Postpartum Hemorrhage; a Major Killer of Woman: Review of Current Scenario

Abstract
Postpartum Hemorrhage is one of the most common causes of maternal mortality worldwide accounting for 127,000 deaths annually. PPH is a preventable condition and early timely intervention can prevent development of this dreadful condition. One such intervention that is highly recommended is Active Management of Third Stage of Labor. It is the only intervention known to prevent PPH. Though even with different interventions and blood transfusion facility, maternal deaths cannot be brought down to zero. Significant reduction can only be achieved by better education of women about maternal health. The main purpose of this study is to know the recent global and national prevalence of PPH, its prevention as well as management at an early stage, so as to reduce the overall burden of deaths resulting from PPH.

Method: The literature regarding PPH was searched from various English language journals and published peer-reviewed articles on PubMed, MEDLINE, Embase and Google Scholar till 2015.

Keywords: Active management of third stage of labor; Cesarean section; Maternal mortality; Oxytocin; Postpartum Hemorrhage; Vaginal delivery; Controlled cord traction

Introduction
Postpartum hemorrhage (PPH) is defined as any blood loss >500 ml following vaginal delivery and >1000 ml after cesarean section [1]. Definitions vary in various parts of world and are often based on inaccurate estimates of blood loss [1-4]. It can also be defined as fall in hematocrit >10% [5,6]. PPH is often classified as primary, occurring within 24 hours of birth and is more common form of PPH [7,8] or secondary defined as bleeding in excess of normal lochia after 24 hours and up to six weeks postpartum [9]. In addition, it can also be classified as third or fourth stage depending on whether it occurs during or after delivery of placenta respectively. According to WHO estimates PPH is leading cause of maternal mortality and morbidity worldwide and is responsible for nearly one-quarter (25%) of all maternal deaths [10,11]. Worldwide it is responsible for 127,000 deaths annually [12]. Half of these total maternal deaths occur in Africa and Asia, where PPH is one of the leading causes of maternal mortality [8]. Hence, the risk of woman dying due to pregnancy or childbirth in her lifetime is about one in six in the developing countries as compared to 1:30,000 in Northern Europe [13], and 1:3,700 in United States of America [14]. According to latest WHO figures, 10.5% of all live births were complicated with PPH, and around 13,795,000 women suffered PPH with 13,200 maternal deaths in the year 2000 [15].

Incidence
Global
PPH is one of the major causes of maternal mortality around the world with a reported incidence of 2–11% [16-18] (Figure 1 & 2). The exact rates may differ according to data source, country as well as assessment method with prevalence of 10.6% when measured by objective assessment of blood loss and 7.2% when measured by subjective techniques. According to a systematic review the prevalence of PPH with ≥500 ml of blood loss was 10.5% in Africa, 8.9% in Latin America and Caribbean, 6.3% in North America and Europe, and 2.6% in Asia [19]. Another similar systematic review reported slightly higher prevalence rates, with similar regional variation: 26% in Africa, 13% in North America and Europe, and 8% in Latin America and Asia [20]. On the other hand the prevalence of PPH with ≥1000 ml of blood loss was significantly lower in both reviews with estimates of 1.9 to 2.8% [19,20]. Similar studies reported that global prevalence of severe PPH (blood loss ≥1000 ml) was 10.5% amongst women who had live birth in year 2000 [21]. Carnoli et al. [19] also reported a global prevalence of PPH ≥500 ml as 6.09% and of PPH ≥1000 ml as 1.86% [19]. Prevalence of PPH ≥500 ml ranged from 2.55% in Asia to 10.45% in Africa. Also the prevalence of primary and Secondary PPH is approximately 6% and 1.86% of all deliveries, respectively [19].

Though the overall prevalence of PPH is low in developed countries as compared to developing nations, but several studies have reported a rise in rates of PPH in these developed regions also [22-28]. In United States, the prevalence has increased from 2.3% in 1994 to 2.9% in 2006, a 26% increase [29]. Also the National statistics of US suggest that approximately 8% of total maternal deaths are caused by PPH. Furthermore it was reported that the rate of PPH increased from 1.5% in 1999 to 4.1% in 2009, and rate of atomic PPH rose from 1% in 1999 to 3.4% in 2009 [25].

Indian
The maternal mortality ratio (MMR) in India between 2007 and 2009 was 212, which is far away from the Millennium Development Goal 5 target for India: 109 maternal deaths per
100,000 live births [30]. With 56,000 maternal deaths, India accounted for 19% of global burden of maternal deaths in 2010 [31], though it has only 16% of global population. The level of MMR in India has declined from over 750 in the sixties to about 400 in the nineties [32,33]. It has further declined from 254 in 2004-2006 to 212 in 2007-2009 [30], but it has not yet reached the desired levels. PPH is a frequent complication of delivery and its reported incidence in India is 2%-4% after vaginal delivery and 6% after cesarean section with uterine atony being the most common cause (50%) [34]. Furthermore, latest figures report PPH as the contributory cause of 19.9% of maternal mortality, that is anywhere from 78,000 [35] to 117,000 [11] maternal deaths in India. As reported by Registrar, General, India and Centre for Global Health Research 2001-2003; the five most common direct causes of pregnancy-related mortality in India were hemorrhage (38%), sepsis (11%), unsafe abortion (8%), hypertensive disorders (5%) and obstructed labor (5%) [35]. The remaining 34% of maternal deaths were due to unspecified indirect causes [35].

Various studies in different regions of India report different prevalence of PPH. A study in North east region of India reported 94 maternal deaths/102525 live births, out of these, 53.19% women died due to hemorrhage accounting for about 21.27% of total deaths [36]. Similar studies reported prevalence of 22.7% in Delhi [37] and 28.57% in Orissa [38]. Hemorrhage was also found to be the major cause of maternal mortality in West India, accounting for 24.6% of maternal deaths in that region [39]. Mukherji et al [40]. reported that 58% of maternal deaths due to hemorrhage were actually due to PPH, resulting from lack of provision of emergency transport at community level [40].

**Figure 1:** Maternal mortality ratio (per 100,000 live births), 2010.

**Causes of PPH**

PPH can result from many causes that are broadly divided into; Atonic, Traumatic and Mixed. A recent randomized trial in the United States reveal that, birth weight, labor induction and augmentation, chorioamnionitis, magnesium sulfate use, and previous PPH can all lead to increased risk of PPH [41].

The Risk factors for PPH include [42,43]:

a) Antenatal risk factors: Antepartum hemorrhage in this pregnancy; Placenta praevia (increases risk by 12 times); Suspected or proven placental abruption; Multiple pregnancy (increases risk by 5 times); Over-distended uterus (polyhydramnios or macrosomia); Pre-eclampsia or pregnancy-induced hypertension (4 times risk); Grand multiparity (four or more pregnancies); Previous PPH (3 times risk) or previous history of retained placenta; Asian ethnic origin (2 times risk); Existing uterine abnormalities; Maternal age (≥40 years); Maternal anemia.

b) Intrapartum risk factors: Induction of labor (Twice risk); Labor of >12 hours (2 x risk); Emergency caesarean section (4 times risk); Retained placenta (5 times risk); episiotomy (5 times risk); Baby weight >4 kg (2 x risk); Maternal pyrexia in labor (2 x risk).
c) Pre-existing maternal coagulopathy: Haemophilia A or B; Von Willebrand’s disease.

d) Another study reported that PPH is also linked with obesity. It was found that, the risk of atomic uterine hemorrhage rapidly rises with rising Body Mass Index (BMI); in women with a BMI > 40, the risk was 5.2% with normal delivery and 13.6% with instrumental delivery [44].

Another way of describing the causes of PPH is “four T’s” [45,46]:

i. Tone: uterine atony, distended bladder.

ii. Trauma: lacerations of the uterus, cervix, or vagina.

iii. Tissue: retained placenta or clots.

iv. Thrombin: pre-existing or acquired coagulopathy.

Ways to prevent PPH

PPH is one of the third stage complications which every obstetrician faces once in her lifetime and is very challenging most of the times. Despite of improvements in management, early PPH still remains a significant cause of maternal morbidity and mortality in developing countries [47,48]. One of the ways to prevent PPH is Active management of the third stage of labor (AMTSL). It is considered to be the “gold standard” to reduce the incidence of PPH. It combines nondrug interventions with administration of uterotonics drugs [49].

It is a combination of

a. Uterotonic administration (preferably Oxytocin) immediately upon delivery of baby,

b. Early cord clamping and cutting, and

c. Gentle cord traction with uterine counter traction when the uterus is well contracted (Brandt-Andrews maneuver).

Studies have compared AMTSL with expectant management and found a substantial reduction in the occurrence of PPH by approximately 60-70% [50]. These findings were also reflected in a retrospective cohort study with historical controls conducted in a developing country, which also found a significant reduction in incidence of PPH after implementation of AMSTL [51].

The International Confederation of Midwives and International Federation of Gynecology and Obstetrics further state: “Every attendant at birth needs to have the knowledge, skills and critical judgment needed to carry out AMTSL for preventing postpartum haemorrhage” [52]. Hence, it is recommended that all women should benefit from AMTSL, the only intervention known to prevent PPH [53].

Furthermore the most recent Cochrane review of active versus expectant management of third stage of labor including seven studies, indicate a significant reduction in risk of PPH with AMTSL [54]. Though controlled cord traction was an initial component of AMTSL, but, three RCTs assessing AMTSL with and without cord traction found no significant difference in the risk of PPH [55-57]. Similarly regarding cord clamping, it was initially thought that early cord clamping was better, but latest studies indicate that the timing is not important [49]. The findings were further confirmed by an updated review of the Cochrane Collaboration researchers in 2013, which observed no significant differences in the risk of PPH between early and late cord clamping [58]. Also a recent review of seven RCTs investigating the efficacy of oxytocin, three with intramuscular (IM) and four with intravenous (IV) preparations, showed that oxytocin is the best uterotonic to reduce the risk of PPH [59]. Intraumbilical administration of oxytocin was also found to cause significant reductions in blood loss [60,61]. Similarly for the use of other uterotonics, a 2011 review of ergot alkaloids containing six studies (RCTs and quasi-RCTs) found a significant reduction of PPH when administered in third stage of labor [62].

Studies report that a longer-acting oxytocin derivative, carbetocin, single dose (100 micrograms), licensed in UK specifically indicated for prevention of PPH in context of caesarean delivery is at least as effective as oxytocin by infusion [63,64].

A Long Way Forward

The vast disparities between regions and countries in maternal health have long been known. The most recent estimates show that in 2008, maternal mortality ratios ranged from 290 maternal deaths per 100,000 live births in developing countries to just 14 in developed countries [65]. The fact that an estimated 385,000
women die each year during pregnancy, delivery and the postpartum period suggests inadequate overall progress toward reproductive health, including maternal health or MDGs [13, 65, 66]. Furthermore, there is a growing body of evidence showing that even within countries; maternal health outcomes are inequitably distributed, with the poorest likely to be most disadvantaged. In some settings, improvement in national maternal mortality ratio hides the existence of persistent internal inequities, some of which continue to increase even when aggregate trends improve [67]. There is growing interest, therefore, in comparing maternal health outcomes between communities with different social and economic development contexts. Resources, power and access to opportunities are unequally and unfairly distributed across social categories, creating social gradients that disadvantage people in lower social positions [68].

| Intervention | WHO Recommendations |
|--------------|----------------------|
| Active management of the third stage of labor | Involves combination of interventions, including: cord clamping and cutting; controlled cord traction; and use of an uterotonic agent |
| Controlled Cord Traction | In settings where skilled birth attendants are available, controlled cord traction is recommended for vaginal births if the care provider and the parturient woman regard a small reduction in blood loss and a small reduction in the duration of the third stage of labor as important (weak recommendation, high-quality evidence) In settings where skilled birth attendants are unavailable, controlled cord traction is not recommended (strong recommendation, moderate-quality evidence) Only skilled provider can administer |
| Cord Clamping | Late cord clamping (in 1 to 3 minutes) is recommended for all births while initiating simultaneous essential newborn care (strong recommendation, moderate-quality evidence) Early cord clamping (less than 1 minute) is not recommended unless the neonate is asphyxiated and needs to be moved immediately for resuscitation (strong recommendation, moderate-quality evidence) Only skilled provider can administer |
| Uterine Massage | Sustained uterine massage is not recommended as an intervention to prevent PPH in women who have received prophylactic oxytocin (weak recommendation, low-quality evidence) Postpartum abdominal uterine tonus assessment for early identification of uterine atony is recommended for all women (strong recommendation, very low-quality evidence) Only skilled provider can conduct routine uterine tone assessment. |
| Oxytocin | Oxytocin (10 IU, IV/IM) is the recommended uterotonic drug for the prevention of PPH (strong recommendation, moderate-quality evidence) Only skilled provider can administer |
| Ergometrine | In settings where oxytocin is unavailable, the use of other injectable uterotonics, like ergometrine/methylergometrine or fixed drug combinations of oxytocin and ergometrine) is recommended (strong recommendation, moderate-quality evidence) Only skilled provider can administer |
| Misoprostol | In settings where oxytocin is unavailable, oral misoprostol (600 μg) is one of the recommendations (strong recommendation, moderate-quality evidence) Skilled and unskilled providers can administer; women can self-administer as well |

Relationships with male partners are another factor that affects women’s health. The level of a husband’s education is also a major determinant of skilled attendance at birth, indicating that women might need to take husband’s/partner’s permission before taking decisions related to care [69,70]. Hence, by bringing behavioral changes at individual and family levels, one can facilitate women’s and their families’ health, awareness of potential obstetric and neonatal risk, increasing their knowledge of good pregnancy and delivery care, equipping them with skills to take health-enhancing decisions, and building

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self-efficacy for requesting assistance from other community members or local health authorities [71]. Diffusion of new knowledge and awareness can be facilitated by media messages, outreach workers, or community members themselves. The concept of “birth preparedness” - where pregnant women, their families, and the wider community are encouraged to anticipate potential complications and develop strategies for transporting women to medical facilities prior to or at the onset of labor - is another way of preventing maternal morbidity and mortality. Additionally, healthcare systems in developing countries may not be able to provide comprehensive care to patients as a result of limited access to resources. These upstream factors need to be considered alongside clinical management and intervention in the pursuit of worldwide reduction in maternal deaths due to PPH. Hence, a lot needs to be done at individual, community and political levels to promote maternal health and to reduce the burden of maternal deaths in India.

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References

1. Rath WH (2011) Postpartum hemorrhage - update on problems of definitions and diagnosis. Acta Obstet Gynecol Scand 90(5): 421-428.
2. Kavie JA, Khafi H, Stoltzfus RJ, Witter F, Tielsch JM, et al. (2006) Measurement of blood loss at childbirth and postpartum. Int J Gynaecol Obstet 95(1): 24-26.
3. Stafford I, Diddy GA, Clark SL, Belfort MA (2008) Visually estimated and calculated blood loss in vaginal and cesarean delivery. Am J Obstet Gynecol 199(5): 519.e1-519.e7.
4. Schorn MN (2010) Measurement of blood loss: review of the literature. J Midwifery Womens Health 55(1): 20-27.
5. Wainscot MP (2004) Pregnancy, postpartum hemorrhage.
6. Smith JR (2004) Postpartum Hemorrhage.
7. World Health Organization (2008) Reducing the Burden: Postpartum Hemorrhage. p. 1-8.
8. Khan KS, Wojdyla D, Say L, Gremezoglu AM, Look PFA (2006) WHO analysis of causes of maternal death: a systematic review. Lancet 367(9516): 1066-1074.
9. Magnann EF, Evans S, Chauhan SP, Laneau G, Fisk AD, et al. (2005) The Length of the Third Stage of Labor and the Risk of Postpartum Hemorrhage. Obstet Gynecol 105(2): 290-293.
10. World Health Organization (2012) WHO Recommendations for the Prevention and Treatment of Postpartum Haemorrhage. World Health Organization, Geneva.
11. World Health Organization (2007) Maternal mortality in 2005: estimates developed by WHO, UNICEF, UNFPA and the World Bank, WHO, Geneva, Switzerland.
12. World Health Organization (2008) Reducing the Burden: Postpartum Hemorrhage.
13. Ronsmans C, Graham WI (2006) Lancet Maternal Survival Series steering group. Maternal mortality: who, when, where, and why. Lancet 368(9542): 1189-1200.
14. Karoshi M, Keith L (2009) Challenges in managing postpartum hemorrhage in resource-poor countries. Clin Obstet Gynecol 52(2): 285-298.
15. Cameron MJ, Robson SC (2006) Vital statistics: an overview in A Textbook of Postpartum Hemorrhage. In: CB-Lynch, et al. (Eds.), A Comprehensive Guide to Evaluation, Management and Surgical intervention, Sapiens Publishing (1st edn.). p. 17-34.
16. Anderson FWJ (2009) Maternal mortality: an enduring epidemic. Clinical Obstetrics and Gynecology 52(2): 214-223.
17. Oyelese Y, Scora WE, Mastrolia R, Smulian JF (2007) Postpartum hemorrhage. Obstetrics and Gynecology Clinics of North America 34(3): 421-441.
18. Mercier FJ, Van de Velde M (2008) Major obstetric hemorrhage. Anesthesiol Clin 26(1): 53-66.
19. Carroli G, Cuesta C, Abalos E, Guimenez AM, et al. (2008) Epidemiology of postpartum haemorrhage: a systematic review. Best Pract Res Clin Obstet Gynaecol 22(5): 999-1012.
20. Calvert C, Thomas S, Ronsmans C, Wagner KS, Adler AJ, et al. (2012) Identifying regional variation in the prevalence of postpartum haemorrhage: a systematic review and meta-analysis. PLoS One 7(7): e41114.
21. Abou Zahr C (2003) Global burden of maternal death and disability. Br Med Bull 67: 1-11.
22. Ford JB, Roberts CL, Simpson JM, Vaughan J, Cameron CA (2007) Increased postpartum hemorrhage rates in Australia. Int J Gynaecol Obstet 98(3): 257-243.
23. Joseph KS, Rouleau J, Kramer MS, Young DC, Liston RM, et al. (2007) Investigation of an increase in postpartum hemorrhage in Canada. BJOG 114(6): 751-759.
24. Knight M, Callaghan WM, Berg C, Alexander S, Bouvier-Colle MH, et al. (2009) Trends in postpartum hemorrhage in high resource countries: a review and recommendations from the International Postpartum Hemorrhage Collaborative Group. BMC Pregnancy Childbirth 9: 55.
25. Lutomski JE, Byrne BM, Devane D, Greene R (2012) Increasing trends in atonic postpartum haemorrhage in Ireland: an 11-year population-based cohort study. BJOG 119(3): 306-314.
26. Mehrabadi A, Hutchton JA, Lee L, Kramer MS, Liston RM, et al. (2013) Epidemiological investigation of a temporal increase in atonic postpartum haemorrhage: a population-based retrospective cohort study. BJOG 120(7): 853-862.
27. Mehrabadi A, Hutchton JA, Lee L, Liston RM, Joseph KS (2012) Trends in postpartum hemorrhage from 2000 to 2009: a population-based study. BMC Pregnancy Childbirth 12: 108.
28. Rossen J, Okiand I, Nilsen OB, Eggebø TM (2010) Is there an increase of postpartum hemorrhage, and is severe hemorrhage associated with more frequent use of obstetric interventions? Acta Obstet Gynecol Scand 89(10): 1248-1255.
29. Callaghan WM, Kuklina EV, Berg CJ (2010) Trends in postpartum hemorrhage: United States, 1994-2006. Am J Obstet Gynecol 202(4): 351.e1-353.e6.
30. Registrar General of India (2011) Sample registration system bulletin on maternal mortality in India 2007-2009. Office of the Registrar General of India, New Delhi, India.
31. World Health Organization, UNICEF, UNFPA, The World Bank (2012) Trends in maternal mortality: 1990 to 2010. WHO, UNICEF, UNFPA
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32. United Nations (2015) UN Millennium Development Goals.
33. Bhat PN, Naveenatham K, Rajan SL (1995) Maternal Mortality in India: Estimates from a Regression Model. Stud Fam Plann 26(4): 217-232.
34. Amy JJ (1998) Severe Postpartum Hemorrhage: A Rational Approach. Natl Med J India 11(2): 86-88.
35. (2006) Registrar, General, India and Centre for Global Health Research, Maternal Mortality in India, 1997-2003: Trends, Causes and Risk Factors, New Delhi: Registrar General, India. p. 1-40.
36. Devi KP, Singh LR, Singh LB, Singh MR, Singh NN (2015) Postpartum Hemorrhage and Maternal Deaths in North East India. Open Journal of Obstetrics and Gynecology 5: 635-638.
37. Dutta DK (2012) Insight Maternal Mortality, an Indian Facebook. Jaypee Brothers Medical Publishers Pvt. Ltd, New Delhi, India. p. 1-4.
38. Bhat RP, Navada MH, Rao SV, Ngarathra G (2013) Evaluation of Obstetric Admissions to Intensive Care Unit of Tertiary Referral Center in Coastal India. Indian Journal of Critical Care Medicine 17(1):34-37.
39. Sharma N (2001) Maternal mortality - a retrospective study of ten years. J Obstet Gynaecol Ind 51: 60-62.
40. Mukherji J, Ganguly RP, Saha SK (2001) Maternal mortality due to haemorrhage with emphasis on post partum haemorrhage. J Obstet Gynaecol Ind 51: 130-133.
41. Jackson KW, Albert JR, Schemmer GK, Elliot M, Humphrey A, et al. (2001) A randomized controlled trial comparing oxytocin administration before and after placental delivery in the prevention of postpartum hemorrh. Am J Obstet Gynecol 185(4): 873-877.
42. Royal College of Obstetricians and Gynecologists (2011) Prevention and management of postpartum haemorrhage. Green-top Guideline No. 52, p. 1-24.
43. (2014) Intrapartum care: care of healthy women and their babies during childbirth, NICE Clinical Guidelines [CG190].
44. Blomberg M (2011) Maternal obesity and risk of postpartum hemorrhage. Obstet Gynecol 118(3): 561-568.
45. Lalonde A (2012) FIGO Guidelines: Prevention and treatment of postpartum hemorrhage in low-resource settings. Int J Gynaecol Obstet 117(2): 108-118.
46. Society of Obstetrics and Gynecology of Canada (2008) Postpartum hemorrhage. ALARM Manual. (15th edn).
47. Kwast BE (1991) Postpartum hemorrhage: its contribution to maternal mortality. Midwifery 7(2): 64-70.
48. World Health Organization (1991) Maternal Mortality: A Global Factbook. WHO Geneva, Switzerland.
49. World Health Organization (WHO) WHO Recommendations for the Prevention and Treatment of Postpartum Haemorrhage. WHO, Geneva, Switzerland, p. 1-48.
50. Begley CM, Gyte GM, Murphy DJ, Devane D, McDonald SJ, et al. (2010) Active versus expectant management for women in the third stage of labour. Cochrane Database Syst Rev (7): CD007412.
51. Geelhoed D, Visser L, Agordzo P, Asare K, Leeuwen JS, et al. (2002) Active versus expectant management of the third stage of labor in rural Ghana. Acta Obstet Gynecol Scand 81(2): 172-173.
52. International Confederation of Midwives, International Federation of Gynaecology and Obstetrics (2004) Joint statement management of the third stage of labour to prevent post-partum haemorrhage. The Hague, ICM, FIGO, London.
53. Kongnyuy EJ, Mlava, G, Broek Nvd (2008) Using Criteria-Based Audit to Improve the Management of Postpartum Haemorrhage in Resource Limited Countries: A Case Study of Malawi. Matern Child Health J 13(6):873-878.
54. Begley CM, Gyte GM, Devane D, McGuire W, Weeks A (2011) Active versus expectant management for women in the third stage of labour: Cochrane Database Syst Rev (11): CD007412.
55. Althabe F, Alemán, Tomasso G, Gibbons L, Vitureira G, et al. (2009) A pilot randomized controlled trial of controlled cord traction to reduce postpartum blood loss. Int J Gynaecol Obstet 107(1): 4-7.
56. Deneux-Tharaux C, Sentilhes L, Maillard E, Closset E, Vardon D, et al. (2013) Effect of routine controlled cord traction as part of the active management of the third stage of labour on postpartum haemorrhage: multicentre randomised controlled trial (TRACOR). BMJ 346:f1541.
57. Guiménezoglu AM, Lumbiganon P, Landoulsi S, Widmer M, Abdel-Aleem H, et al. (2012) Active management of the third stage of labour with and without controlled cord traction: a randomised, controlled, non-inferiority trial. Lancet 379(9827): 1721-1727.
58. McDonald SJ, Middleton P, Dowswell T, Morris PS (2013) Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes [review]. Cochrane Database Syst Rev 7: CD004074.
59. Cotter AM, Ness A, Tolosa JR (2001) Prophylactic oxytocin for the third stage of labour: [review]. Cochrane Database of Systematic Reviews 4: CD001808.
60. Güngördük K, Asicioglu O, Besimoglu B, Gündördük OC, Yıldırım G, et al. (2010) Using intravascular vein injection of oxytocin in routine practice with active management of the third stage of labor: a randomized controlled trial. Obstet Gynecol 116(3): 619-624.
61. Puri M, Taneja P, Gami N, Rehan HS (2012) Effects of different doses of intravascular oxytocin on the third stage of labor. Int J Gynaecol Obstet 118(3): 210-212.
62. Liabsuetrakul T, Choobun T, Peeyananjarassri K, Islam QM (2007) Prophylactic use of ergot alkaloids in the third stage of labour [review]. Cochrane Database Syst Rev (2): CD000546.
63. Boucher M, Horbay GL, Griffin P, Deschamps Y, Desjardins C, et al. (1998) Double-blind, randomized comparison of the effect of carboplatin and oxytocin on intraoperative blood loss and urine tone of patients undergoing caesarean sections. J Perinatol 18(3): 202-207.
64. Dansereau J, Joshi AK, Helewa ME, Donan TA, Lange IR, et al. (1999) Double-blind comparison of carboplatin versus oxytocin in prevention of uterine atony after caesarean section. Am J Obstet Gynecol 180(3 Pt 1): 670-676.
65. WHO (2010) Trends in Maternal Mortality: 1990 to 2008. Estimates developed by WHO, UNICEF, UNFPA and The World Bank. World Health Organization, Geneva.
66. Countdown Coverage Writing Group; Countdown to 2015 Core Group, Bryce J, Daelmans B, Dwivedi A, et al. (2008) Countdown to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. Lancet 371(9620): 1247-1258.

67. Houweling TAJ, Ronsmans C, Campbell OMR, Kunst AE (2007) Huge poor-rich inequalities in maternity care: an international comparative study of maternity and child care in developing countries. Bull World Health Organ 85(10): 745-754.

68. CSDH (2008) Closing the gap in a generation: health equity through action on the social determinants of health. Final report of the commission on Social Determinants of health. WHO, Geneva, pp. 1-256.

69. Gabrysch S, Campbell O (2009) Still too far to walk: literature review of the determinants of delivery service use. BMC Pregnancy and Childbirth 9: 34.

70. Paul BK, Rumsey DJ (2002) Utilization of health facilities and trained birth attendants for childbirth in rural Bangladesh: an empirical study. Soc Sci Med 54(12): 1755-1765.

71. Morrison J, Thapa R, Hartley S, Osrin D, Manandhar M, et al. (2012) Understanding how women’s groups improve maternal and newborn health in Makwanpur, Nepal: a qualitative study. Int Health 2(1): 25-35.