



# A SURVEY OF DRUGS UTILIZED IN PRIMARY POST PARTUM HAEMORRHAGE AT A TERTIORY CARE TEACHING HOSPITAL

Dr Sheetal Hathila, \*Dr Chetan G. Parmar, Dr A J Singh,  
Dr G H Dumra

Junior lecturer, \*Assistant professor, Dean and professor Banas medical college, Professor and Head  
Department of Pharmacology AMC MET Medical College, Maninagar, Ahmadabad

## Abstract

**Introduction:** The most common type of obstetric hemorrhage is postpartum haemorrhage (PPH), mainly primary PPH. Primary PPH is defined according to WHO as blood loss of 500 ml in the first 24 h postpartum. Definitions vary in various parts of world and are often based on estimation of blood loss. It can also be defined as fall in haematocrit >10%. Major cause of avoidable visits to emergency room and hospitalizations at the time of very. **Materials and Methods:** It is Prospective, Observational study, approximately 115 prescriptions analysed. Written informed consent was taken from the eligible patients included in the study. Drugs data collected by reviewing the prescriptions prescribed. Data of all the 115 patients enter in Microsoft excel 2007 and analysed by using SPSS version 20.0 Software. Prescription pattern was evaluated by using WHO core drug prescribing indicators and US-FDA Drug Risk. **Results:** Among 115, only 34 (29.5%) patients had antenatal check-ups at least 3 visits while rest 81 (70.43%) were not booked. Maximum cases were between age group of 21-25 Which contribute to 57 (49.56%). Among 115 cases, 19 patients had medical disorders, among them most Common was hypertension which contribute to 10 cases (43.47%) followed by sickle cell disease 7 (30.43%). Only 3(13.04%) suffered from diabetes and cardiac diseases. **Conclusion:** Our study concludes that visual estimation of postpartum blood loss is an inaccurate method to determine the amount of blood loss in PPH, resulting in underestimation and misdiagnosis of PPH. Multigravidas have been found to have higher incidence of PPH. Regular antenatal check-ups and improvement obstetric education are mandatory to decrease the incidences of PPH. Apart from mechanical measures and oxytocin alone, some other Uterotonics drugs were needed to control the PPH, in patients with inadequate antenatal car.

**Keywords:** Primary postpartum haemorrhage, Uterotonic drugs, Survey of drugs

## INTRODUCTION

Drugs play an important role in improving maternal health and promoting Safe, rational and efficacious use of drugs during pregnancy prevents morbidity and mortality in mother and foetus. Oxytocin, methyl ergometrine, carboprost and misoprostol are different medical preparations used as uterotonics for prophylaxis and treatment of PPH. The main purpose of this study is to evaluate and generate accurate data which help in management of PPH at an early stage, so as to reduce the overall burden of maternal deaths resulting from PPH.

## MATERIALS AND METHODS

All patients admitted for delivery & ending up in PPH or presenting with PPH in outpatient department, casualty or referred from outside as PPH were included in this study. The data was collected from all the patients irrespective of age in a pre-designed Case report form after taking written informed consent from the patients and/or patient's relatives (Annexure 1). The Case report form includes patient's demographic details, indoor number, pregnancy duration, provisional diagnosis / chief complaints, investigations and treatment. All maternal complications were noted and recorded in prescription.

## INCLUSION CRITERIA

- (1) All patients admitted for delivery & ending up in PPH or presenting with PPH in outpatient department, casualty or referred from outside as PPH
- (2) Willingness to give written informed consent
- (3) Follow up for 24h to note outcome



## EXCLUSION CRITERIA

- 1) Patients with history of coagulation disorder
- 2) Patients who were taking heparin & warfarin.
- 3) Ante-partum haemorrhage
- 4) Not willing to give consent.
- 5) Known hypersensitivity to prostaglandin administration
- 6) Unconscious and patients unable to respond to verbal questions

## RESULTS

The demographic data

Table 1: Total number of booked and unbooked cases and

Type	No of cases	%
Booked	34	29.56
Unbooked	81	70.43
Total	115	100

Age in years	No of cases	%
16-20	9	7.82
21-25	54	46.9
26-30	38	33.04
31-35	12	10.43
36-40	2	1.73

	115	100
--	-----	-----

Among 115, only 34 (29.5%) patients had antenatal check-ups at least 3 visits while rest 81 (70.43%) were not booked. As youngest age group was 18 & oldest was 39 years, hence above class Interval was taken. Maximum cases were between age group of 21-25 which contribute to 57 (49.56%). The mean age was 25.5±4.14 years.

Table 2: Parity wise distribution of cases

Parity	No of cases	%
Primigravida	39	33.91
Multigravida	71	61.73
Grand multigravida	5	4.34
Total	115	100

Among 115 cases, most of them i.e. 72 (61.73%) were Multigravida.

Table 3: Medical condition related to cases

MEDICAL Condition	No of cases	%
Cardiac diseases	3	13.04
Hypertension	10	43.47
Diabetes mellitus	3	13.04
Sickle cell disease	7	30.43
Total	23	100

Among 115 cases, 19 patients had medical disorders, among them most Common was hypertension which contribute to 10 cases (43.47%) followed by sickle cell disease 7 (30.43%). Only 3(13.04%) suffered from diabetes and cardiac diseases.



Table4 Relation between hemodynamics at the time of child birth and post-partum anemia

	No of cases	Post-partum Hb < 7%
Hemodynamically stable (HB>11)	68 (100%)	15 (22.6%)
Hemodynamically unstable (HB<11)	47 (100%)	36 (77.3%)
Total	115(100%)	51 (100%)

Out of total 115 patients, 47 Hemodynamically unstable patients (36, 77.3%) decrease Hb which was higher than Hemodynamically stable patients (15, 22.6%) and it is highly statistically significant. (p<0.01, z=3.16).

Table5 Drug use pattern in primary PPH patients

Drug use pattern in primary PPH patients(n=115)	
	49(42.6%)
oxytocin + Methylergometrine	
oxytocin + Methylergometrine +carboprost	31(26.9%)
Oxytocine+ carboprost	25(21.7%)
Methylergometrine+ Misoprost	6(5.21%)
oxytocin+Methylergometrine+carboprost+blood transfusion	3(2.6%)
oxytocin+Methylergometrine+blood transfusion	1(0.86%)

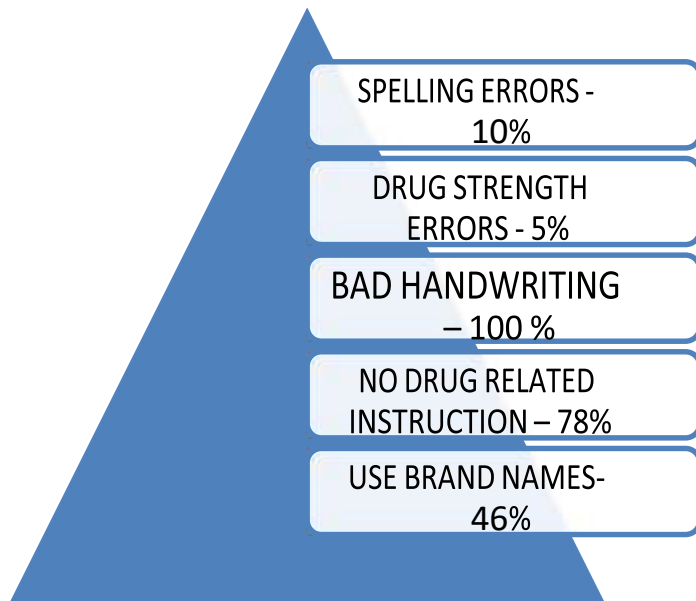
Out of total 115 primary PPH patients 49(42.6%) were cured with oxytocin + Methylergometrine regimen followed by oxytocin + Methylergometrine +carboprost 31(26.9%),Oxytocine+ carboprost25(21.7%), Methylergometrine+Misoprost6(5.21%), oxytocin+Methylergometrine+car boprost+blood transfusion 3(2.6%), oxytocin+Methylergometrine+blood transfusion1(0.86%).

Table 6Analysis of adverse drug reaction Analysis of Adverse Drug Reactions

Suspected Drug	Adverse Drug Reaction	No	Causality	Severity	Preventability	Treatment
WHO Modified assessment Hartwig and and Seigel Thornton's scale	Modified Schumock criteria		treatment		Symptomatic	
Oxytocin	Nausea and treatment	15	Possible	Mild	Not	Symptomatic vomiting preventable
Methylergometrine+ blood transfusion	Hypersensitivity reaction		2	Possible	Mild	Not preventable Symptomatic treatment
Misoprostol+ Methylergometrine	Shivering, Fever	1	Possible	Mild	Not preventable	Symptomatic treatment
Oxytosine+ Methylergometrine	Hyper tension		2	Possible	Mild	Not preventable Reassurance

In our study, most of the ADRs were mild according to Modified Hartwig and siegel scale. All ADRs were not preventable according to Modified Schumock and Thornton's criteria. Nausea and vomiting was found to be the most common side effect of intravenous oxytocin during this study, followed by Hypersensitivity reaction, Hypertension, Shivering and fever.

Figure:1 Errors in prescription.



A total of 115 medicine administration errors (AEs) were observed during the study period. Of these, The most common errors in prescription has been bad handwriting(100%) followed by no drug related instruction(78%) , use brand names(46%), spelling errors (10%)and drug strength errors ( 5%).<sup>5</sup>

## DISCUSSION

Measurements of blood loss in patients who developed primary PPH in our study period, was done by visual estimation and general examination of patient. Laboratory tests including haemoglobin, haematocrit were performed. Immediate resuscitative measures like intravenous access, fluid replacement and catheterization were done. The initial evaluation included clinical examination. From treatment point of view medical intervention included use of oxytocins, ergot alkaloids. Prostaglandins have been added subsequently for management of primary post-partum haemorrhage. Where prophylactic dose of oxytocin was already given a repeat dose of 20 units in 500 ml of intravenous oxytocin was administered. Slow intravenous injection of methylergometrine 0.2 mg was given in normotensive patients, while in hypertensive cases a further 10 units of oxytocin were given in case of slow response. Lastly prostaglandins were administered to control atonic haemorrhage that was unresponsive to oxytocin and / or ergometrine. PGE was used rectally and failed response was treated with additional intramyometrial PGF2 alpha. Different surgical procedures like manual removal of placenta, suturing of genital tract tears, bimanual uterine compression and packing, bilateral uterine artery ligation and caesarean hysterectomy were performed to control haemorrhage where medical management failed. The important steps in the management of PPH are predicting PPH and assessment of blood loss during third stage of labour. WHO recommends using blood collected in calibrated vessel plus soiled pads for blood loss measurement. In our study, measurement of blood loss was done by direct visualisation of blood in pad and diagnosis of PPH was made clinically by findings of pelvic examination, Monitoring of pulse, blood pressure, shock index, bleeding during fourth stage of labour, condition of uterus and risk factors.

According to study of Lertbunnaphong et al visual estimation of blood loss was found to be inaccurate, resulting in underestimation, with low correspondence (27.6%) and poor agreement (Cohen's kappa coefficient 0.07;  $p < 0.05$ ), compared with objective measurement using the drape. Two-thirds of cases of immediate PPH (65.4%) were misdiagnosed using visual estimation.<sup>5</sup>

But Chohasn A et al data supported our study and mentioned that other methods for measurement of blood loss are often difficult to use and time consuming; while, direct visual estimation is feasible and reliable if done carefully.<sup>6</sup>

The booking status is an important contributing factor for prevention of primary hemorrhage. The WHO recommends a minimum of eight antenatal care visits which identified risk factors of primary post-partum haemorrhage like anemia, pregnancy induced hypertension, Abruptio of Placenta, Placenta previa.<sup>4</sup>

As 70.43% of the patients in our study were unbooked. In line with this thinking, the absence of regular antenatal care means that medical risk factors that increase the risk of PPH often go undetected. This reflects the very poor standard of obstetric care of pregnant patients in our study centre area.

In our study, maximum proportion of primary PPH was reported in 21-25 years age group (46.9%) followed by 26-30 (38%). The mean age in this study was  $25.5 \pm 4.14$ . This is in consonance with study of Kumar R et al in which primary





PPH was high in more than 25 years of age group<sup>8</sup>. Similar to our result, age group analysis by Patel DM et al Revealed those patients

within the age group 21-27 years presented with maximum primary PPH.<sup>9</sup>

In our study 40.86% cases were hemodynamically unstable which was more compared to Limaye et al 18%.<sup>12</sup> the commonest complication encountered in patients with post-partum hemorrhage was anemia (77.3%) due to excessive blood loss. Anemia is shown to be the most common cause of morbidity in few other studies. Prior studies have demonstrated that severe anemia may impair myometrial contractility resulting from impaired transport

of haemoglobin and oxygen to uterus causing tissue enzymes and cellular dysfunction.<sup>7</sup> Most common cause in our study was Uterine atony without other associated causes was the major identified cause of primary postpartum haemorrhage, but this occurred in only 36% of women, which is much lower than the reported prevalence of at least 70% in Kodla CS et al study.<sup>11</sup> The blood vessels pass through the myometrial muscle cells and after delivery these muscle fibers contract effectively causing occlusion of the blood vessels. This is the primary mechanism of hemostasis after delivery. So atony of the uterus can cause massive primary PPH and death in spite of normal coagulation system.

Retained placental tissues can lead to uterine atony. In our study, patients with combined placenta tissues and uterine atony were categorised under the group of retained placental tissues of 18.9% among severe haemorrhage group was higher than previous reported prevalence of 10%.<sup>11</sup> Genital tract trauma accounted for only 13.94%, which is less than the figure reported in the literature of 20%. It can be also due to proper obstetric care through labour and vaginal delivery procedures. Our data included 7 cases without an identified cause, and hence were probably due to uterine atony that was not recognised clinically.

In our study uterotonic was used in almost all cases. However, oxytocin was used in 80% of the cases only. IV infusion of 20-40IU of oxytocin in 500 or 1000 mL of NS is considered an acceptable alternative regimen which will help the uterus to remain retracted. The infusion was given in 100% of cases. placental delivery is commonly done by controlled cord traction, it was not documented. Each and every patient in our study underwent mechanical treatment in form of uterine massage and controlled cord traction, as these are standard measures of preventing PPH. But uterine massage documented only in 60% prescription.

Among the 90 medically treated patients 13 (43.3%) were cured completely with oxytocin + Methylergometrine and did not require any further management. 25 needed repeat oxytocine + carboprost (21.7%) as ergometrine could not be given because they were hypertensive. Hemodynamic deterioration, patient1(0.86%) shall be managed as per routine therapeutic method immediately using oxytocin + Methylergometrine + blood transfusion. In 1(0.86%) patient oxytocin + Methylergometrine + blood transfusion had to be used to maintain uterine contraction.

Out of 9 (33.3%) cases which were not cured with both the therapies i.e. oxytocin and ergometrine, misoprostol per rectal was used and 3 out of them needed additional

intramyometrial carboprost. The study in Peoples Medical College, Nawab Shah showed that the haemorrhage was controlled by oxytocin in 46.11% cases and 25% patients required PGE2 to control PPH. The results are also comparable to the study conducted by Tammy, in which the patients receiving oxytocin required more than one uterotonic agents to control PPH.<sup>6</sup>

In Dr. Praveena Gungam et al study, to compare the effect of rectal misoprostol and IM oxytocin in primary PPH, the use of additional uterotonics in misoprostol group is 15% and 9% in oxytocin group. The use of additional uterotonics in misoprostol group is statistically significant, with  $p < 0.05$ .<sup>17</sup> This is comparable with the largest ever trial conducted by WHO on misoprostol use in third stage of labour involving >9000 women demonstrated higher proportion of women requiring additional uterotonic drugs.<sup>95</sup>

Comparing the drug risk categories for pregnancy, introduced by US food and drug administration (FDA), in our study majority of drugs were from category A 82.21% which is the safest category followed by category B 15.64% category C 2.15% and category D 0.00%. No drugs were prescribed from category X which is absolutely contraindicated in pregnancy. The similar pattern of category distribution was seen in the study done in Netherland in which from category A 81.7% category B 10.9%, category C 6.3% category D 1.1%, category X 0.0%.<sup>23</sup> In our study, most of the ADRs were mild according to Modified Hartwig and siegel scale. All ADRs were not preventable according to Modified Schumock and Thornton's criteria. Nausea and vomiting was found to be the most common side effect of intravenous oxytocin during this study, followed by Hypersensitivity reaction, Hypertension, Shivering and fever.

## CONCLUSIONS

Our study concludes that visual estimation of postpartum blood loss is an inaccurate method to determine the amount of blood loss in PPH, resulting in underestimation and misdiagnosis of PPH. Multigravidas have been found to have higher



incidence of PPH. Regular antenatal checkups and improvement obstetric education are mandatory to decrease the incidences of PPH.

Apart from mechanical measures and oxytocin alone, some other Uterotonics drugs were needed to control the PPH, in patients with inadequate antenatal care. This study has also provided the data of the association between hemodynamically unstable patients at the time of labour and post-partum anemia, requiring emergency management. Further studies with larger sample size to confirm these findings are required. ADRs were self-limiting or managed symptomatically in majority of the cases. Causality assessment of the majority of ADRs was 'possible' by WHO UMC scale as failure to dechallenge the drug in most of the cases.

The weakness of this study is that the practices were not observed directly. The timings of uterotonic drugs administration were not documented.

**ACKNOWLEDGEMENTS:** None

**CONFLICTS OF INTEREST:** None

**FUNDING:** Nil

## REFERENCES

- Taj Mahal History and Pictures at [http://www.indianchild.com /taj\\_mahal.html](http://www.indianchild.com /taj_mahal.html). Postpartum haemorrhage | National Health Portal of India [nhp.gov.in/disease/gynaecology-and-obstetrics/postpartum-haemorrhage](http://nhp.gov.in/disease/gynaecology-and-obstetrics/postpartum-haemorrhage) Accessed 20 January 2018
- Kumar N. Postpartum hemorrhage; a major killer of woman: review of current scenario. *Obstet Gynecol Int J*. 2016;4(4):00116.
- WHO recommendations for the prevention and treatment of postpartum haemorrhage. Geneva: World Health Organization; 2012. Available at [http://apps.who.int/iris/bitstream/10665/75411/1/9789241548502\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/75411/1/9789241548502_eng.pdf). Accessed 25 november 2017.
- Ministry of Health and Family Welfare, Government of India has released guidelines as "Guidance Note on Prevention and Management of Postpartum haemorrhage" <https://www.nhp.gov.in/disease/gynaecology-and-obstetrics/postpartumhaemorrhage> Accessed 27 november 2017.
- Lertbunnaphong T, Lapthanapat N, Leetheeragul J, Hakularb P, Ownon A. Postpartum blood loss: visual estimation versus objective quantification with a novel birthing drape. *Singapore medical journal*. 2016 Jun; 57(6):325.
- Chohan A, Butt F, Mansoor H, Falak T. PRIMARY POST PARTUM HAEMORRHAGE: OUTCOME OF DIFFERENT TREATMENT MEASURES. *Biomedica*. 2006 Jan; 22:16-20.
- Uthman SG, Garba MA, Danazumi AG, Mandara MU. How Birth Interval and Antenatal Care Affects Postpartum Haemorrhage Prevention in Maiduguri, Nigeria. *Journal of Applied Pharmaceutical Science*. 2013 Mar 1;3(3):36.
- Kumar R. Prevention of maternal mortality: why success eludes us? *Indian journal of public health*. 2002;46(1):3-7.
- 10] Al-Zirqi I, Vangen S, Forsen L, Stray-Pedersen B. Prevalence and risk factors of severe obstetric haemorrhage. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2008 Sep 1;115(10):1265-72.
- Kodla CS. A study of prevalence, causes, risk factors and outcome of severe obstetrics haemorrhage. *J Sci Innovative Res*. 2015;4(2):83-7.
- Limaye HR. Maternal and fetal outcome in obstetric emergency cases referred from rural areas. *J Obstet Gynaec in India*. 1982; 32:520-9.
- Frass KA. Postpartum hemorrhage is related to the hemoglobin levels at labor: Observational study. *Alexandria Journal of Medicine*. 2015;51(4):333-7.
- Patel MM, Jain M. A study on active management of third stage of labour as per WHO guidelines: efficacy and complications. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2016 Dec 16;5(1):803.