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■ Original Article

The Effectiveness of Rectal Misoprostol after Child Birth in Reduction of Postpartum Blood Loss at the National Hospital Abuja

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ABSTRACT

Background: Over the years postpartum haemorrhage (PPH) remained an important cause of maternal morbidity and mortality. Efforts to reduce the incidence of PPH resulted in the introduction of active management of third stage of labour. The use of rectal misoprostol in the immediate postpartum period has been reported to reduce postpartum haemorrhage. ***Aim of the study:*** The study seeks to determine the efficacy of administering prophylactic 600 microgram rectal misoprostol immediately after the delivery of placenta in reducing postpartum blood loss. **Methods:** This was a prospective comparative study in which eligible consenting parturients were randomized into two groups. In addition to other measures of active management of third stage of labour, the study group received 600 micrograms of rectal misoprostol immediately after delivering the placenta. The primary outcomes measured were estimated blood loss and haemoglobin change from the intrapartum value. The secondary outcomes were misoprostol side effects and need for blood transfusion. **Results:** Three hundred and twenty parturients were recruited for the study but 318 were analysed. One hundred and fifty-three were randomised to study group while 165 were in control group. There were statistically significant differences in the estimated mean blood loss and mean haemoglobin change of the two groups (P<0.0001). The estimated mean blood loss and mean haemoglobin change in the study group were 153 ± 45.1ml and 0.5 ± 0.2g/dl respectively; while in the control group were 230.6 ± 76.9ml and 0.8 ±0.3g/dl respectively. Thirty seven percent of control group had estimated blood loss = 250mls while 2.6% of study group had estimated blood loss = 250mls. Only 1 person in study and 2 persons in control groups received blood transfusion. Sixteen (9.7%) in control group and 6 (3.9%) in study group received additional

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uterotonic agent. The difference was statistically significant with p value of 0.005. Fifteen (9.8%) of the study group had abdominal pain, 24 (15.7%) had shivery and 9 (5.9%) had nausea. However, only shivering reached statistical significance (p=0.028). All the recorded side effects were self-limiting and there was no maternal death. **Conclusion:** Prophylactic 600 microgram rectal misoprostol given immediately after delivery of the placenta is effective in reducing postpartum blood loss and the need for blood transfusion.

Keywords: Misoprostol, postpartum haemorrhage, haemoglobin change.

Introduction

Pregnancy and child birth involve significant health risks even among women without existing health problems. A report in 2014 revealed that about 830 women died from pregnancy and childbirth complications around the world daily. Almost all of these deaths (about 99%) occurred in low-resource income settings, and most could have been prevented.[1] For every maternal death, 20-30 women suffer varying degrees of disability.[2] Many of the deaths and complications arise from severe bleeding during and after pregnancy and child birth.[3]

Postpartum haemorrhage (PPH) is the single most important cause of maternal death worldwide.[4,5] Postpartum haemorrhage occurs in about 10.5% of births and accounts for over 130 000 maternal deaths annually.[6] In our environment, postpartum haemorrhage is the commonest cause of maternal mortality.[7,8,9] Even if a woman survives postpartum haemorrhage, she can be severely affected and suffer from continuing health problems. Postpartum haemorrhage contributes about 6.7-25% of the 58,500 maternal deaths recorded in Nigeria every year.[7,10,11,12] University of Port Harcourt Teaching Hospital (UPTH) 2011 annual report showed that the maternal mortality rate at UPTH was 792.1/100,000 deliveries with primary PPH accounting for 17.3% of the maternal deaths.[13] A study in North-central Nigeria reported that PPH accounted for 34% of maternal mortality.[14] While another study in Enugu reported PPH as responsible for 18% of maternal mortality.[15]

Uterine atony is the commonest cause of PPH. A study from Ilorin, reported that is responsible for 70% of postpartum haemorrhage.[16] Other causes include retained products of conception, uterine inversion, genital tract laceration and ruptured uterus.[16] Active management of labour has been largely employed in labour management for over a decade and is known to reduce blood loss by about 30%.[8] Despite that, many women still lose significant amount of blood during and after delivery.[9] Most of these women in developing countries go into labour with borderline haemoglobin values, thus minimal blood loss may become critical.[17]

Primary postpartum haemorrhage (PPH) is the most common form of major obstetric haemorrhage. Traditionally, PPH is referred to as the loss of 500 ml or more of blood from the genital tract within 24 hours of the birth of a baby.[18] It is also defined as loss of any amount of blood from the genital tract that causes cardio-pulmonary compromise in the first 24hrs of childbirth. Blood transfusion which may alleviate the anaemia and shorten hospital stay in some cases is not without risks as it carries risks of blood transfusion reactions and infections, especially Human Immunodeficiency Virus (HIV) and Hepatitis B.[19] Unavailability of blood bank in most hospitals in the rural settings makes prompt transfusion impossible when needed thus contributing to poor outcome. In many centres where blood bank is available, poor supply of electricity affects proper functioning of the blood bank. Poor or non-existence of referral system also affects prompt referral of patients to other facilities. Invariably, most rural healthcare centres do not have adequate facilities to handle postpartum haemorrhage. Consequent upon the fact that PPH may be fatal or result in serious adverse medical problems, any

method which will help to reduce postpartum blood loss will be of great importance.

Misoprostol is a synthetic analogue of prostaglandin E1. It is heat stable and effective uterotonic agent which can be used for the treatment of uterine atony. Unlike other uterotonic agents, it is relatively inexpensive (<1 Dollar), can be taken orally, introduced vaginally, rectally or sublingually, does not need refrigeration, and has a long shelf-life.[20] Its advantages in obstetrics and gynaecology especially for prevention and management of postpartum haemorrhage has been demonstrated in some studies.[21,22,23]

Several studies have examined the role of misoprostol in preventing PPH and proven its safety and efficacy.[23] Efficacy of misoprostol in reducing postpartum blood loss thus preventing PPH has been demonstrated in some reports in Afghanistan, Indonesia, Nepal, Tanzania, Ethiopia and Nigeria.[24-29]

A recent meta-analysis provided evidence to support recommendation for prophylactic use of misoprostol in preventing primary postpartum haemorrhage.[30] In a community where there is availability and use of misoprostol after childbirth, there is usually a reduced frequency of excessive bleeding and the need for emergency referral following postpartum haemorrhage as compared with data from a control area where misoprostol was not available.[31]

Misoprostol is not without some documented side effects. When used in appropriate dosage for prevention of postpartum blood loss, these side effects are tolerable and ranges from nausea and vomiting to shivering, high grade pyrexia, bronchospasm, cramping pains and diarrhoea. These side effects are related to dose and route of administration.[32,33,34] Its side effects on the new born are insignificant as misoprostol appear in negligible quantity in colostrum following maternal exposure.[35] Since most women in resource poor economic settings are anaemic in pregnancy, little amount of blood loss may have severe consequences including maternal death. Thus, this study, seek to examine whether prophylactic use of misoprostol with Active Management of Third Stage of Labour will be a strong tool in the hands of obstetricians and midwives in reducing maternal morbidity and mortality resulting from postpartum blood loss. If effective, this would also reduce the problems associated with the need for transfusion of blood and blood products in management of severe haemorrhage.

Methods

This was a prospective comparative study conducted in the Department of Obstetrics and Gynaecology of one secondary hospital in Nasarawa state and one tertiary hospital in Abuja, Nigeria. The study was over a period of six months, May to October 2018. Approval for the study was obtained from the institutions Ethics Committee and written informed consent was obtained from the parturient. A minimum sample size of 264 participants was estimated for the study. However, a sample size used for the study was 320. The criteria for inclusion in the study were parturient in active phase of labour with anticipated spontaneous vaginal delivery, term pregnancy and singleton pregnancy in cephalic presentation. Patients who met the inclusion criteria were recruited consecutively as they presented for admission in the labour ward. Information obtained included patient's age, marital status, educational level, occupation, booking status, parity, gestational age and intrapartum haemo-globin level.

Randomisation

A random sequence of numbers was computer generated using a sample size of 320. Sequentially numbered packs containing three white tablets of misoprostol (manufactured by Piramal Healthcare UK Limited, Morpeth Whalton Road, Northumberland NE61 3YA, United Kingdom) or a placebo, were prepared using the random numbers to determine their content. One hundred and fifty-five packs contained 600 microgram of misoprostol each while another 165 packs contained the placebo. The drug and placebo were prepared in batches by a pharmacist who was not involved in the study and was stored in the labour ward cupboard. All were designated with the random

numbers. Both groups received Active Management of Third Stage of Labour by a midwife or medical doctor that conducted the delivery, but were not involved in the assessment of blood loss or final analysis of the results. The designation of the packs was only known to the pharmacist and this was made known to the research team at the time of final analysis. As patients were recruited, they were given the drug from the pool of already prepared packs.

Clinical Procedure

Once labour was confirmed, about two millilitres of maternal peripheral blood was collected from all consented pregnant women for haemoglobin estimation. The sample was collected from the forearm of each participant by venepuncture technique into sterile EDTA container. The sample bottle labelled with patient unique identification number which included patient's study number and hospital number.

Measurement of Blood Loss

To ensure accurate measurement of blood loss, a combination of direct measurement and gravimetric methods were used. Difference in haemoglobin levels before and after delivery was determined.

After the delivery of the baby and the immediate clamping of the umbilical cord, two pre-weighed under pads were spread underneath the patient to optimize blood collection. 10IU of oxytocin was then injected slowly intramuscularly, as part of the routine active management of the third stage of labour as practiced in the centres. Thereafter, an assistant would open the assigned packet and hand the enclosed tablets to the accoucheur for insertion as far into the rectum as the index finger could go immediately after delivery of the placenta. The placenta was delivered by controlled cord traction and if episiotomy was given, it was repaired promptly. After inserting the rectal tablets, the accoucheur removed the outer pair of gloves and continued with the cleaning of the parturient. Subsequently, the tone of the uterus was assessed quarter hourly until two hours postpartum by the researcher or the labour ward registrar who had been trained for this purpose, and an additional uterotonic was administered if the uterus was adjudged to be atonic.

The under pads measurement of blood loss was taken by the researcher or the labour ward registrar once bleeding had subsided, by weighing the pads and subtracting the pre-weight. Subsequent blood losses up till two hours postpartum were measured by the application of perineal pads of known weight to the perineum. These pads were then weighed two hours postpartum, and the blood loss estimated from the pads and linens weight gain as: 1g≈ 1ml. The patients' vital signs were also recorded two hours postpartum and the occurrence of specific side effects such as shivering, pyrexia or vomiting noted. If the clinical condition remained stable, the parturient was transferred to the Postnatal Ward thereafter. However, in the event that bleeding persisted, subsequent management was in accordance with the laid down protocol for the management of primary postpartum haemorrhage.

In the Postnatal Ward, another venous blood sample is collected 24 hours postpartum for haemoglobin level check. This was compared with the intrapartum measurement to determine the change in haemoglobin level. Any need for blood transfusion was then decided in line with the blood transfusion policy of the department, withholding blood transfusion if haemoglobin is=8g/dl or more and patient is not symptomatic.

Data Collection

The study data collection sheet was used to obtain information on socio-demographic characteristics, the intrapartum and postpartum blood loss, direct and gravimetric estimated blood loss.

Data Analysis

The result was collated and data analysed with the aid of Statistical Package for Social Science (SPSS) version 23. A p-value less than 0.05 at 95% confidence interval was regarded as statistically significant. Continuous data were described using

means and standard deviation while categorical variables were described using percentages. Chi square test or Fisher's exact test where appropriate was used to test the significant difference between categorical variables while test of significance for continuous variables were analysed using T-test. Baseline analysis involved comparing of the baseline characteristics between the two study arms. Hypothesis testing was done to determine if there is a significant difference in amount of postpartum blood loss between patients who received prophylactic misoprostol and the control group.

Result

A total of 320 parturients were recruited and participated in this study, but two of them were excluded from statistical analysis due to incomplete assessment of haemoglobin change. Analysis was thus based on 318 parturients (Misoprostol=153 or 48.1%; placebo=165 or 51.9%). The groups were similar regarding important baseline characteristics such as age, parity, occupation, level of education and intrapartum haemoglobin as shown in Table 1. This made it possible to attribute any differences observed between the groups to the respective treatments (misoprostol or placebo) administered. As shown in Table 2, the intrapartum haemoglobin in both study and control groups was 11.5 ± 1.3. The estimated blood loss in study group was 153 ± 45.1 while that of control group was 230.6 ± 76.9. This difference was statistically significant with p-value of <0.0001. The change in intrapartum haemoglobin level in the study group was 0.5 ± 0.2 while that of control group was 0.8 ± 0.3. This was statistically significant with P-value of <0.0001. As shown in Table 3, in the study group, only 2.6% had estimated blood loss = 250mls while that of control group were 37%. This was statistically significant (<0.0001).

The need for additional uterotonics was 16(9.7%) in control group and 6(3.9%) in study group. The result showed a statistically significant difference between the two groups (p<0.005). The commonest side effect in the misoprostol group was shivering in 24 (15.7%) as shown in Table 4. However, there were no observed statistically significant differences in the side effects in the two groups except for shivering. Women who had misoprostol had higher incidence of shivering than the placebo group (15.7% vs 6.7%; p=0.028).

Table 1: Baseline Characteristics of Study (Misoprostol) and Control (Placebo) Groups

Variables	Misoprostol (*n*=153)	Placebo (*n*=165)	Overall (*n*=318)	Test of significance Test value; *P*
Maternal Age (years)	27.2 ± 5.1	28.2 ± 5.0	28.0 ± 5.1	0.816[t]; 0.415*
Maternal Age Group (years)				
≥ *24 years* [N (%)]	46 (30.1)	46 (27.9)	92 (28.9)	
25 - *34 years* [N (%)]	95 (62.1)	101 (61.2)	196 (61.6)	
35 - *44 years* [N (%)]	12 (7.8)	18 (10.9)	30 (9.4)	0.932[a]; 0.627*
Gestational Age (weeks)	39.0 ± 1.0	39.0 ± 1.1	39.0 ± 1.1	0.276[t]; 0.783*
Baby's weight (kg)	3.2 ± 0.4	3.2 ± 0.4	3.2 ± 0.4	0.059[t]; 0.953*
Educational Status				
Primary [N (%)]	42 (27.5)	36 (21.8)	78 (24.5)	
Secondary [N (%)]	46(30.1)	50 (30.3)	96 (30.2)	
Tertiary [N (%)]	65 (42.5)	79 (47.9)	144 (45.3)	1.539[a]; 0.0.463*

Marital Status					
Single	[N (%)]	7 (4.6)	3 (1.8)	10 (3.1)	
Married	[N (%)]	144 (94.1)	159 (96.4)	303 (95.3)	
Single ever married	[N (%)]	2 (1.4)	3 (1.8)	5 (1.5)	0.290[a]; 0.352*
Booking Status					
Unbooked	[N (%)]	46 (27.9)	38 (24.8)	84 (26.4)	
Booked	[N (%)]	119 (72.1)	115 (75.2)	234 (73.6)	0.378[e]; 0.313*

t = Test; a = Chi-Square test; e = Fisher's exact test; * = Not statistically significant at P>0.05;

Table 2: Estimated Blood loss and Haemoglobin change in Women that received Misoprostol (Study group) and those that received Placebo (Control group)

Variables	Misoprostol (*n*=153)	Placebo (*n*=165)	Overall (*n*=318)	Test of significance Test value; *P*
Intrapartum Hb (Mean ± SD)	11.5 ± 1.3	11.5 ± 1.3	11.5 ± 1.3	0.402t ; 0.688*
Postpartum Hb (Mean ± SD)	10.9 ± 1.4	10.6 ± 1.3	10.8 ± 1.5	1.806t ; 0.070*
HB difference (Mean ± SD)	0.5 ± 0.2	0.8 ± 0.3	0.7 ± 0.3	9.123t; <0.0001**
Estimated Blood Loss (Mean ± SD)	153 ± 45.1	230.6 ± 76.9	193.5 ± 79.1	9.945t; <0.0001**

t = t Test; * = Not statistically significant at P>0.05; ** = Statistically significant at P<0.0001

Table 3: Outcome variables of parturient randomized to rectal misoprostol and placebo

Variable	Placebo (*n*=165) N (%)	Misoprostol (*n*=153) N (%)	Odds ratio (95% CI)	P
Episiotomy				
No	132 (80.0)	114 (74.5)		
Yes	33 (20.0)	39 (25.5)	1.364 (0.808- 2.318)	0.150*
Blood transfusion				
No	163 (98.2)	152 (99.3)		
Yes	2 (1.2)	1 (0.7)	0.536 (0.048- 5.974)	0.528*
Added Uterotonics (Oxytocin)				
No	149 (90.3)	147 (96.1)		
Yes	16 (9.7)	6(3.9)	0.155 (0.035- 0.703	0.005**
Estimated Blood loss				
<250mls	104 (63.0)	149 (97.4)		
= 250mls	61 (37.0)	4 (2.6)	0.046 (0. 016- 0.130)	<0.0001**

* = Not statistically significant at P>0.05; ** = Statistically significant at P<0.01

Table 4: Side effects on women that received misoprostol and those that received placebo

Variable	Placebo (*n*=165) N (%)	Misoprostol (*n*=153) N (%)	P-value
No side effect	116 (70.3)	96 (62.7)	0.170*
Abdominal Pain	19 (11.5)	15 (9.8)	0.493*
Dizziness	12 (7.3)	7 (4.6)	0.251*
Headache	2 (1.2)	1 (0.7)	0.564*
Nausea	4 (2.4)	9 (5.9)	0.166*
Shivery	11 (6.7)	24 (15.7)	0.028**
Fever	1 (0.6)	1 (0.7)	-

*= Not statistically significant at P>0.05; ** = Statistically significant at P<0.05

Discussion

Recent systematic review concluded that ergometrine plus oxytocin, carbetocin, and misoprostol plus oxytocin were more effective in preventing primary postpartum haemorrhage than the current standard oxytocin.[36] Misoprostol plus oxytocin combination evidence is less consistent which could be as a result of different routes and doses used in the studies.[36]

To the best of our knowledge, the possible role of rectal misoprostol as an adjunct to oxytocin for prevention of PPH in patients with no identifiable risk factors has not been previously studied in our locality.

This study showed that there was significant difference between adjunctive rectal misoprostol (600μg) plus active management of third stage of labour compared to active management of third stage of labour only, with respect to the mean estimated blood loss following delivery of the baby and change in intrapartum haemoglobin level. The difference between intrapartum and postpartum haemoglobin level was significantly higher in control group (0.8 ± 0.3g/dL) compared to the study group (0.5 ± 0.2g/dL) at t=9.123; p<0.0001. Also, the estimated blood loss was significantly higher among women in control (230.6 ± 76.9g/dL) than women in the study group (153 ± 45.1g/dL) and t=9.945; P<0.0001. Both groups were the same in terms of having same socio-demographic characteristics and no identifiable risk for developing PPH. This finding is similar to the study by Mirteimouri et al[37] which showed that adjunctive misoprostol can decrease postpartum hemorrhage and also can decrease amount of blood loss compared to oxytocin. Shrestha et al[38] showed that misoprostol is as effective as oxytocin in preventing PPH.

This finding is consistent with the results of other studies done in Nigeria and around the world. At Ile-Ife, Nigeria, Afolabi et al[29] established that prophylactic administration of misoprostol in the third stage of labour could significantly reduce the incidence of primary PPH from 18% to 5%. The study was a prospective randomised controlled clinical trial in which 200 parturients at term who had vaginal delivery were randomly assigned into two groups: oral misoprostol and intramuscular oxytocin, after the delivery of the baby and the clamping of the umbilical cord. The study was unlike this study in which misoprostol was evaluated for use in augmentation of the routine Active Management of Third Stage of Labour.

However, the findings of our study were inconsistent with that of Hofmeyr et al[39] in a hospital-based, decentralized, multi-centre, randomized, placebo-controlled, double-blind trial, in which 1103 women were enrolled in 4 hospitals in Ibadan Nigeria, Johannesburg South Africa and Kampala Uganda. Participants received

a sublingual dose of 400 microgram of misoprostol or a placebo, in addition to standard Active Management of the Third Stage of Labour, after vaginal birth. The study found no benefit when 400 micrograms of sublingual misoprostol was used to augment Active Management of Third Stage of Labour; though the route of administration and dose of the drug differs with this study.

One of the strengths of our study is the employment of an objective method of blood loss measurement (change in haemoglobin level), and use of two methods of blood loss estimation (direct and gravimetric methods) rather than visual estimation as was done in many previous misoprostol studies[40,41,42] with the result that the mean blood loss for each group could be more accurately and reliably determined. Additionally, the blinding (parturient blinded) design significantly eliminates bias, as the occurrence of shivering, abdominal cramp, nausea or vomiting which are recognized as common side effects of misoprostol occurred in both arms of the study groups.

The estimated mean blood loss was higher (230.6 ± 76.9mL) in the control group than in the study group (153 ± 45.1mL), the difference was statistically significant ($p<0.0001$). The value in the control group was higher than the 217 ± 197mL reported by Gharoro and Enabudoso in Benin using visual estimation.[43] This is not unexpected, as visual estimation is known to be associated with significant underestimation of blood loss[44,45] whereas direct and gravimetric methods used in our study has been shown to possess a high level of accuracy relative to photo spectrometry which is the gold standard for blood loss estimation.[42]

Using similar methodology to this present study for blood loss measurement in two hundred low risk parturients in India, Gupta et al[46] reported a mean intrapartum blood loss of 161.67 ± 76.81mL in those that received misoprostol which was higher than the 150.97 ± 69.14mL recorded in patients receiving oxytocin for active management of the third stage of labour, but the difference was not statistically significant. The difference in the relationship that was observed between the study and control arms in our study most probably due to difference in the context. In our study both arms received oxytocin as the standard for active management of third stage, the study group received in addition, 600μg misoprostol rectally.

One randomized-controlled trial was identified in the literature evaluating the role of adjunctive misoprostol in the prevention of post-partum haemorrhage in patients with no known risk factors. In that study, Mirteimouri et al[37] randomized 400 parturients with no risk factors for PPH to receive either rectal misoprostol (400μg) or placebo after delivery. The study showed a reduction in the need for additional uterotonics among the misoprostol group. There was also a significant reduction in the need for blood transfusion or hysterectomy in the misoprostol group, and their haematocrit drop was less.

Our study also showed a significant reduction in the need for additional uterotonics among the study group, there was rare need for blood transfusion, and drop in haemoglobin level was less in the study group compared to the control group. Rectal misoprostol though has slow uptake but a prolonged duration of action compared to oral and sublingual misoprostol.[39] This makes it a suitable route of administration in case of prevention of PPH as it has fewer side effects and it would have attained its peak level by the time uterine atony and PPH would be developing had it not been given.[32,34]

This study attested to the safety of misoprostol when used prophylactically in prevention of postpartum bleeding. Ninety-six (62.7%) of the study group had no side effects of the drug compared to 116 (70.3%) in the control group. Fifteen (9.8%) of the study subjects had abdominal pain, 24(15.7%) had shivering, 9(5.9%) had nausea, 7(4.6%) had dizziness and only 1(0.7%) had fever. Of all these side effects, only shivery reached statistical significance (15.7% vs 6.7%; P= 0.028). These side effects were mainly self-limiting.

This finding was consistent with that of Afolabi et al, Derman et al, Sanghvi et al, that corroborated the safety profile of misoprostol when used for

prevention and management of postpartum haemorrhage.[14,31,40] The studies similarly reported the side effects of misoprostol to include nausea, vomiting, diarrhoea, shivering and abdominal cramps. These side effects were largely self-limiting and dose dependent as was observed in the present study.

Conclusion

This study shows that prophylactic 600 microgram rectal misoprostol given following active management of third stage of labour further reduces postpartum blood loss. There is therefore reduced need for blood transfusion especially in those with no identifiable risk for primary postpartum haemorrhage. It also has good safety profile and not associated with any major adverse effects. Because of these advantages, misoprostol should be considered for inclusion in the delivery packs for easy access and use especially in the primary health care centres.

Declaration of Conflict of Interest

No conflict of interest declared.

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References

1. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB and Daniels JD et al. Global Causes of Maternal Death: A WHO Systematic Analysis. Lancet Global Health, 2014;2(6): e323-e333. doi: 10.1016/ S2214-109X (14)70227-X.
2. UNFPA, Trends in Maternal Mortality: 1990-2010. UNFPA. Accessed 20th May 2012. Available at: https://www.unfpa.org/public/global
3. Nazir N, Shehzad S and Mehmood M. Rectal Misoprostol versus Intravenous Oxytocin in the Active Management of the Third Stage of Labour. APMC 2016;10(4):206-212
4. Nabila T, Mehnaz K and Rashida P. Effectiveness of misoprostol in the prevention of postpartum hemorrhage. PJMHS. 2015;9 (1):268-270
5. AbouZahr C. Global burden of maternal death and disability. Br Med Bull 2003; 67:111
6. AbouZahr C. Global burden of maternal death and disability. In: Rodeck C, ed. Reducing maternal death and disability in pregnancy. Oxford: Oxford University Press; 2003:1-11
7. Ajenifuja KO, Adepiti CO and Ogunniyi SO, Postpartum haemorrhage in a teaching hospital in Nigeria: a 5-year experience. Afr Health Sci. 2010; 10(1): 71-74.
8. Nkwocha GC, Anya SE and Anya AE. Obstetric mortality in a Nigerian general hospital. Niger J Med 2006; 15:75-6.
9. Oladapo OT, Akinola OI, Fawole AO, Adeyemi AS, Adegbola O and Loto OM et al.; Nigerian AMTSL Group. Active management of third stage of labour: evidence versus practice. Acta Obstet Gynecol Scand 2009; 88 (11): 1252-1260.
10. Ezugwu EC, Agu PU, Nwoke MO and Ezugwu FO. Reducing maternal deaths in a low resource setting in Nigeria, Nigerian J. of Clinical Practice 2014; 17: 62-66
11. WHO. Attending to 136 Million births every year, make every mother and child count. World Health Organization. Geneva 2005:62-63.
12. Derman RJ, Kodkany BS, Goudar SS, Geller SE, Naik VA and Bellad MB, et al. Oral misoprostol in preventing postpartum haemorrhage in resource poor communities: a randomized control trial. Lancet 2006; 368:12481253
13. University of Port Harcourt Teaching Hospital: Obstetrics and Gynaecology Annual report 2011.
14. Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, Shackelford KA, Steiner C and Heuton KR et al. Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014 Sep 13;384(9947):980-1004.

doi: 10.1016/S0140-6736(14)60696-6. Epub 2014 May 2.
15. Chukudebelu WO and Ozumba BC. Maternal mortality at the University of Nigeria Teaching Hospital, Enugu: a 10-year survey. Trop J Obstet Gynaecol (Special Edition) 1988;1:236.
16. Adetoro OO. Primary PostPartum Haemorrhage in a University Hospital in Nigeria. West African Journal of Medicine 2008; (11)3 :172-178.
17. Bias JM, Eskes M, Bonsel GJ and Bleker OP. Postpartum haemorrhage in nulliparous women: incidence and risk factors in low and high risk women. A Dutch population-based cohort study on standard (>or =500ml) and severe (>or = 1000ml) postpartum haemorrhage. Eur J Obstet Gynecol Reprod Biol. 2004; 115:166172.
18. Mousa HA, Blum J, Abou El, Senoun G, Shakur H and Alfirevic Z. Treatment for primary postpartum haemorrhage. Cochrane Database Syst Rev. 2014;2: Cd003249
19. International centre for diarrhoeal disease research, Bangladesh Study of Blood-transfusion Services in Maharashtra and Gujarat States, India. J Health Popul Nutr. 2009; 27(2): 259-270.
20. Andersen JT, Mastrogiannis D, Andersen NL, Petersen M, Broedbaek K and Cejvanovic V et al. Diclofenac/misoprostol during early pregnancy and the risk of miscarriage: a Danish nationwide cohort study. Arch Gynecol Obstet 2016; 294(2):245-50.
21. Owonikoko KM, Arowojolu AO and Okunlola MA. Effect of sublingual misoprostol versus intravenous oxytocin on reducing blood loss at Cesarean section in Nigeria: a randomized controlled trial. J Obstet Gynaecol Res 2011 ;37(7):715-21.
22. Prata N, Sreevisa A, Greig F, Walsh J and Potts M. Setting priorities for safe motherhood interventions in a resource-scarce setting, Health Policy. 2010; 94:113
23. Bradley S, Prata N, Young-Lin N and Bishai DM. Cost-effectiveness of misoprostol to control postpartum haemorrhage in low-resource settings. Int J of Gynecol and Obstet 2007; 97: 52-56
24. Sanghvi H, Ansari N, Prata NJV, Gibson H, Ehsan AT and Smith JM. Prevention of postpartum hemorrhage at home birth in Afghanistan. Int J Gynaecol Obstet. 2010; 108:27681.
25. Sanghvi H, Wiknjosastro G, Chanpong G, Fishel J, Ahmed S and Zulkarnain M. Prevention of postpartum haemorrhage study, West Java, Indonesia. Baltimore, MD: JHPIEGO, Maternal and Neonatal Health Programme; 2004.
26. Rajbhandri S, Pun A, Hodgins S and Rajendra PK. Prevention of postpartum haemorrhage at home birth with use of misoprostol in Banke District, Nepal. Int J Gynaecol Obstet. 2006; 94:143144.
27. Prata N, Mbaruku G, Campbell M, Potts M and Vahidinia F. Controlling postpartum haemorrage after home births in Tanzania. Int J Gynecol Obstet. 2005; 90:5155.
28. Prata N, Gessessew A, Abraha AK, Holston M and Potts M. Prevention of postpartum haemorrhage: options for home birth in rural Ethiopia. Afr J Reprod Health. 2009;13:8795
29. Afolabi EO, Kuti O, Orji EO and Ogunniyi SO. Oral misoprostol versus intramuscular oxytocin in the active management of the third stage of labour. Singapore Med J 2010; 51(3): 207
30. Conde-Agudelo A, Nieto A, Rosas-Bermudez A and Romero R. Misoprostol to reduce intraoperative and postoperative hemorrhage during cesarean delivery: a systematic review and meta-analysis. Am J Obstet Gynecol. 2013;209(1):4041
31. Maternal and Neonatal Health Program. Preventing postpartum hemorrhage: a community-based approach proves effective in rural Indonesia. Baltimore USA: MNH Program, 2005.
32. Tang OS, Gemzell-Danielsson K and Ho PC. Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects. Int J Gynaecol Obstet 2010; 99 (Suppl 2):160167.
33. Lumbiganon P, Hofmeyr J, Gülmezoglu AM, Pinol A and Villar J. Misoprostol dose-related shivering and pyrexia in the third stage of labour. WHO Colaborative Trial of Misoprostol in the Management of the Third Stage of Labour. BJOG 1999; 106: 304-308.
34. Aubert J, Bejan-Angoulvant T and Jonville-Bera AP. [Pharmacology of misoprostol (pharmacokinetic data, adverse effects and teratogenic effects)]. J Gynecol Obstet Biol Reprod (Paris). 2014;43(2): 114-22.
35. Vallera C, Choi LO, Cha CM and Hong RW. Uterotonic Medications: Oxytocin, Methylergonovine, Carboprost, Misoprostol. Anesthesiol Clin. 2017;35(2):207-219.
36. Gallos DI, Williams HM and Price MJ. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis, Cochrane Database of Systematic Reviews, 2018 DOI: 10.1002/ 14651858.CD011689.
37. Mirteimouri M, Tara M, Teimouri B, Nahid S and Vaezi A. Efficacy of Rectal Misoprostol for Prevention of Postpartum Hemorrhage, Iran J Pharm Res. 2013 Spring; 12(2): 469474. PMCID: PMC3813228, PMID: 24250623.
38. Shrestha A, Dongol A, Chawla CD and Adhikari RK. Rectal misoprostol versus intramuscular oxytocin

for prevention of postpartum hemorrhage. Kathmandu Univ Med J (KUMJ). 2011;9(33):8-12.
39. Hofmeyr GJ, Fawole B, Mugerwa K, Godi PN, Blignaut Q and Mange L et al. Administration of 400 micrograms of misoprostol to augment routine active management of the third stage of labour. International journal of Gynaecology and Obstetrics. 2011; (112) 2:98-102.
40. Gülmezoglu AM, Forna F, Villar J and Hofmeyr GJ. Prostaglandins for preventing postpartum haemorrhage. Cochrane Database Syst. Rev. 2007:CD000494.
41. Hanan MF, Al Kadri, Bedayah K, Al Anazi and Hani MT. Visual estimation versus gravimetric measurement of postpartum blood loss: a prospective cohort study. Archives of Gynecology and Obstetrics 2011; 283(6): 1207- 1213
42. Patel A, Goudar SS and Geller SE. Drape estimation vs. visual assessment for estimating postpartum haemorrhage. Int J Gynecol Obstet, 2006;93:220-224
43. Gharoro EP, Enabudoso EJ. Relationship between visually estimated blood loss at delivery and postpartum change in haematocrit. J Obstet Gynaecol 2009;29(6):517-520
44. Hill JA, Fadel HE, Nelson MC, Nelson RM and Nelson GH. Blood loss at vaginal delivery. South Med J 1986 ;79 :188 92.
45. Gahres EE, Albert SN and Dodek SM. Intrapartum blood loss measured with Cr51-tagged erythrocytes. Obstet Gynecol 1962; 19:45562.
46. Gupta B, Jain V and Aggarwal N. Rectal misoprostol versus oxytocin in the prevention of postpartum haemorrhage A pilot study. Int J Gynecol Obstet. 2006;94(Suppl. 2): S139-S140.