Efficacy of Rectal Misoprostol in Active Management of Third Stage of Labour in Comparison with Oxytocin

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Abstract:

Background: Third stage of labour is defined as the time from delivery the baby to complete delivery of the placenta and its attached membranes.

Most common complications of the third stage of labour are postpartum hemorrhage (PPH). Active management of third stage of labour (AMTL) prevents PPH. Misoprostol is a prostaglandin E1 analogue has been suggested as an alternative of the routine prophylactic oxytocic agents in AMTL. Rectal route had been chosen because it avoids gastrointestinal side effects.

Objectives: To asses effectiveness of (400 mcg) rectally administered misoprostol tablet in the AMTL in comparison with standard oxytocin regimen.

Patients and Methods: In prospective case-control study, 100 women were randomized, 50 patients received either 400mcg misoprostol tablets rectally (study medication) the other 50 received 10 IU oxytocin in 500 ml Ringer lactate solution IV. As a method of AMTL. Patient with risk factor for PPH had been excluded. A comparison between the two groups in their amount of blood loss, drop in hemoglobin level from admission to 24 hr. after delivery, duration of third stage of labour and any side effects appear done.

Results: Maximum amount of blood loss in both groups of the study was 440 ml, so we had no case of PPH. There was no stastically significant difference in mean blood loss, mean difference in Hb level (gm/dl) on admission and 24 hours after delivery, and duration of third stage of labour found between study groups [p values= 0.138, 0.227, 0.08 respectively]. More shivering occurs in cases but the difference was not significant.

Conclusions: Misoprostol in a dose of 400 mcg rectally shows promising results, it seems safe and effective drug that can be used in the management of third stage of labour.

Keywords: Rectal misoprostol, Third stage of labour, Active management.

Introduction:

Pregnancy and child birth involve significant health risks even for women with no pre-existing health problems.

Taj Mahal one of the seven wonders of the world, a monument dedicated to the memory of Queen Mumtaz who died because of severe postpartum hemorrhage (PPH) is a grim reminder of maternal mortality that can affect any woman in child birth [(1)].

PPH still remains one of the leading causes of maternal deaths indeveloping world [(2)]. While PPH in industrialized countries is more often due to obstetric interventions such as induction of labour, epidural anesthesia, and caesarean section the leading causes of PPH in the developing world are retained placenta, uterine atony and genital tract injury [(3)]. For this reason it is important to consider any interventions that may minimize this complication.

Active management of third stage of labour is recommended by the world health organization (WHO) [(4)], it has also been recommended by the international confederation of midwives

and the international confederation of gynecologist and obstetrician to decrease risk of PPH [5].

Third stage of labouris defined as the period between the delivery of the infant and delivery of the placenta and its attached membranes, this normally lasts 5-10 minutes, can last up to 30 minutes [6, 7, 8].

Active management of third stage of labour includes interventions designed to speed up delivery of the placenta by increasing uterine contractions to prevent PPH [9]. This generally involve routine prophylactic administration of uterotonic agents before delivery of the placenta (sometimes with delivery of anterior shoulder or with crowning of the head), early cord clamping and controlled cord traction [10, 11, 12].

There are markedly polarized views between those who believe in active management and those who believe in physiological management of the third stage of labour [13].

In rural communities, the lack of access to skilled birth attendance who are able to administer parentral oxytocic agents, the high incidence of anemia in pregnancy, the lack of availability of safe blood transfusion services and the lack of refrigeration to store the oxytocic agent worsens the outcome of PPH [14, 15].

The availability of an easily administered, affordable and thermo-stable preparation for routine management of third stage of labour may have considerable benefits in preventing PPH and perhaps reduce maternal morbidity and mortality in the third world, where atonic post-partum hemorrhage is common due to high multiparity and prolonged labour [16].

Current oxytocic drugs are far from ideal ,particularly for routine use in developing countries, where simple routes of administration and stable, inexpensive drugs are needed [17].

Oxytocin is made in the supraoptic and paraventricular nucleus of the hypothalamus and is released into the blood from the posterior lobe of the pituitary gland [18]. Oxytocin is commercially available in the United States as syntocinonand pitocin, which is not effective by mouth; the half-life of intravenously infused oxytocin is approximately 3 minutes. It is metabolized by hepatic oxytocinases and its excretion is biliary and renal [19].

Misoprostol is a prostaglandin E1 analogue originally marketed for the treatment of peptic ulcer disease. Its uterotonic features have been confirmed in the fields of labour induction and induction of abortion [20].

The role of misoprostol as an agent in the third stage of labour has been investigated because the drug is thermo-stable and enterally administered, it has potential to be a widely used intervention. Orally formulated tablets administered via rectal route have been suggested as a lifesaving treatment for severe PPH [21]. The use of rectally administered misoprostol is preferred around the world [22].

Patients and Methods:

A case-control study conducted between December 1, 2015 and June 31st, 2016 in Azadi Teaching Hospital, Kirkuk, Iraq.

A total of 100 women who had been involved in our study (50 patients studied women and 50 patients controls) were admitted to the labour room of Azadi Teaching Hospital. Women included in the study were in active labour when vaginal delivery was anticipated. Consent was taken from all ladies involved; after taking a good

history, they were subjected to physical and obstetric examination to exclude high risk patients, with laboratory investigation as hemoglobin and hematocrit level to exclude anaemia which was one of the exclusion criteria, blood group and Rh group for all study subjects on admission to delivery room was done.

The chosen pregnant ladies were judged to be at low risk of postpartum hemorrhage therefore the criteria for exclusion were:

1. Placenta previa.
2. Previous history of PPH.
3. Anemia.
4. Antipartum hemorrhage.
5. Non cephalic presentation
6. Parity more than 4.
7. Multiple pregnancy.
8. Intrauterine fetal death.
9. Uterine fibroid.
10. Patient on anticoagulant therapy.
11. Primgravida.
12. Gestational age less than 37 weeks.
13. Polyhydramnious.
14. History of previous scar.
15. History of allergy to prostaglandins.

Women were divided into two groups, 50 in each group who were actively managed for their third stage of labour.

In group 1(cases): patient received 400 mcg misoprostol tablets rectally [Cytotic ® tablet 200 mcg] immediately after delivery of the baby and clamping of the umbilical cord.

Group 2(controls): patient received 10 international units (IU) oxytocin IV [Oxytocin injection BP, 10 IU, in 500 cc Ringer lactate or Normal saline solution (which was prepared beforehand) as rapid infusion immediately after delivery of placenta and clamping of the umbilical cord. A pad was put under the buttock (weighed before) to estimate amount of blood loss.

We follow both groups by:

1. Placenta delivered completely or not (signs of placental separation include a gush of blood, lengthening of the umbilical cord, and the uterine fundus becomes firmer and globular after the placenta detaches).
2. Time from administration of the drugs till delivery of the placenta.
3. Amount of blood loss was calculated from number of pads, weight of each pad was before using it (25gm), then weigh it after 1 hour after delivery of placenta, number of clots and weight of each clot. For weighing the pads and clots, we use special plastic balance (3kg). We calculate the amount of blood loss in grams in which 1gm of blood loss assumed to be equal to 1 ml of blood loss [23]. The cases was followed up to one hour after delivery for side effects of misoprostol and oxytocin [Diarrhea, Headache, vomiting, abdominal pain, shivering] and any signs of hypovolemia. Blood pressure, pulse rate and temperature were checked after one hour from delivery of placenta.
4. Hemoglobin level in gram/ deciliter redone 24 hours after delivery.

The main outcomes measured were amount of blood loss after delivery and difference in hemoglobin levels in grams/ deciliter on admission and 24 hours after delivery. Primary postpartum hemorrhage is defined as a postpartum blood loss of more than 500 ml, Other outcomes measured was duration of the third stage of labour, delivery of the placenta whether completely delivered or not, and development of any side effects.

Statistical analysis:

All statistical analysis (frequency distribution, T-test for difference between two means, P value more than 0.05 was regarded non-significant) done by using SPSS version 15.

Results:

In this study a total of 100 women who fulfill the inclusion criteria of the study divided into two groups:

Group 1 (cases):

Involved 50 women actively managed in their third stage of labour by using 400 mcg misoprostol rectally immediately after delivery of the baby and clamping of the cord.

Group 2 (controls):

Involved 50 women actively managed in their third stage of labour by 10 IU oxytocin IV in 500 cc Ringer lactate solution immediately after delivery of the baby and clamping of the cord.

The analysis of the data, showed no statistically significant difference between the two groups in relation to the demographic characteristics [age, gravidity, parity, gestational age, hemoglobin level] of the studied population as summarized in table (1). The mean maternal age was 26.2±4.8 years in cases versus 27.6 ± 5.34 years in control (p value 0.30). Mean gestational age was 39.44 ± 1.31(weeks) in study group versus 39.12 ± 1.18 in controls (p value 0.190). Mean gravidity was 3.04± 0.83 in misoprostol group versus 3.26 ± 0.82 in controls. Mean hemoglobin level on admission 11.45 ± 1.01 gram/ deciliter in cases versus 11.15± 0.93 gram/deciliter in controls (p value 0.130).

Regarding delivery of placenta, the placenta delivered completely in all cases of both groups, i.e. we had no case of retained placenta in our study.

Mean time for delivery of placenta was 6.26 ± 3.82 minutes in misoprostol group versus 5.14 ± 1.73 minutes in oxytocin group. There was no statistical significant difference between the study groups (p value of 0.08) table (2). The most common time for complete delivery of placenta was five minutes in both groups [about (58%) of the cases had delivery of the placenta within five minutes versus (66%) of the controls].

The mean amount of blood loss in misoprostol group (cases) was 141.5± 88.98 (ml) versus 113.6 ± 50.92(ml) with [p value of 0.138] therefore there was no statistically significant difference between the two groups in the mean amount of blood loss table (2).

Maximum amount of blood loss in our study was 440 ml which mean that we did not have any case of PPH.

The mean change in hemoglobin level, which is defined as the difference in Hb level in gm/ dl on admission and 24 hours after admission. This was 0.816 ±0.74 (gm/dl) in misoprostol group versus 0.65±0.61 (gm/dl) in oxytocin group with a p value of 0.227 which was statistically non-significant as shown in table (2).

Table (3) shows the difference in development of side effects in each group. More shivering occurs in misoprostol group (three of the cases versus one of the control) and more abdominal pain (three of the cases versus none in controls), however more vomiting occur in oxytocin group (one of the controls versus none of the cases). These differences was statistically non-significant p value= 0.744.

Mean change in hemoglobin level, defined as the difference in Hb level in gm/ dl on

admission and 24 hours after admission [anemia is one the risk factors for PPH].
The most common time for complete delivery of placenta was five minutes in both groups [58% of the cases versus 66% of the controls] [prolonged duration of third stage of labour increases risk of PPH].
Maximum amount of blood loss in our study was 440 ml no case of PPH.

More blood loss in misoprostol group, but the difference was not significant.
There was more shivering (3) of the cases in misoprostol group versus (1) in intravenous oxytocin group, more abdominal pain (3) versus none intravenous oxytocin group and more vomiting in oxytocin group versus none in misoprostol, however these differences was statistically none significant (P-value 0.744).

Table (1): Representing demographic characteristic between cases (misoprostol group) and control (oxytocin group).

		Misoprostol group Mean ± St. D	Oxytocin group Mean ± St. D	P value	
Demographic characteristic	Maternal age (years)	26.20 ± 4.80	27.60 ± 5.34	0.300	Non -significant
	Gravidity	3.04 ± 0.83	3.26 ± 0.82	0.180	
	Parity	1.84 ± 0.86	2.14 ± 0.85	0.080	
	Gestational age(weeks)	39.44 ± 1.31	39.12 ± 1.18	0.190	
	Hb level on admission (gm/dl)	11.45 ± 1.01	11.15 ± 0.93	0.130	

Table 2: Outcomes indicative of blood loss.

Title	Misoprostol group	Oxytocin group	P value	
mean hemoglobin level change	0.816 gm/dl	0.74 gm/dl	0.227	Non-significant
mean amount of blood loss	141.5 ml	113.3 ml	0.138	
duration of third stage of labour	6.26 minutes	5.14 minutes	0.0 82	

Table (3): Side effects of the drugs in both groups.

		Grouping into Cases and Control				P Value
		Cases		Control		
		Count	%	Count	%	
Side Effects	Diarrhea	0	0%	0	0%	0.744 (non significant)
	Headache	0	0%	0	0%	
	Vomiting	0	0%	1	2%	
	Abdominal pain	2	4%	0	0%	
	Fever	0	0%	0	0%	
	Shivering	2	4%	1	2%	
	Abdominal pain and Shivering	1	2%	0	0%	
	None	45	90%	48	96%	
Total		50	100%	50	100%	

Discussion:

Primary post-partum hemorrhage can be defined as blood loss of 500 ml or more within 24 hours after birth, the majority can be prevented by the use of prophylactic uterotonic agents in the third stage of labour and timely and appropriate management [24].

Maternal iron deficiency anemia is a major public health and nutritional problem in the world [25]. Therefore in countries were many women having severe anemia during pregnancy, even a relatively small reduction of post-partum blood loss could be clinically relevant.

For centuries, the uterotonic agent of choice has been oxytocin with or without supplemental ergot preparations such as ergometrine or methergine, both oxytocin and methergine are unstable at room temperature and thus require special temperature and light storage conditions to remain effective [26].

This study evaluates the effectiveness of rectally administered misoprostol in active management of third stage of labour.

According to the results of our study there was no stastically significant difference in the mean maternal age (p value 0.30). This result was nearest to the results of a study done by Ayaad and Abu Omer (2004) in Jordan [27], in this study the mean maternal age in misoprostol group was 23±4.3 (years) versus 23 ± 4.9 (years) in oxytocin. The mean age in our study was higher than that study, this may be due to difference in the communities from which the studied populations chosen, however it agree with our study in that there was no statistical significant difference in the mean maternal age in both groups (p value 0.280).

Ayaad and Abu Omer(2004) [27] found the mean gestational age of 39.57 weeks in misoprostol group versus 38.85 weeks in oxytocin group, these results was near to the results in our study. Both studies show no statistically significant difference between the misoprostol and oxytocin groups (P values was 0.06 and 0.190 respectively).

The mean hemoglobin level prior to delivery (on admission) in our study was 11.45 ± 1.01 gram/ deciliter in cases versus 11.15 ± 0.93 gram/ deciliter in controls (p value 0.130), this mean that there wasn't significant difference statistically between the two groups. This was in agreement with a study done by Kemik Gul et al(2006) [28] in Turkey, They found that there was no statistically significant difference between the groups (200 mcg rectal misoprostol,400 mcg rectal misoprostol and 10 IU oxytocin) in hemoglobin level prior to delivery [F3.28,p=0.52].

The maximum amount of blood loss in our study was 440 ml which mean that we have no cases of postpartum hemorrhage. This result disagrees with a study done by Caliskan et al (2002) in Turkey [29]. In that study there was more PPH in misoprostol group .These differences between our study and their study may be due to larger sample sizes in their study (1606 women) also using of combined oxytocic drugs in one arm of their study (oxytocin 10 IU plus methylergometrine).

The mean amount of blood loss after delivery was 141.5 ml in cases versus 113.3 ml in controls and this difference was statistically not significant (p value 0.138). This was in agreement with other studies as following:

A study done by Parson et al (2007) [30]. Also in a study done by Ayaad and Abu Omer, 2004 [27], in both studies there was no statistically significant difference between the treatment groups in amount of blood loss after delivery. They concluded that rectal misoprostol was as effective as oxytocin in minimizing blood loss in third stage of labour.

Another study done by Chaudhuri P et al (2010) [31], show lower amount in

intraoperative and postoperative blood loss in misoprostol group than in the oxytocin group which was statistically significant difference they concluded that rectal misoprostol could be an effective alternative to oxytocin in preventing blood loss after caesarian delivery.

Hemoglobin level change, mean the difference in hemoglobin level in gram/ deciliter on admission and 24 hours after delivery. In our study mean hemoglobin level change in cases was 0.816 gm/ dl versus 0.74 gm/ dl in controls, p value =0.227. There was no statistical significant difference between the two groups of the study. D. Edwar Z. Khosho and Dr. Weaam (2013) [32] also a study by Karkanis et al (2002) [33], found no significant difference in Delta [Hb] was observed between the two groups; (P value=0.62, P value=0.35 respectively).

The duration of third stage of labour is important since the prevalence of postpartum hemorrhage increase with increase in duration of third stage.

Regarding mean time of placental delivery (duration of third stage of labour) in our study, in misoprostol group was 6.26 minutes versus 5.14 minutes in oxytocin group, p value 0.82 . This result was statistically not significant. This was in agreement with the results of a study done by Dr. Edwar Z. Khosho and Dr. Weaam (2013) [32] in which the length of third stage of labour was statistically non-significant between both groups.

The risk of retained placenta increase with prolonged third stage of labour, in our study the placenta was completely delivered in all patients of both groups and we have no case of retained placenta.

Regarding development of side effects in our study we had more shivering in misoprostol group [(3) in cases versus (1) in controls], and more abdominal pain [(3) in cases versus (0) in controls] but less vomiting [(1) in oxytocin group versus (0) in misoprostol group]. These differences were statistically non-significant [p value 0.744].

These results was in agreement with other studies done by Masoumeh Mirteimouri et al (2013) [34], and Kemik Gul et al (2006) [28]. They found no significant difference in development of side effects between the groups; they conclude that rectal misoprostol seems to be safe in management of third stage of labour and prevention of postpartum hemorrhage.

The results of our study disagree with the results of the study done by Parson et al (2007) [30], which found more shivering in misoprostol group (7.5% in misoprostol group versus 0.9% in oxytocin group) which was highly significant p value =0.001. This may be because of higher dose of misoprostol used (800 mcg).

Conclusions:

- Misoprostol may be used as an alternative to oxytocin in the management of third stage of labour.
- Rectal misoprostol was effective in reducing amount of blood loss, and shortening the duration of third stage of labour.
- Rectal misoprostol seems to be effective and safe in preventing postpartum hemorrhage.

References:

[1]. Manthan M. Patel, Mahrima Jain, 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, 2016Jan; 5(1):80-83.
[2]. Abdel- Alem H, El Nashar I, Abdel – Alem A Management of sever postpartum hemorrhage with misoprostol. Int J Gynecol Obstet; (2001). 72:75-81.
[3]. PA3 TH. Preventing post partum hemorrhage: took it for providers. Condensed version. Washington DC 2004. [Medline].
[4]. International confederation of midwives, International confederation of gynecologists and obstetrician's, Joint Statement: Management of third stage of labour to prevent post-partum hemorrhage, J Midwifery Women's Health, 2004, 99:76-77.
[5]. WHO, Active management of the third stage of labour, 2014/RHR/ 14, 18.
[6]. Phlip N. Baker, Louise C. Kenny, Obstetrics by ten teachers: 19th edition, 338 Euston Road, London NWI 3BH, HODDER ARNOLD, 2011, 202.
[7]. Andres Lopez Bernal, Errol R. Nortwiz, The normal mechanisms of labour, D. Keith Edmonds, Dewhurst's Text book of Obstetrics and Gynecology, UK, Wiley –Black Well, 2012, 260.
[8]. Alan H. Decherny, Lauren Nathan, David Geffen, Normal labour and delivery, Current Obstetrics and Gynecologic diagnosis and treatment, 9th edition, California, 2003:10:213-259.
[9]. Campbell S., editor labour. Obstetrics by ten teachers. 17 edition. London: Arnold, 2000, .P.P.101-141.
[10]. Philip N. Baker editor Labour, obstetric by ten teachers, 18th edition, London: Edward Arnold. 2006, Chapter 17. pp. 255-275.
[11]. Royal college of obstetricians and gynecologists, Prevention and management of postpartum hemorrhage, Green Top Guideline No.52, London RCOG; 2015, 4.
[12]. David M. Luesly, Philip N. Baker, Obstetrics & Gynecology An evidence – based book for MRCOG: second edition, 338 Euston Road, London, Edward Arnold, 2010,361.
[13]. Michael S.R, Alan M.Z. chang Postpartum hemorrhage and other problems of the third stage James DK, Weiner CP, Steer PJ, Gonik B High Risk pregnancy :management options .3rd edition .U.S.A :Elsevier: 2006. pp 1559-1578.
[14]. Bamigboye AA, Hofmeyr GJ, Merell DA). Rectal misoprostol in the prevention of postpartum hemorrhage: A placebo controlled trial.1998, AMJ Obstetric Gynecology; 179: 1043-1046.
[15]. Marcella J. Gowan, Active management of third stage of labour by skilled birth Attendants in a rural regional hospital in southern Ethiopia, A qualitative case study, Doctor of Education (EdD), 2015, 20.
[16]. Caliskan, BurcuAykan, Nilgun Ozturk, Berna Dilbaz, Serdar Dilbaz, Ali H Is rectally or orally administered misoprostol and oxytocin more effective in prevention of postpartum hemorrhage when compared with oxytocin alone? (2003). Artemis J; 4(4):38-44.
[17]. Surbek DV, Fehr PM, Hosli I, Holzgreve W. Oral misoprostol for third stage of labour: A randomized placebo-controlled trial. Obstet Gynecol; 1999, 94:255-258.
[18]. TakayanagiYetal. Pervasive social deficit, but normal parturition, in oxytocin receptor deficient mice. Proc NathAcadsci USA; 2005. 102: 96- 101 PMID.
[19]. Cunningham F G, Leveno KJ, Bloom SL, Hauth JC, Glistap L, Wenstrom KD. Normal labour and delivery. Williams's obstetrics. 22 editions. New York. Chicago: Mcgraw-hell. 2005. PP 430-439.
[20]. El-Refaey H, Rajasekar D, Abdalla M, Calder L, Templeton A. Induction of abortion with mifepristone and oral or vaginal misoprostol. N Engl J Med; 1995, 332: 983-987. [Free Full Text].
[21]. Lokugamage AU, Sullivan KR, Niculescue I, Tigere P, Onyangunga F, El-Refaey H, et al A randomized study comparing rectally administered misoprostol versus syntometrine combined with an oxytocin infusion for the cessation

of primary postpartum hemorrhage. Acta Obstet Gynecol Scand 2001. Sep; 80:835.
[22]. Rehan-Uddin Khan, Hazem El-Refaey, MD. Pharmacokinetics and adverse effect profile of rectally administered misoprostol in the third stage of labour. The American College of Obstetricians and Gynecologists. Elsevier. MAY 2003, Vol.101, No.5, PART 1.
[23]. Cardoso P, Hoj L, Nielson BB, Hvidman L, Neilsen J, Aaby P. Effect of sublingual misoprostol on severe postpartum hemorrhage in a primary health center in Guinea-Bissau: randomized double blind clinical trial. BMJ, 2005.331:723.
[24]. WHO, Recommendations on the use of utertonics for the prevention of post-partum hemorrhage during third stage oflabour, 21, Jan, 2018.
[25]. GholamerzaBafar, MasoumaShohani, Ali Soleymani, Milad Azami, Maternal anemia during pregnancy and small for gestational age: a systematic review and meta-analysis, The journal of maternal-fetal and neonatal medicine, 2018, 1-7.
[26]. Kundodyiwa TW, Majoko F, Rusakaniko S. Misoprostol versus oxytocin in the third stage of labor. Int J GynecolObstet; 2001, 75:235-241.
[27]. Ayaad I, Abu Omer A, Prevention of postpartum hemorrhage by rectal misoprostol: A randomized control trial. Middle East J of Family Medicine; 2004, vol. 5(5).
[28]. Kemik Gul O, Asli Somunkiran, Ismail Ozdemir, Oguz Yucel, Evaluation of the efficacy of rectal misoprostol versus intravenous oxytocin in prevention of postpartum hemorrhage. Turk Jinekoloji ve Obstetrik Dernegi; (2006), 3(3): 162- 166.
[29]. Caliskan E, Meydanli MM, Dilbaz B, Aykan B, Sonmezer M, Haberal A. Is rectal misoprostol really effective in the treatment of third stage of labour? A randomized controlled trial. Am J Obstet Gynecol; 2002, 187(4):1038-1045.
[30]. Parsons SM, Walley RL, Crane JM, Mathews K, Hutchens D, Rectal misoprostol versus oxytocin in the management of third stage of labour. J Obstet Gynecol Can. 2007, Sep; 29(9): 711-8.
[31]. Chaudhuri P., Baerjee GB, Mandal A, Rectally administered misoprostol versus intravenous oxytocin infusion during cesarean delivery to reduce intraoperative and postoperative blood loss, Int J Gynaecol Obstet., 2010, 109(1):25-9.
[32]. Dr. Edwar Z. Khosho, Dr. Weaam F. Almahfooth. Rectal misoprostol versus oxytocin in the management of third stage of labour, Iraqi Academic Scientific Journals, 2013, 7.issue 1, 68-76.
[33]. Karkanis SG, Caloia D, Saleniek ME, Kingdom J, Walker M, Meffe F, Windrim R, Randomized control trial of rectal misoprostol versus oxytocin in third stage management. J Obstet Gynecol Can. (2002); 24(2):149-54.
[34]. Masoumeh Mirteimouri, Fatemeh Tara, Batool Teimouri, Nahid Sakhavar, Afsana Vaezi,Efficacyof rectal misoprostol for prevention of post-partum hemorrhage, IJPR 2013,12 (2):469-474.