

EFFECTIVENESS OF RECTAL MISOPROSTOL IN CESSATION OF POST PARTUM HAEMORRHAGE

Samia Nasreen, Shehla Baqai*, Bushra Iftikhar**, Sumaira Bukhsh***, Muhammad Kamran****

Pakistan Naval Ship Shifa Hospital Karachi, *Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, **Combined Military Hospital Malir/National University of Medical Sciences (NUMS) Pakistan, ***Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, ****Armed Forces Institute of Mental Health/ National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine the efficacy of rectal misoprostol in management of Post Partum Haemorrhage in third stage of labour.

Study Design: Interventional study.

Place and Duration of Study: Gynaecology and obstetrics department at PNS Shifa Hospital Karachi, from Sep 2012 to Mar 2013.

Material and Methods: All singleton and multiple pregnancies of gestation 37-42 weeks, who presented in labour room to deliver and had prolonged second stage of labour (n=112) were enrolled in the study. Patients, who were having coagulopathy, abruption, placenta previa, and allergy to prostaglandins were excluded from the study. Third stage was managed actively according to hospital standard routine. Hemoglobin was measured at the time of admission and repeated after delivery in patients having PPH. Blood was estimated by weighing all gauzes and packs. If blood loss more than 500ml one hour after delivery and all traumatic causes and retained placenta were excluded, 600µg (3 tablets) of misoprostol were given per rectally, which were inserted up to a digit depth. After one hour total amount of blood loss was calculated. The data were then entered in a proforma and analyzed.

Results: Majority (44.6%) of the women were 26-33 years of age, 8.9% had PPH with fall in hemoglobin by 1.5-2 gms/dl. Ninety percent of the patients responded to rectal misoprostol.

Conclusion: Active management of third stage of labour has a definite role in the preventive of PPH. Rectal administration of misoprostol should be considered for control of PPH in low resource settings like ours as it was found effective in the study.

Keywords: Blood loss, Hemoglobin level, Misoprostol, Prolonged labour, Postpartum hemorrhage.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Primary postpartum haemorrhage (PPH) is the leading cause of maternal morbidity and mortality especially in developing countries¹. Maternal mortality globally is estimated at 529,000 deaths per year and created major demands on health care systems². The WHO estimates that obstetric hemorrhage complicates 10.5% of all live births in the world³. Timely management of PPH reduces maternal mortality⁴. The solution in developing countries like Pakistan is a management option which is simple

to administer with no special storage requirement, cheap and easily available⁵. Misoprostol, a prostaglandin E-1 analogue is a revolutionary medicine, not only suitable for remote areas but also in hospital settings⁶. Overall PPH is responsible for 25% of maternal deaths in Pakistan. In Pakistan misoprostol is reportedly used only in hospital settings⁷. Unfortunately we are not aware of misoprostol use in PPH as alternative or additive therapy^{8,9}, as there are no proper statistics available on maternal health in our country. Lots of work has been done in last two decades for the role of misoprostol in PPH¹⁰. There is a strong association between prolonged labour and postpartum hemorrhage¹¹, but there is no local

Correspondence: Dr Samia Nasreen, SD-138 Falcon Complex Malir Cantt Karachi Pakistan

Email: saminanasreen104164@gmail.com

Received: 11 Aug 2016; revised received: 10 Apr 2017; accepted: 25 Apr 2017

guidelines available for its appropriate dose and route of its administration¹². Aim of the study was to outline a protocol for use of misoprostol in women in postpartum hemorrhage.

MATERIAL AND METHODS

This interventional study was carried out in department of gynae and obstetrics at 600 bedded PNS Shifa Hospital Karachi for a period of six months. The study was approved by the ethical committee of the hospital. All patients between 20 and 40 years of age having single or multiple

obstetrical history were noted. Third stage of labour was managed actively according to FIGO standard protocol, that is 10 i.u of syntocinon, was given at the moment when anterior shoulder was delivered. Brandt Andrew method was used to deliver the placenta. Bimanual uterine message was done. For estimation of blood loss, bed pans were used and placed beneath buttocks of patients, and weighing all gauzes and packs (which were pre weighted) and collected in a plastic bag. Difference in weight was noted in

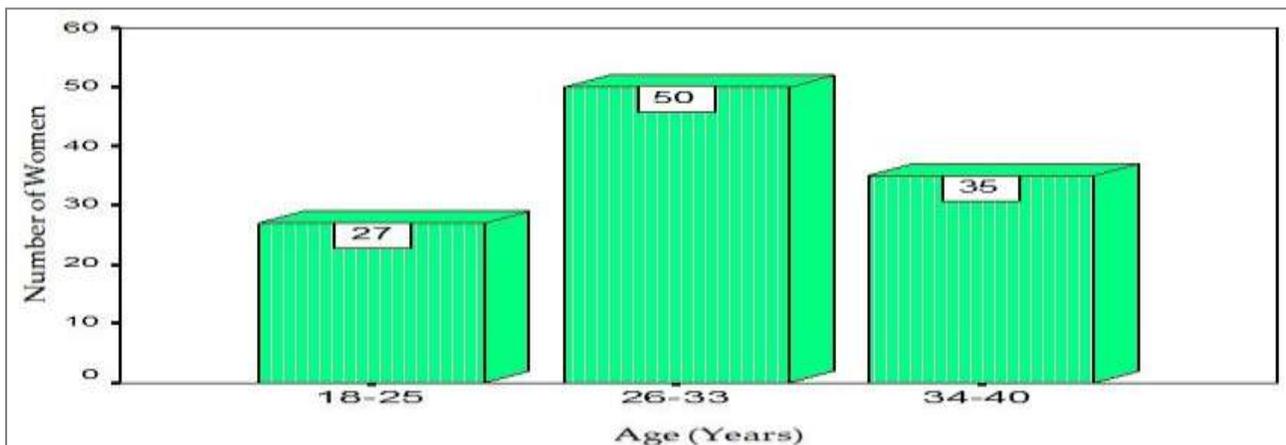


Figure-1: Age distribution patients (Mean ± SD) age = 30.31 ± 5.60 years.

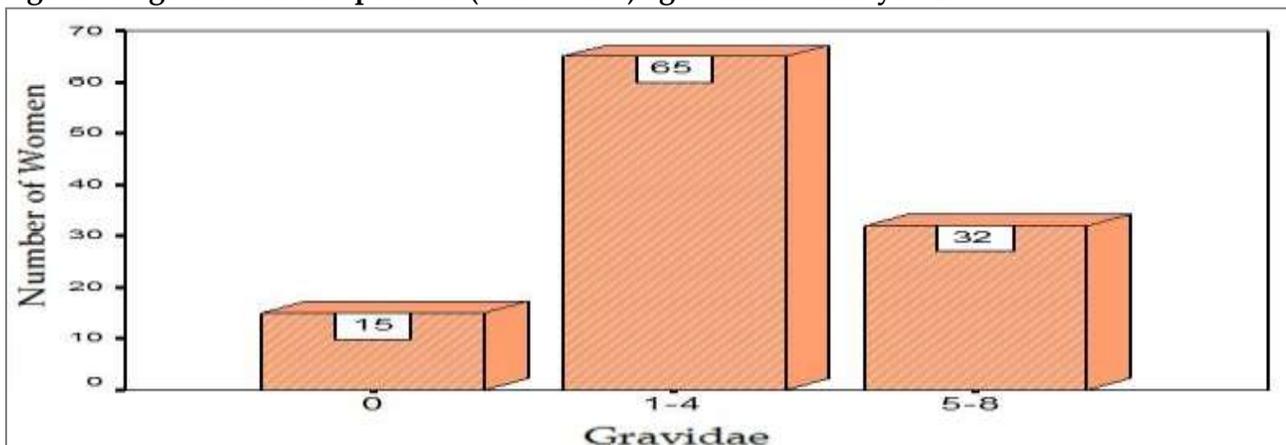


Figure-2: The Pauty among the patients.

pregnancies at term with prolonged labour and PPH were included. Causes of PPH other than atony were excluded. Informed consent was taken from each patient when they came to labour room.

Maternal record including age, weight, parity, hemoglobin levels and previous

grams and one gram of blood was taken equal to one ml of blood loss approximately. Blood loss was estimated from delivery till one hour postpartum. If blood loss was more than 500ml and all traumatic causes and retained placenta was excluded and patient had given informed consent for trial, 600mcg (3 tablets) of misoprostol

were given per rectally, which were inserted up to a digit depth.

Data Analysis

Statistical package for social sciences SPSS version 13.0 was used for analysis of statistics. Descriptive statistics was used to calculate mean and standard deviation for variables like age of patient; frequencies and percentages for parity, gravida, blood loss and postpartum hemorrhage after misoprostol treatment.

while most of the patients were of the age group 26 to 33 years (44%) as shown in fig-1. Out of 112 women, 15 (13.3%) were primiparous (Para 0+0), 95 (84.8%) were multiparous (para 1-5) and only 2 (1.8%) were grand multiparous (Para>5) as shown in fig-2. Blood loss measurement after misoprostol treatment has shown that 102 (91.1%) women were observed with blood loss <500 ml followed by 9 (8%) with blood loss 500-1000 ml and only one (0.9%) had blood loss >1000 ml

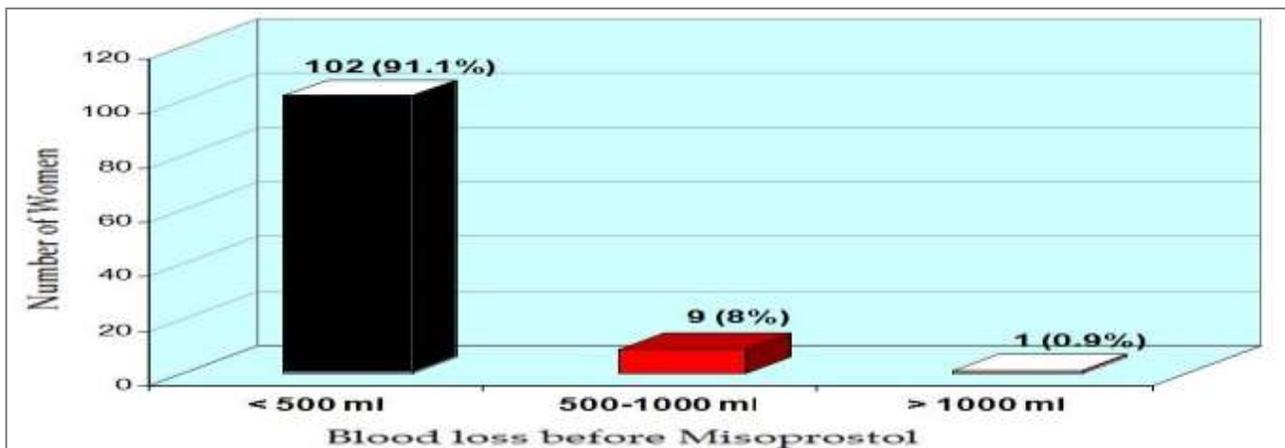


Figure-3: Blood loss after misoprostol treatment (n=112).

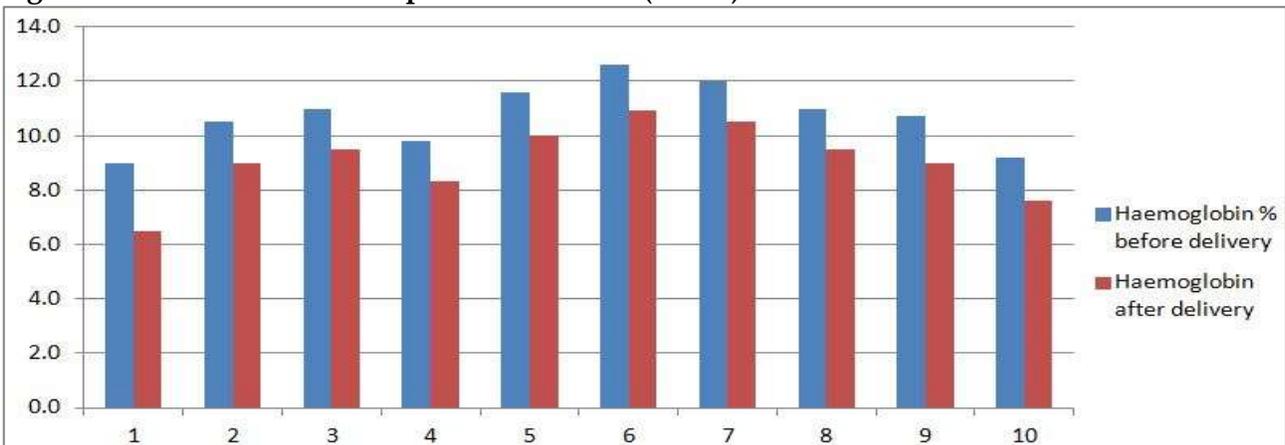


Figure-4: Haemoglobin level before and after delivery.

Stratification according to age and gravidae was done to evaluate the effect of these variables on occurrence of PPH.

RESULTS

Rectal misoprostol was used for the treatment of post-partum hemorrhage in 112 women with mean age of 30.31 ± 5.6. The age group of patients in study was 18 to 40 years,

(fig-3).

Thus, the frequency of postpartum hemorrhage was 8.9%, fall of hemoglobin level is noted in patients having PPH between 1.5 to 2gms/dl which is shown in the (fig-4). Among 27 women of age group 18-25 years, PPH occurred in only one (3.7%) woman, among 50 women of age group 26-33 years, PPH occurred in 6 (12%)

women while among 35 women of age group 34-40 years, PPH occurred in three (8.6%) women. The incidents of PPH increases with parity as only 6.7% of primigravida had post partum haemorrhage as compared to 12.5% in multigravida. One patient did not respond to the misoprostol and needed further intervention. Among 15 women of primigravidae, PPH occurred in only one (6.7%) woman, among 65 women of gravidae 1-4, PPH occurred in 5 (7.7%) women while among 32 women of gravidae 5-8, PPH occurred in 4 (12.5%) women.

DISCUSSION

In low income countries maternal mortality is mostly caused by post-partum hemorrhage. It is observed that in sub Saharan Africa¹³, 40 maternal deaths have been reported per 100,000 births. While in United Kingdom¹ maternal death is observed in 100,000 births.

These statistics need intervention to decrease maternal mortality¹⁴. Lack of training and storing facility for oxytocic agents, non-availability of trained birth attendants for administration of parenteral uterotonic agents and non-availability of blood transfusion facility in rural areas further worsens the consequences of post-partum hemorrhage¹⁵.

Prolonged labour¹³ and multi-parity leads to an increased risk of post-partum hemorrhage because of uterine atony in third world, leading to increased maternal mortality and morbidity¹⁶.

Alternative uterotonic preparations which are cheap, easy to administer and store may contribute to the treatment of post-partum hemorrhage and thus help low income countries in decreasing maternal morbidity and mortality¹⁷. In a study by Bamigboye et al. Four ninety one women were observed. These women were given 400mcg of misoprostol rectally or 1 ampoule of syntometrine intramuscularly randomly after the delivery. Results showed that hemoglobin, postpartum blood loss and length of third stage of labour were similar¹⁸. In a descriptive study in Egypt by H Abdul Aleem and colleagues, out of 18 women with severe hemorrhage because of

atony, 16 had responded to misoprostol (88.2%). These women previously received oxytocin, methylergometrine and enzaprost but were not responding. In this study 1000mcg of misoprostol was given before resorting lastly to surgical intervention. In four cases only 600mcg misoprostol was available in theatre, and thus was used so. The above mentioned study concluded that cases of postpartum hemorrhage because of uterine atony not responding to other uterotonics can be treated effectively with misoprostol¹⁹. Our results matched the results of H Abdul-Aleem's as post-partum haemorrhage was controlled in 102 (91.1%) out of 112 patients. In 10 patients misoprostol was not effective. Out of these 10 patients, 9 (8.9%) patients had blood loss of 500-1000ml, and only one (0.9%) had blood loss >1000ml. These results are promising and encouraging use of misoprostol in treatment of postpartum haemorrhage, which is no doubt a low cost solution for postpartum haemorrhage in our setups. Postpartum haemorrhage occurred with significant higher frequency in grand multiparas (para>5). Rate of PPH was almost doubled than that of primigravidas (para 0) and multiparas (para 1-5). These results matched with results of Munim who noticed three times higher incidence of PPH in grand multipara.

Misoprostol, a prostaglandin E1 analogue and is marketed for treatment of peptic ulcer. In countries where it is registered it is not approved for any use in pregnancy and also not approved in post-partum hemorrhage. Because misoprostol is heat stable, easy available, every midwife carry this in her bag²⁰. Oxytocin is not recommended to be replaced by misoprostol in PPH²¹, instead it is required to be available to doctors working in rural health posts and to the midwives conducting home deliveries in remote areas. In these settings it is not practically possible to administer parenteral oxytocics and misoprostol will prove an easy treatment options for women dying of PPH, as non-availability of easy to use, carry and store uterotonic agents is major hurdle to prevent life threatening post-partum hemorrhage in developing world²². From our

knowledge we know that as compare to oxytocin or ergometrine, misoprostol is easy to use (no equipment needed), multiple routes of administration (rectal and oral), easy to store in room temperature for longer time (several years), thermostable and with fewer side effects including shivering and hyperthermia. Additionally it can be given safely in hypertensives²³. Practical advantage of rectal route is to avoid gastrointestinal side effects²⁴. Several studies have proved that misoprostol rectally is effective in treatment of post-partum hemorrhage in third stage of labour¹⁴. Although we are still unable to determine rate of transmucosal absorption of rectal misoprostol. Postpartum haemorrhage when related to the age among 27 women of age 18-25 years of age PPH was not controlled in only one (3.7%) in 50 women of age group 26-33 years, PPH was not controlled, ie 6 (12%), While among 35 women of age group 34-40 years PPH, was not controlled in 3 (8.6%). In our country where women has lesser access to contraception and control over their family size²⁵, we frequently see women of higher age group getting pregnant. However in this study the results matched with Robert's who proved that there is no relationship of age with PPH¹⁸.

Worldwide and especially in our country postpartum haemorrhage is the major killer of women and there is a need to consider measures to reduce this complication. In patients with PPH, rectal route appears practical and preferable to vaginal and oral administration and thus preventing PPH. Further studies are warranted in Pakistan to increase awareness about misoprostol among rural health workers, where most deliveries occur.

CONCLUSION

Active management of third stage of labour has a definite role in the preventive of PPH. Rectal administration of misoprostol should be considered for control of PPH in low resource settings like ours as it was found effective in the study.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author

REFERENCES

1. World Health Organization. The World Health Report 2005. Make every mother and child count. Geneva: WHO, 2005.
2. Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF, WHO analysis of causes of maternal death: A systematic review, *Lancet* 2006; 367(9516): 1066-74.
3. Department of Reproductive Health and Research, World Health Organization. Maternal Mortality in 2000: Estimates Developed by WHO, UNICEF, and UNFPA. Geneva: WHO 2004.
4. Smith JM, Baawo SD, Subah M, Sirtor-Gbassie V, Howe CJ, Ishola G, et al. Advance distribution of misoprostol for prevention of postpartum hemorrhage (PPH) at home births in two districts of Liberia. *BMC Pregnancy Childbirth* 2014; 14(1): 189.
5. Rajaei M, Karimi S, Shahboodaghi Z, Mahboobi H, Khorgoei T, Rajaei F. Safety and efficacy of misoprostol versus oxytocin for the prevention of postpartum hemorrhage. *J Pregnancy* 2014; 713879.
6. Ejembi C, Shittu O, Moran M, Adiri F, Oguntunde O, Saadatu B, et al. Community-level distribution of misoprostol to prevent postpartum hemorrhage at home births in northern Nigeria. *Afr J Reprod Health* 2014; 18(2): 166-75.
7. Musa AO, Ijaiya MA, Saidu R, Aboyeji AP, Jimoh AA, Adesina KT, et al. Double-blind randomized controlled trial comparing misoprostol and oxytocin for management of the third stage of labor in a Nigerian hospital. *Int J Gynaecol Obstet* 2015; 129(3): 227-30.
8. Atukunda EC, Brhlikova P, Agaba AG, Pollock. Civil Society Organizations and medicines policy change: A case study of registration, procurement, distribution and use of misoprostol in Uganda. *Soc Sci Med* 2015; 130: 242-9.
9. Marret H, Simon E, Beucher G, Dreyfus M, Gaudineau A, Vayssière C, et al. Overview and expert assessment of off-label use of misoprostol in obstetrics and gynaecology: review and report by the Collège national des gynécologues obstétriciens français. *Eur J Obstet Gynecol Reprod Biol* 2015; 187: 80-4.
10. Mobeen N, Durocher J, Zuberi N, Japan N, Blum J, Wasim S, et al. Administration of misoprostol by trained traditional birth attendants to prevent postpartum haemorrhage in homebirths in Pakistan: A randomized placebo controlled trial. *BJOG* 2011; 118(3): 353-61.
11. Lu MC, Muthengi E, Wakeel F, Fridman M, Korst LM, Gregory KD. Prolonged second stage of labour and postpartum hemorrhage. *J Matern Fetal Neonatal Med* 2009; 22(3): 227-32.
12. Zuberi NF, Durocher J, Sikandar R, Babar N, Blum J, Walraven G, Misoprostol in addition to routine treatment of postpartum hemorrhage: a hospital-based randomized-controlled trial in Karachi. Pakistan, *BMC Pregnancy Childbirth* 2008;8(40): 1-8.
13. Webber GC, Chirangi B. Women's health in women's hands: A pilot study assessing the feasibility of providing women with medications to reduce postpartum hemorrhage and sepsis in rural Tanzania. *Health Care Women Int* 2014; 35(7-9): 758-70.
14. Spangler SA, Gobezyayehu AG, Getachew T, Sibley LM. Interpretation of national policy regarding community-based use of misoprostol for postpartum hemorrhage prevention in Ethiopia: a tale of two regions. *J Midwifery Women's Health* 2014; 59(Suppl-1):S83-90.

15. Geller SE, Adams MG, Kelly PJ, Kodkany BS, Derman RJ. Postpartum haemorrhage in resource poor settings. *Int J Gynaecol Obstet* 2006; 92: 202-11.
 16. Nasreen H, Nahar S, Mamun MA, Afsana K, Byass P. Oral misoprostol for preventing postpartum haemorrhage in home births in rural Bangladesh: how effective is it, *Glob Health Action* 2011; 4: 10.3402/gha.v4i0.7017.
 17. Weeks AD, Ditai J, Ononge S, Faragher B, Frye LJ, Durocher J, et al. The MamaMiso study of self-administered misoprostol to prevent bleeding after childbirth in rural Uganda: a community-based, placebo-controlled randomised trial. *BMC Pregnancy Childbirth* 2015;15(1): 219.
 18. Bamigboye AA, Hofmeyr GJ, Merrel DA. Rectal misoprostol in the prevention of postpartum hemorrhage: a placebo controlled trial. *Am J Obstet Gynaecol* 1998; 179(4): 1043-6.
 19. Miller S, Lester F, Hensleigh P. Prevention and treatment of postpartum haemorrhage: new advances for low resource settings. *J Midwifery* 2004; 49: 283-92.
 20. Millard C, Pollock AM, Brhlikova P. Commentary Evidence versus influence in the WHO procedure for approving essential medicines: misoprostol for maternal health. *BMJ* 2014; 349: g4823.
 21. Priya GP, Veena P, Chaturvedula L, Subitha L. Arch, A randomized controlled trial of sublingual misoprostol and intramuscular oxytocin for prevention of postpartum hemorrhage. *Arch Gynecol Obstet* 2015; 292(6): 1231-7
 22. EL-Refaey H, Rodeck C. Postpartum haemorrhage: Definitions, medical and surgical management. A time for change. *Br Med Bull* 2003; 67: 205-17.
 23. Bell S, Passano P, Bohl DD, Islam A, Prata N, Training traditional birth attendants on the use of misoprostol and a blood measurement tool to prevent postpartum haemorrhage: lessons learnt from Bangladesh. *J Health Popul Nutr* 2014; 32(1): 118-29.
 24. Leon W, Durocher J, Barrera G, Pinto E, Winikoff B, Dose and side effects of sublingual misoprostol for treatment of postpartum hemorrhage: What difference do they make. *BMC Pregnancy and Childbirth* 2012; 12:65.
 25. Gani N, Ali TS. Prevalence and factors associated with maternal postpartum haemorrhage in Khyber Agency Pakistan. *J Ayub Med Coll Abbotabad* 2013; 25(1-2): 81-5.
-