipitate labour</td>
</tr>
<tr>
<td>Oxytocin augmentation</td>
</tr>
<tr>
<td>Manual removal of placenta</td>
</tr>
<tr>
<td>Use of uterine relaxants</td>
</tr>
<tr>
<td>Deep anaesthesia</td>
</tr>
<tr>
<td>Magnesium sulphate</td>
</tr>
<tr>
<td>Intrinsic factors</td>
</tr>
<tr>
<td>Previous postpartum haemorrhage</td>
</tr>
<tr>
<td>Antepartum haemorrhage</td>
</tr>
<tr>
<td>Obesity</td>
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<tr>
<td>Age &gt; 35 years</td>
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Multiple pregnancies, polyhydramnios and fetal macrosomia cause uterine over-distension.

The odds ratio to develop PPH from fetal macrosomia and multiple pregnancies are 1.8 (95% CI 1.4 to 2.3) and 2.2 (95% CI 1.5 to 3.2) respectively (Magann et al., 2005). In the presence of twin-twin transfusion syndrome, the odds ratio increases to 5.1 (95% CI 1.5 to 15.7) (Magann et al., 2005). On contrary, Carroli et al. did not find any relationship between multiple pregnancies with occurrence of uterine atony (Carroli et al., 2008). A study based data obtained from Nationwide Inpatient Sample (NIS), a large public use administrative dataset in the United States, had reported an association of polyhydramnios with uterine atony requiring blood transfusion in the odds ratio of 1.9 (95% CI 1.2-3.1) (Bateman et al., 2010).

Intrapartum factors such as induction of labour, prolonged labour, oxytocin exposure and abnormal third stage are also recognised to associate with uterine atony. Induction of labour had an odds ratio of 1.5 (95% CI 1.2 to 1.7) (Magann et al., 2005) and was the cause of 17% of uterine atony requiring blood transfusion (Bateman et al., 2010).
Prolonged usage of oxytocin in labour contributes to uterine atony. Grotegut et al. had demonstrated that massive PPH secondary to uterine atony was significantly higher in women who were exposed to oxytocin (Grotegut et al., 2011). The authors proposed that persistent oxytocin administration causes desensitisation of oxytocin receptors which further contributed into uterine atony.

The presence of uterine fibroids or connective tissue disorders may hinder the myometrium contractility thus leading to uterine atony. However, the existing data are conflicting with regards to relationship between uterine fibroids and uterine atony. Patients with connective tissue disorders are at a higher risk of PPH as compared to the general population (Kominiarek & Kilpatrick, 2007) which is explained by poor connective tissue support. Hence, uterotonic agents would be the first-line treatment for these conditions.

Though identification of risk factors is essential, they have only moderate positive predictive value (Callaghan et al., 2010) as uterine atony can happen in any women with no apparent risk factor. Therefore, although early detection is important, timely and appropriate management is also crucial.

MANAGEMENT STRATEGIES

Prevention of PPH
Post-partum haemorrhage is preventable in many ways. Prevention begins early in high-risk women, as early as in preconception period. Prevention and optimisation of anaemia allows better tolerability to variable severity of PPH. Induction and augmentation of labour should be made with clear indications, performed judiciously by skilled birth attendants.

Women at high-risk of PPH should be delivered at tertiary centres with well-equipped operation theatre, intensive care unit and blood transfusion services. The International Federation of Gynaecology and Obstetrics (FIGO) promotes active management of the third stage of labour (AMTS) in all women in order to reduce the incidence of postpartum haemorrhage (Leduc et al., 2009).

Family planning
Low contraceptive prevalence rate leads to high fertility among women. In 2007, based on the United Nation Statistics Division report, contraceptive prevalence rate among married women (aged 15 to 49 years old) was at 54% (Department of Economic and Social Affairs,
United Nations Statistics Division, United Nation, 2010). In the CEMD report from 2001 to 2005, up to 70% of maternal deaths were recognised in women who did not practise contraception. This reflects high parity contributing to more than half of maternal deaths was due to PPH during the same period (Division of Family Health Development, Ministry of Health, 2005).

**Risk assessment and stratification**

Uterine atony, the commonest cause of PPH, is best prevented by ensuring that immediate haemostasis is achieved by effective myometrial contractility (Mukherjee & Arulkumaran, 2009). Uterine blood vessels supplying the placental bed pass through the myometrium.

However, in uterine atony, there is failure of myometrial contractions leading to impaired vasoconstriction of these blood vessels, resulting in excessive blood loss.

Nevertheless up to 60% of women with PPH have no identified risk factors (Mukherjee & Arulkumaran, 2009). Thus, constant awareness, early detection, timely resuscitation and management skills are necessary to overcome this problem.

<table>
<thead>
<tr>
<th>Colour codes</th>
<th>Associated risk factors</th>
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<tbody>
<tr>
<td>WHITE</td>
<td>primigravida, age &lt;18 or &gt;40,gravida 6 and above, spacing &lt; 2 years or &gt;5 years, short stature &lt;145 cm, single mother</td>
</tr>
<tr>
<td>YELLOW</td>
<td>Mothers with HIV positive or Hepatitis B positive, blood pressure &gt;140/90 and &lt;160/110 mmHg with no proteinuria, diabetes, gestation &gt; EDD +7 days.</td>
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<tr>
<td>GREEN</td>
<td>Rhesus negative, pre-pregnancy weight &lt;45 kg, medical problem excluding diabetes and hypertension, previous gynaecological surgery, drug/alcohol addiction, unsure of last menstrual period, recurrent miscarriage, previous obstetrics history (previous caesarean section, gestational hypertension, diabetes, intrauterine death, baby &lt;2.5 or &gt;4 kg, third degree perineal tear, retained placenta.</td>
</tr>
<tr>
<td>RED</td>
<td>eclampsia, pre-eclampsia, heart disease, breathlessness on exertion, uncontrolled diabetes, antepartum haemorrhage, symptomatic anaemia, prelabour rupture of membrane, preterm contractions, abnormal fetal heart rate &lt;110/min after 26 weeks and &gt;160/min after 34 weeks</td>
</tr>
</tbody>
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Table 2. Colour coding system based on risk factors, used in antenatal clinics in Malaysia as cited by Ravindran et al. in 2003 (Ravindran et al., 2003)

**Risk management and monitoring system**

Risk management includes incidence reporting, clinical practice guidelines review, near miss audits and CEMD. Standardised practice among all healthcare personnel is achievable by complying the clinical practice guidelines and hospital protocols. Incidences reporting
involving a retrospective detailed documentation of adverse events are done by staffs. The whole document is reviewed by the risk management team to determine any preventable or substandard care. This is followed by a series of event including audit, re-audit, staff education and training to improve in subsequent care.

Obstetrics near miss events are inclusive of massive PPH and peri-partum hysterectomy (Upadhyay & Scholefield, 2008). Audits of these events allow risk identification and implementation of preventive measures. Brace et al. reported that massive PPH was the major maternal morbidity in Scotland from 2003 to 2005 with the incidence of 3.7 per 1000 births (Brace et al., 2007). Up to 40% of near missed events received suboptimal care (Upadhyay & Scholefield, 2008).

Implementation of CEMD has allowed access of information with regards to the cause of death, areas of substandard care and identification of high risk women (Neilson, 2009). Each maternal death is studied and analysed in detail followed by expert’s recommendation. CEMD was introduced back in 1991. To date there has been several published reports over the past two decades. This allows identification of deficiency in the health care system. The MOH had put tremendous efforts and resources allocation into improvising the health care system. This is evident by a marked reduction in MMR in recent years (Division of Family Health Development, Ministry of Health, 2005).

**Non-pharmacological/ Mechanical strategies**

Varatharajan et al. evaluated the outcome of management for massive PPH using the algorithm ‘HAEMOSTASIS’ (Help; Assess and resuscitate; Established diagnosis; Massage of uterus; Oxytocin infusion and prostaglandins; Shift to operation theatre; Tamponade test; Apply compression sutures; Systematic pelvic devascularisation; Interventional radiology and Subtotal/total hysterectomy) The algorithm was found to provide a logical management pathway to reduce blood transfusions, hysterectomy, admissions to intensive care units and also maternal deaths.

**Uterine massage**

Uterine massage is performed by rubbing or stimulating the fundus of the uterus. It is hypothesised that massage releases local prostaglandins that promote uterine contractility hence reduces bleeding. Systematic review has shown that uterine massage is effective in
preventing PPH. controlled trial involving 200 women who were allocated to either uterine massage or no uterine massage following active management of third stage.

Women who received uterine massage had lesser amount of bleeding and requirement for additional uterotonic agents.

In groups; intramuscular oxytocin after delivery of the anterior shoulder, sustained uterine massage for 30 minutes followed by delayed oxytocin or received oxytocin and uterine massage immediately after delivery. It was found that oxytocin was more superior in controlling haemostasis as compared to sustained uterine massage.

Uterine massage performed immediately after administration of oxytocin did not show significant additional benefit as compared to oxytocin alone. The limitation of this trial was that, it was unable to demonstrate the effect of uterine massage on the amount of blood loss in the absence of oxytocin as this was non-ethical.

**Aortic compression**

Aortic compression can assist in controlling the amount of blood loss by decreasing the blood flow at the distal end including uterine artery (Riley & Burgess, 1994). Aortic compression is achieved via applying pressure with the flat surface of the knuckles above the contracted uterus and slightly to the left (Figure 1). Absence of femoral pulse indicates correct and complete occlusion of the aorta. It is crucial to release and re-apply the pressure every 30 minutes to allow intermittent blood flow to the lower limbs. Aortic compression is a simple intervention that can be used while preparing for a definitive management or during the transfer of patient from a district hospital to another tertiary hospital.
External aortic compression devices have been described by several authors (Winter, 1939; Soltan et al., 2009). These have been shown to be effective in reducing the resuscitation time and also the amount of blood being transfused with minimal side-effects reported.

However, these devices are not readily available in our setting especially in district hospital setting. According to CEMD report in the year 2000, 6.6% of PPH mortality had occurred during transfer of patients. Such simple device can be applied by any health care provider (with minimal training) would be of great value in reducing maternal morbidity and mortality.

**Bimanual compression**

Bimanual compression is performed by inserting the right hand into vagina at anterior surface of the uterus and the left hand is on abdomen at the fundus towards the posterior surface of uterus. The uterus is compressed between the two hands to minimise bleeding (Figure 2). This technique can be used as a temporary measure while patient is being stabilised for definitive treatment.
Uterine tamponade

In the past, sterile roller gauze had been used to pack the uterine cavity to reduce blood loss during massive PPH caused by uterine atony (Douglass, 1955). Despite its effectiveness, the popularity of uterine packing has dramatically declined with the wide availability of uterotonic agents (Douglass, 1955).

Nowadays, balloon devices have been recognised as an effective adjuvant strategy for achieving haemostasis in massive PPH in uterine atony. It was hypothesised that intrauterine balloon exert hydrostatic pressure on the uterine arteries resulting in reduced blood loss (Georgiou, 2009). The most commonly described balloon devices are Bakri balloon, Rusch catheter, Sengstaken-Blackmore catheter, Foley catheter and Condom catheter (Airede & Nnadi, 2008; Keriakos & Mukhopadhyay, 2006; Marcovici & Scoccia, 1999; Majumdar et al., 2010; Vitthala et al., 2009).

Bakri balloon is the only device that is specifically designed for uterine tamponade in massive PPH. It is equipped with large drainage channel that allow drainage of blood from the uterine cavity (Georgiou, 2009). Although both Sengstaken-Blackmore and Foley catheter have drainage channel, they are small in size thus prone to blockage by blood clots. In addition, the distal tip of Sengstaken-Blackmore catheter would deter the contact between the balloon surface and the fundus of uterus. The other two catheters (Rusch and Condom catheter) do not have drainage channel and thus result in difficulty in drainage of blood from the uterine cavity (Georgiou, 2009).
The capacity of balloon insufflations differs between various types of balloons. Rusch catheter has the largest capacity of 1500 ml of fluid (Keriakos & Mukhopadhyay, 2006) followed by Bakri balloon with 500 ml (Georgiou, 2009) while both Sengstaken-Blackmore catheter and Condom catheter have the capacity to accommodate 300 ml (Georgiou, 2009).

Foleys catheter has the smallest capacity with 30 ml and the use of multiple Foley catheters have been described (Marcovici & Scoccia, 1999).

Tamponade test’ is used to determine the success of controlling the haemostasis in atonic PPH. A negative ‘tamponade test’ indicate inadequate control of bleeding thus require additional strategies such as applying compressive sutures, systematic pelvic devascularisation or hysterectomy.

The use of concomitant uterotonic agents such as oxytocin and Carbetocin while the balloon is still in-situ is recommended to maintain the tamponade effect (Georgiou, 2009). Antibiotic therapy is also recommended to reduce ascending infection during balloon placement (Keriakos & Mukhopadhyay, 2006). However, there is no consensus on duration of its usage. Most authors remove the balloon within 48 hours. However, variations in the rate of deflation have been reported (Georgiou, 2009).

The adverse effects of the balloon devices reported so far were mainly due to overdistension of the balloon which includes pressure necrosis and uterine rupture. Other reported complications were uterine perforation and air embolism especially if air was used to inflate the balloon. Due to this risk, insufflation of balloon with air is not recommended.

With regards to subsequent fertility, successful pregnancies have been reported following the use of these balloon devices (Georgiou, 2009).

As uterine atony is a significant contributing factor in PPH, balloon tamponade devices may play a major role in pre-hospital emergency management prior to safe transfer to tertiary centre in reducing blood loss, hence lowering morbidity and mortality. However, to date there is paucity of data in addressing this issue.
Pharmacological strategies

Effective uterine contractions are crucial to ensure adequate haemostasis following delivery. Several uterotonic agents have been described to be effective in promoting myometrium contractility hence avoiding the need for surgical intervention.

Oxytocin

Oxytocin is the first line therapy for uterine atony. It acts by stimulating rhythmic uterine contraction particularly in the upper segment. It is administered intramuscularly or intravenously; however the onset of action is delayed if given intramuscularly (3-7 minutes) as compared to immediate onset if given by intravenous route. Furthermore, due to its short plasma half-life of 3 minutes, continuous intravenous infusion is preferred (Breathnach & Geary 2009).

Most centres use the regime of 20 IU oxytocin in 500 ml of crystalloid solution (Breathnach & Geary, 2009; Rajan & Wing, 2010). In., 40 IU oxytocin in 500 ml of crystalloid solution is given over the duration of 6 hours. In certain circumstances, 80 IU oxytocin in 500ml of crystalloid solution has been used effectively.

Adverse effects of oxytocin infusion were mainly related to its anti-diuretic properties resulting in water intoxication, manifesting as headache, vomiting, drowsiness and convulsions (Breathnach & Geary, 2009b). In cases where fluid restriction is indicated, concentrated oxytocin via infusion pump is recommended.

Ergometrine

As opposed to oxytocin, ergometrine results in sustained myometrial contraction. As it also acts on the vascular smooth muscle, it is not suitable for those with hypertension, migraine, heart disease and peripheral vascular disease such as Raynaund’s syndrome. It is given as 0.25 mg intramuscularly or intravenously with rapid clinical effect within 2 to 5 minutes that can persist up to 3 hours. Ergometrine is metabolised in the liver and has a plasma half-life of 30 minutes. A repeat dose of ergometrine can be given after 5 minutes if the uterus is still not well contracted. Nausea, vomiting and dizziness are commonly reported side-effects (Breathnach & Geary 2009b).
Syntometrine consists of 5 IU oxytocin and 0.5 mg ergometrine in a single preparation. This preparation results in a rapid onset of uterine contraction due to its oxytocic properties and sustained contractility from the ergometrine component (Rajan & Wing, 2010).

**Carbetocin**

Carbetocin is a long-acting synthetic oxytocin analogue that is administered via intramuscular or intravenous route. The recommended dose is 100 μg. Carbetocin has the advantage of rapid onset of action, within 2 minutes, similar to oxytocin with additional benefit of longer duration of action. These actions do not differ by the route of administration. However, intramuscular Carbetocin (120 minutes) had been reported to give a longer uterine contraction as compared to intravenous route (60 minutes) (Rath, 2009).

Side effects of carbetocin include headache, hypotension, tremor, flushing, abdominal pain and nausea. Rarely, it was associated with dizziness, chest pain, dyspnoea, metallic taste, vomiting, back pain and chills (Rath, 2009).

Randomised controlled trials have found Carbetocin to be associated with lesser requirement for additional uterotonic agents and uterine massage in high risk patients after caesarean deliveries (Su et al., 2007). However, there was no significant difference in the amount of blood loss and rate of PPH between Carbetocin and oxytocin in these women.

Furthermore, a single dose of Carbetocin was found to be more convenient than oxytocin infusion that require intravenous line and is time-consuming (Su et al., 2007).

There are three randomised controlled trials assessing the use of Carbetocin following vaginal delivery. Boucher et al. compared Carbetocin with 2-hour 10 IU oxytocin infusion in 160 women with at least one risk factor for PPH (Boucher et al., 2004). The number of women requiring uterotonic intervention (either additional uterotonic agents or uterine massage) was significantly lower in the Carbetocin group (Boucher et al., 2004). Leung et al. randomised 329 women to intramuscular Carbetocin and intramuscular syntometrine and found no difference in the decline of haemoglobin two days after delivery (Leung et al., 2006). Although the rate of PPH was lower in the Carbetocin group, it was not statistically significant (Leung et al., 2006). About 120 women were randomised to Carbetocin and Syntometrine groups had showed lower haemoglobin drop in the Carbetocin group (Nirmala
et al., 2009). All three studies had shown Carbetocin to be associated with lower incidence of adverse effects.

Carbetocin is not widely available in developing countries. In., though it is available, its use is restricted to high risk cases due to its higher cost.

Misoprostol
Misoprostol is a synthetic analogue of prostaglandin E1 that has uterotonic properties (Hofmeyr & Gulmezoglu, 2008). Although it has been used widely as uterotonic agents in certain developed country misoprostol has only been registered for therapeutic use in refractory gastro-duodenal ulcers, and has not been made legally available for pregnancy in view of safety concerns in pregnancy (Health Technology Assessment Unit, Ministry of Health., 2003).

Misoprostol is a cheap and effective uterotonic agent that can be administered via oral, sublingual, vaginal or rectally. The onset of action is slower if given rectally with more favourable side effects. Adverse effects of misoprostol are dose-related and commonly reported are diarrhoea, shivering and pyrexia (Breathnach & Geary, 2009).

A Cochrane review has concluded that misoprostal administered at a dose of 600 mcg was effective in reducing blood loss after compared to placebo (Gulmezoglu et al., 2007).

However, it was found to be less superior to oxytocin in preventing PPH. More recent trials have challenged the superiority of oxytocin. Several studies have shown that there were no difference in the amount of blood loss between misoprostol and oxytocin (Hofmeyr & Gulmezoglu, 2008; Parsons et al., 2006). In fact, Parsons et al. found that those who received misoprostol required less additional uterotonic (Parsons et al, 2006).

Due to its cost and easy storage, misoprostol may indeed be of value to prevent PPH in low resource setting where oxytocin may not be readily available (Moeen et al., 2011; Nasreen et al., 2011).

Carboprost/Haemabate
In,, carboprost is used as second-line therapy for uterine atony-related PPH that has failed to respond to either oxytocin or syntometrine. It is an analogue of PG F2α and acts on smooth muscle resulting in myometrial contractions. The recommended dose is 0.25 mg and it can be
given as intramuscular or intramyometrial injection. Intramyometrial administration can be performed trans-abdominally or under direct vision during caesarean deliveries.

The clinical effect is faster if given intramyometrial (peak within 5 minutes) as compared to intramuscularly (peak within 15 minutes). A maximum dose of 2mg (8 doses) can be given at 15 minutes interval (Breathnach & Geary, 2009).

Commonly reported adverse effects are nausea, vomiting, diarrhoea, pyrexia, bronchospasm and systemic hypertension. Therefore contraindication to its usage would be those with cardiac and pulmonary disease (Breathnach & Geary, 2009).

**Surgical intervention**

In most cases, the use of non pharmacological approach and uterotonic agents are able to curb massive bleeding due to uterine atony. Those who are not responding to these interventions may require surgical interventions. Multidisciplinary support involving anaesthetists and haematologists expertise is essential to ensure an optimal outcome.

**B-Lynch compression sutures**

In the atonic uterus, the vessels especially at the placental bed are unable to contract to secure bleeding. B-Lynch suture, which was first reported in 1997, comprises of vertical compression suture on the uterine vascular system. The reported success rate was 91.7% (95% CI 84.9%-95.5%) (Doumouchtsis et al., 2007). It is a simple, quick and life-saving procedure to combat bleeding from a lax uterus.

Before performing this procedure, its efficacy should be predicted by doing manual compression of the uterus. The surgeon’s left hand is placed behind the uterus while the right hand compresses the lower segment of the uterus just above the bladder reflection. If the amount of bleeding reduces, the compression suture is likely to be effective.
Fig. 3: A puncture 3 cm from the right lower edge of the uterine incision and 3 cm from right lateral border made and threaded through the uterine cavity to emerge at the upper incision margin 3 cm above and its lateral border. Then, the suture is looped over the uterine fundus 3-4 cm from the right border before it being pulled downward vertically to enter the posterior uterine wall at the same level of the first puncture site. The suture is passed through the cavity and emerged on the left uterine border horizontally before it is brought up to the fundus and looped anteriorly. After the needle has passed through the uterine cavity and brought out 3 cm anteriorly and below the incision margin on the left, the two lengths of catgut are pulled tight, while the assistant continuously compressed on the uterus. A knot applied anteriorly to secure the tension.

Lloyd-Davis position is preferred when performing this procedure as the vaginal bleeding can be assessed simultaneously. B-Lynch suture is performed by using absorbable sutures with round bodied needle. The technique B-Lynch suture application is described in Figure 3. B-Lynch surgical technique is relatively safe and allows fertility preservation. Two uterine necroses were reported. (Joshi & Shrivastava M, 2004; Treloar et al., 2006) However, these two cases had received numerous comments and queries regarding the suturing techniques. In one of the comments, B-Lynch had stated among 948 successful cases of B-Lynch sutures worldwide only seven cases failed. (B-Lynch, 2005) Allam et al reviewed 10 case reports involving a total of 38 women who underwent B-Lynch surgical technique for massive PPH.
There were 36 successful cases with 2 failures reported. Till date, no known post-operative mortality reported (Allam & B-Lynch, 2005).

**Hayman suture**

Hayman uterine compression suture (Figure 4) is another method which has been described to arrest bleeding in uterine atony. This technique does not require lower segment hysterotomy therefore it is a good option when PPH occurs following vaginal delivery (Hayman et al., 2002). It is faster, easier and less traumatic to the uterus. The success rate of this procedure is approximately 93.75% (Nanda & Singhal, 2011). However, it may entrap blood within the uterine cavity and subsequently induces haematometra, pyometra and uterine necrosis.

![Fig. 4: This procedure involves making two stitches approaching from below the bladder reflection anteriorly to the posterior wall of the uterus at the same level. The knots are placed at the fundus while the uterus is being compressed by an assistant simultaneously.](image)

**Vascular ligation/Occlusion**

Currently there is no evidence or consensus regarding the superiority of one treatment to another in massive PPH. The limitations are depending on the availability and experience of surgeons, facilities, and local policies. In the past, laparotomy has been advocated to facilitate devascularisation. Vascular ligation is advocated following failure of compression sutures before resorting to hysterectomy is considered, especially when fertility is of concern.
However with recent advancement of less invasive radiological intervention, it has become a viable alternative to vascular ligation.

**Bilateral uterine artery ligation**

This easier technique with fewer complications was first described by Waters in 1952 (Waters, 1952). It involves a low abdominal approach like in Pfannenstiel incision. The uterus is exteriorised and pulled upward to facilitate identification of uterine vessels. An absorbable suture is placed 2 cm below the bladder reflection on both sides of the uterus avoiding the ureters. This technique occludes the ascending branch of uterine vessels, with reported success rate of 80-96% (Morel et al., 2011). This procedure is technically safe other than possible risk of ureteric injury.

**Bilateral internal iliac (hypogastric artery) ligation**

This is one of the oldest surgical technique (Figure 5) introduced as early as 1960’s (Sziller et al., 2007). It requires a good knowledge of anatomy to avoid inadvertent injuries to the external iliac vessels and ureters. The success rate of internal iliac artery ligation varies between 42-93% (Morel et al., 2011). Incorrect ligation entails high risks of limbs ischaemia, gluteal claudication, further bleeding and possible ureteric and nerve injury.

![Diagram](image.png)

(EIA: external iliac artery; EIV: external iliac vein; CIA: common iliac artery; CIV: common iliac vein; IIA: internal iliac artery; U: ureter)

Fig. 5: The broad ligament is opened and traced upward until at the level of bifurcation of common iliac artery parallel to the sacroiliac curvature. The ureter is commonly on the medial leaf of the broad ligament after crossing the bifurcation of common iliac
artery. The vascular sheath needs to be cleared for better visualisation and recognition, minimising inadvertent ligature and venous injury. The internal iliac is a branch of medio-inferior after the bifurcation of common iliac artery. By using a right angle forceps to isolate this vessel, an absorbable ligature is placed 1 to 2 cm below the bifurcation. Following this, a distal pulse at femoral artery is checked to ensure its patency. The same procedure is repeated to the contra-lateral side.

**Embolisation**

Uterine artery embolisation is relatively a new technology in managing PPH. It is only available in tertiary hospitals and it requires an interventional radiologist with the attending obstetrician. This procedure requires haemodynamic stability. Ideally, anticipation of its role is best done pre-operatively example in morbidly adherent placenta. However, uterine atony related PPH often unpredictable hence its use is limited. In cases where balloon tamponade has partially reduced bleeding, concurrent use of uterine artery embolisation may be of value to avoid hysterectomy for conserving fertility.

The success rate of emergency uterine artery embolisation for refractory uterine atony ranges from 70 to 100% (Soncini et al., 2007). As pelvic vasculature is very rich in anastomosis, both sides of uterine artery occlusion are required to ensure its effectiveness. Possible complications include procedure failure with persistent bleeding, infection, vascular injury, postoperative pain and fever. The overall risk is approximately 5% (Soncini et al., 2007). However the reproductive function following this procedure is maintained (Soncini et al., 2007) but may be associated with malpresentation, preterm delivery and PPH.

**Hysterectomy**

Peri-partum hysterectomy for PPH is a difficult decision to make but a life saving definitive procedure. Although this is usually the last resort however early consideration should be given in selected cases especially when fertility is of less concern and in morbidly adherent placenta. The incidence varies up to 8 per 1,000 deliveries (Lone et al., 2010).

Peri-partum hysterectomy has a morbidity rate of 30-40% (Christopoulos et al., 2011).

Complications include ureteric and bladder injury, persistent bleeding requiring reexploration, pneumonia, and urinary fistula (Christopoulos et al., 2011).
Peri-partum hysterectomy can be performed either as total or subtotal hysterectomy. A total hysterectomy reduces risk of cervical stump malignancy (El-Jallad et al., 2004), but requires longer operating time and has higher rate of urinary tract injuries. A subtotal hysterectomy is faster and safer (Rahman et al., 2008) but regular cervical screening is mandatory.

**DISCUSSION**

Our prevalence of UA was 5.5%. The significant risk factors for UA in our study was multiple pregnancy, delivery before 34 weeks gestation, time spent from 4 cm cervical dilatation to delivery >10 hours, macrosomic baby (≥4000g), past history of macrosomic baby, malaria or preeclampsia within four weeks before delivery and maternal age ≥35 years. Our prevalence of UA was within the range of 4% to 7% found in the literature. We observed no association between UA and chronic hypertension, multiparity, HIV status or labor augmentation. We found a slightly increased risk of UA amongst women with past history of UA, tocolysis within one month before delivery or in the latent phase, induction of labor or labor augmentation, but the difference was statistically insignificant. These findings are in contrast with those of other researchers. The lack of statistically significant difference in our series might be due to our small sample size.

In our study, multiple gestation was significantly associated with UA, even after logistic regression. This has already been noticed elsewhere. This can be explained by the uterus overdistention that is associated with poor response to uterus massage and uterotonics. Delivery before 34 weeks was a risk factor for UA in our study. The explanation is unknown. The uterus might be less sensitive to uterotonics because of insufficient uterotonic receptors. Studies should be carried out to explain this observation. Women who spent more than 10 hours from 4 cm cervical dilatation to delivery were at risk of UA. This might be attributed to uterine muscle exhaustion. Some authors found that prolonged labor was a risk factor for UA, while for others, only prolonged second stage of labor was a risk factor for UA.

Also, women who delivered a baby that weighed 4000g or more were also at risk of UA even after control for confounding factors, as already observed by other researchers. It can be explained by the overdistension of uterus that is associated with poor response to uterus massage and uterotonics. Women with past history of macrosomia were at risk for UA, even after adjustment for confounding factors. This has not yet been observed elsewhere. The mechanism is unknown. Studies should be carried out to explain this. Maternal diseases such as malaria or preeclampsia within four weeks before delivery was a risk factor for UA, even
after logistic regression. Preeclampsia is a known risk factor for UA. The relationship between malaria and UA could be the presence of anemia. Malaria can induce maternal anemia and anemia is a known cause of UA. Maternal age ≥35 was also a risk factor for UA, even after logistic regression. This is contrast with the findings of other researchers.

Finally, fever during labor, whatever the cause was another risk factor in our series. It has been shown that two hours after onset of maternal fever, there is a decline in myometrial contractility.16 Women with fever should be actively managed for prevention of UA. The major limitations of our study were our small sample size due to the fact that the study was carried out in two semi-urban hospitals where there were few deliveries. Moreover, we could not study the impact of anemia on UA given that some women did not have a recent hemogram.

CONCLUSION
1. PPH is a major cause of maternal deaths worldwide and uterine atony is the main attributor. In order to reduce maternal mortality, one of the strategies should be towards primary, secondary and tertiary prevention of uterine atony. Close relationship with ancillary support i.e. blood bank facilities, intensivists and ICU care completes the team in management of atonic PPH.

2. Among previously documented risk factors for uterine atony, only a prolonged second stage of labour in multiparas was found to be significant in this study. Gestational diabetes mellitus, a previously undocumented factor, has also been identified as an independent risk factor. The study calls into question the importance of multiparity and age. Replication of these investigations and operational research into the value of these findings would be required for better prevention or management of uterine atony.

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