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**“Inj.Oxytocin 10IU IM Vs Inj. Oxytocin  
5IU IM + Inj.Methyl Ergometrine 0.2mg  
IM Vs Inj.Carbetocin 100mcg IM during  
AMTSL In vaginal Deliveries – A  
Randomized Controlled Trial”**

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**BY**

**Reg.No: BJ0121016**

**Dissertation**

*Submitted to*

*KAHER, Belagavi, Karnataka,*

*In partial fulfilment of the requirements for the degree of*

**MASTER OF SURGERY (M.S.)**

**In**

**OBSTETRICS AND GYNECOLOGY**

**DEPARTMENT OF OBSTETRICS AND GYNECOLOGY  
JAWAHARLAL NEHRU MEDICAL COLLEGE, KAHER,  
BELAGAVI – 590010, KARNATAKA.**

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**DECEMBER-2024 / JANUARY-2025**

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This is to certify that the dissertation entitled “**Inj.Oxytocin 10IU IM Vs Inj. Oxytocin 5IU IM + Inj.Methyl Ergometrine 0.2mg IM Vs Inj.Carbetocin 100mcg IM during AMTSL In vaginal Deliveries – A Randomized Controlled Trial**” is a bonafide research work done by **Reg. No. BJ0121016**.

  
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With reference to the above, we wish to inform you that your proposed research project titled  
"INTRA MUSCULAR OXYTOCIN 10 UNITS VS OXYTOCIN 5U + ERGOMETRINE  
0.2MG VS CARBETOCIN 100MCG IN REDUCTION OF POST-PARTUM BLOOD  
LOSS- A RANDOMIZED CONTROLLED TRIAL", is ethical and justifiable. The proposed  
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## **LIST OF ABBREVIATIONS USED**

PPH	Post Partum Hemorrhage
MMR	Maternal Mortality Ratio
AMTSL	Active Management of Third Stage of Labour
RCT	Randomized controlled trial
WHO	World Health Organization
HB	Hemoglobin
HCT	Hematocrit
PCV	Packed Cell Volume
CCT	Controlled Cord Traction
IM	Intra-Muscular
HS	Heat Stable
SNOSE	Sequentially Numbered Opaque Sealed Envelop
ACOG	American College of Gynecology
SOGC	Society of Obstetricians and Gynecologists of Canada
CNGOF	French National College of Gynecologists and Obstetricians
CMQCC	California Maternal Quality Care Collaborative
SD	Standard Deviation
CTRI	Clinicals Trials Registry of India
BMI	Body Mass Index
ANOVA	Analysis of Variance

## **ABSTRACT**

**“Inj.Oxytocin 10IU IM Vs Inj.Oxytocin 5IU IM + Inj.Methyl Ergometrine 0.2mg IM Vs Inj Carbetocin 100mcg IM during AMTSL in vaginal deliveries – A Three Arm Randomized Controlled Trial”**

### **Background –**

Obstetric haemorrhage is one of the leading cause of (mainly (PPH) Post Partum Hemorrhage) of maternal mortality, accounting for 35% of maternal deaths worldwide (WHO). In order to achieve SDG goal of 70 prevention of PPH is essential.

Inj Syntometrine (Inj Oxytocin 5IU + Inj Methyl ergometrine 0.5mg) is superior to other uterotonics, with significant side effects mainly due to the higher dose of Inj Methyl Ergometrine. The current study is undertaken with same combination as in Syntometrine but with a lower dose of Inj.Methyl ergometrine of 0.2mg to find out the effectiveness with other uterotonics (Inj.Oxytocin 10IU and Inj.Carbetocin 100mcg).

### **Aims and Objectives –**

**Primary objective -** To compare the effectiveness of the 3 uterotonics which helps in reducing post-partum blood loss.

**Secondary objective –** To assess the requirement of additional uterotonics in management of post-partum bleeding.

### **Methods –**

A three arm randomized controlled trial done, in pregnant women fulfilling the selection criteria, in the labour room of KLE’s Dr. Prabhakar Kore Hospital and Medical Research Centre. Where Group A received Inj Oxytocin 10 IU IM;

Group B received Inj Oxytocin 5IU IM + Inj Methyl ergometrine 0.2mg IM; Group C received Inj Carbetocin HS IM. Post partum blood loss is estimated using calibrated BRASSS V drape, soaked gauze and pad were weighed and pre-delivery and post-delivery hemoglobin and hematocrit were compared.

### **Results –**

Total number of deliveries were 4,093 of which 1,486 were vaginal deliveries. A convenient sample of which 423 participants were screened, 238 participants were eligible where 40 participants were excluded as they underwent emergency caesarean section. Of which 198 participants were randomized into three groups containing 66 participants each. Mean blood loss of each group B ( $186.52 \pm 67.08$ ) which is significantly lower than compared to other groups A and C ( $227.42 \pm 102.34$  ;  $186.52 \pm 70.74$  respectively). Group B also has less participants in having blood loss of > 300ml and 300ml – 500ml . The use of additional uterotonics is also reduced in group B when compared with other groups

### **Conclusion –**

It is evident that the combination of Inj.Oxytocin 5IU IM and Inj.Methyl Ergometrine 0.2mg IM (Group B) is found to be superior in reducing the post partum blood loss and use of additional uterotonics compared to other two groups A and C. Combination of oxytocin and ergometrine is cost effective, due to their low cost compared with carbetocin, this makes more practical choice in many settings and more economical.

### **Key words –**

Post Partum Hemorrhage, Uterotonics, Prevention, Post Partum blood loss, BRASSS V drape.

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## **INTRODUCTION**

Obstetric haemorrhage is one of the leading causes (mainly Post Partum Hemorrhage) of maternal mortality globally.<sup>1</sup> The primary cause of maternal mortality in India, accounting for 47% of recorded cases. This percentage may be even higher in economically disadvantaged states.<sup>2</sup> An essential measure in reducing maternal mortality is the prompt identification and treatment of postpartum haemorrhage (PPH), a condition that is often not accurately recognized in primary healthcare centers in India.<sup>3</sup>

Postpartum haemorrhage (PPH) is , responsible for around 35% of all maternal fatalities globally. The prevalence of postpartum haemorrhage (PPH) is 2%–4% after vaginal delivery and 6% after a caesarean section.<sup>2</sup> The rate of postpartum haemorrhage (PPH) is approximately 12% in rural areas of India where expectant management of labour is prevalent.<sup>8</sup> Postpartum haemorrhage (PPH) can affect 5.8% of women during their initial pregnancy. The likelihood of experiencing a first postpartum haemorrhage (PPH) in a second or third pregnancy is approximately 4%–5%. The likelihood of experiencing a recurrence of postpartum haemorrhage (PPH) in a future pregnancy is as high as 15%. Implementing standardised and multidisciplinary programming can reduce between 54%–93% of maternal deaths caused by obstetric haemorrhage.<sup>4</sup> The majority of fatalities resulting from severe postpartum haemorrhage (PPH) appear to happen within the initial 24 hours following childbirth. The progression of haemorrhage from the compensated to decompensated stage is swift and often goes unnoticed. Therefore, accurate forecasting, prompt identification, and timely intervention are essential for reducing the likelihood of severe postpartum haemorrhage (PPH) or enhancing its clinical results.<sup>5</sup>

Maternal mortality refers to the death of a woman caused by “difficulties during pregnancy, regardless of the stage or location of the pregnancy, childbirth, or within 42 days after the pregnancy ends, excluding unintentional or incidental causes”. Maternal mortality is measured using the “Maternal Mortality Ratio (MMR), which quantifies the number of deaths per 100,000 live births.”<sup>6</sup> Approximately- 20% of maternal fatalities’ are documented in South Asia. India, one of the countries in South Asia, has the “largest number of maternal deaths globally, estimated at 35,000”. This accounts for 12% of the total global maternal mortality.

The “Society of Obstetricians and Gynaecologists of Canada” (SOGC) has provided practical advice on postpartum haemorrhage (PPH). These guidelines ‘urge that active treatment of the third stage of labour, as opposed to expectant management’, should be offered and encouraged to all women as it minimises the risk of PPH. Administering uterotonic medicines effectively prevents postpartum haemorrhage (PPH) and considerably reduces its occurrence, making it a crucial component of active therapy. The administration of Inj Oxytocin 10 IU via intramuscular injection is the recommended treatment for preventing postpartum haemorrhage (PPH) in low-risk vaginal and caesarean deliveries. Healthcare professionals should administer this medicine following the delivery of the front shoulder. An suitable alternative for active management is intravenous infusion of Oxytocin at a dosage of 20 to 40 IU in 1000 mL, administered at a rate of 150 mL per hour. <sup>7</sup> Oxytocin is stored in refrigerator in temperature of 2 degrees to 8 degrees Celsius and requires cold chain.

‘The Royal College of Obstetricians and Gynaecologists’ recommends the use of Ergometrine, an ergot analogue, as a secondary pharmaceutical option for treating uterine atony in cases of postpartum haemorrhage, after oxytocin has been

administered as the primary treatment.<sup>8</sup> Ergometrine is stored in refrigerator in temperature of 2 degrees to 8 degrees celsius and requires cold chain.

Carbetocin, administered as a 100µg intramuscular route or intravenous bolus over 1 minute, can be used instead of a continuous oxytocin infusion after elective caesarean sections to avoid postpartum haemorrhage (PPH) and potentially reduce the need for additional uterotonics. Carbetocin is a synthetic analogue of Oxytocin, a hormone that is known for its long-lasting effects. It is also available in form of heat stable Carbetocin. It was initially described in 1987 and is chemically referred to as 1-deamino-1-monocarbo-(2-O-Methyltyrosine)-oxytocin. The half-life of this substance is 40 minutes, which is approximately 4-10 times longer than oxytocin. Uterine contractions commence within two minutes after intravenous injection of an ideal dosage of 100 µg.<sup>9</sup> It has been hypothesized that a single dosage of carbetocin can mimic the effects of a 16-hour intravenous oxytocin infusion in terms of increasing uterine tone and reducing the risk of postpartum hemorrhage in elective caesarean surgery.<sup>10</sup>

**Need for the Study:**

- Aims to reduce standard dose of Inj Methyl Ergometrine from 0.5mg to 0.2mg and to see if this novel combination is superior to or equally as effective as Inj Syntometrine, as well as to assess if there is a reduction in side effects with lowering the dosage of methyl ergometrine.

## **AIMS AND OBJECTIVES**

### **Primary objective:**

- To determine the effectiveness of uterotonic drugs (Inj Oxytocin 10 IU vs Inj Oxytocin 5 IU + Methyl Ergometrine 0.2mg vs Inj Carbetocin HS 100mcg) which helps in reducing the post partum blood loss.

### **Secondary objectives:**

- To estimate the proportion of women receiving additional uterotonic drugs.
- Women requiring transfusion of blood or blood products.
- Use of additional conservative procedures or use of any surgical interventions to treat postpartum hemorrhage

## **REVIEW OF LITERATURE**

“PPH is defined by the quantity of blood loss following childbirth”. According to “World Health Organisation (WHO)”, “postpartum haemorrhage (PPH) is characterised by a blood loss over 500 mL from the genital tract following vaginal birth”. Nevertheless, a volume of 500 mL is designated as the threshold, which is also regarded as the standard blood loss amount after childbirth. According to the latest “WHO definitions of PPH (2012)”, for vaginal births, “PPH is characterised by blood loss above 500 mL, whereas severe PPH is characterised by blood loss exceeding 1000 mL”. “PPH, in the context of caesarean birth, is characterised by blood loss exceeding 1000 ml”.<sup>11</sup> “According to the American College of Obstetricians and Gynecologists (ACOG), the definition of PPH is cumulative blood loss more than or equal to 1000 ml that is associated with signs or symptoms reflecting hypovolemia within the first 24 hours of the birthing process.”<sup>12</sup> In cases of postpartum haemorrhage (PPH), it is crucial to not only carefully estimate the amount of blood loss but also to closely observe the patient's clinical symptoms. Historically, low systolic blood pressure, increased heart rate, and an elevated respiratory rate are used as indicators of hypovolemia.<sup>13</sup>

### **ETIOLOGY AND RISK FACTORS**<sup>14</sup>

Pregnancy inherently poses a risk for postpartum haemorrhage (PPH); every pregnancy has the potential to lead to PPH. It is crucial to recognise the factors that increase the risk of postpartum haemorrhage (PPH) and take preventive measures. The risk factors for postpartum haemorrhage (PPH) are outlined by Hoveyda et al and have been adapted to cater to the Indian population in the provided table.<sup>15</sup>

**Table 1 - "RISK FACTORS FOR POSTPARTUM HEMORRHAGE**

<b>Maternal issues</b>	
<ul style="list-style-type: none"> <li>• Teenage pregnancy</li> <li>• Elderly primigravida</li> <li>• Multiparity and Grand multiparity (&gt; 4)</li> <li>• Inadequate prenatal visits</li> <li>• low socioeconomic status</li> <li>• Previous postpartum hemorrhage</li> <li>• Previous uterine surgeries</li> <li>• Uterine malformations</li> <li>• Fibroid uterus</li> <li>• Previous cesarean section</li> <li>• Previous instrumental delivery</li> <li>• anemia</li> <li>• Thrombocytopenia</li> <li>• Diabetes</li> </ul>	<ul style="list-style-type: none"> <li>• Cardiac dysfunction</li> <li>• hypertensive disorders</li> <li>• Thyroid dysfunction</li> <li>• Renal and liver disorders</li> <li>• Respiratory disorders</li> <li>• anticoagulant therapy</li> <li>• Viral infections, dengue</li> <li>• Inherited and acquired coagulopathies</li> <li>• hemoglobinopathies</li> <li>• Metabolic syndrome</li> <li>• Post-bariatric surgery</li> <li>• Pregnancy after renal transplant</li> <li>• Multifetal gestation</li> </ul>
<b>Intrapartum</b>	
<ul style="list-style-type: none"> <li>• Induction and augmentation of labor</li> <li>• Precipitate labor and prolonged labor</li> <li>• Obstructed labor</li> <li>• The arrest of labor in the second stage</li> <li>• Trial of labor after cesarean (TOLAC)/ vaginal birth after cesarean (VBAC)</li> <li>• Placenta previa</li> <li>• Placenta accreta syndrome</li> </ul>	<ul style="list-style-type: none"> <li>• Instrumental deliveries</li> <li>• Cesarean section</li> <li>• In-coordinate uterine action (hypotonic &amp; hypertonic)</li> <li>• Prolonged rupture of the membrane (PROM/PPORM)</li> <li>• Chorioamnionitis</li> <li>• Placenta abruption</li> <li>• Arteriovenous malformations</li> </ul>
<b>Postpartum</b>	
<ul style="list-style-type: none"> <li>• Genital tract trauma</li> <li>• Retained placenta</li> <li>• Retained placental tissues</li> </ul>	<ul style="list-style-type: none"> <li>• Uterine inversion, uterine rupture</li> <li>• Subinvolution</li> <li>• Puerperal sepsis</li> </ul>

<b>Fetal issues</b>
<ul style="list-style-type: none"><li>• Polyhydramnios</li><li>• large-for-gestational-age fetus</li><li>• Fetal macrosomia (birth weight greater than 8 lb, 13 oz [4,000 g])</li><li>• Congenitally malformed fetus</li></ul>
<b>Placental issues</b>
<ul style="list-style-type: none"><li>• Placenta previa</li><li>• Placenta abruption</li><li>• Placenta accreta</li><li>• AV malformations</li><li>• Placental abnormalities (battle door placenta, vasa previa etc)”</li></ul>

## **PATHOPHYSIOLOGY**<sup>14</sup>

### **Physiology of uterine contractions**

Gaining knowledge on the physiological aspects of the uterus during full-term and preterm labour is crucial for developing ways to regulate uterine function and address clinical issues associated with childbirth. In the case of regular labour at the end of pregnancy, the chemical alterations in the cervical connective tissue occur before the onset of uterine contractions and the dilation of the cervix. Parturition consists of two primary stages.

- An extending conditioning phase!
- A brief secondary phase (active labor)

The "Conditioning" stage results in cervical softening. The preparation phase in the myometrium, there are changes in transduction mechanisms and synthesis of several proteins, such as connexins, ion channels, and receptors sensitive to uterotonics. Reducing the production of nitric oxide causes the uterus to lose its ability to relax.

### **Uterine atony**

The understanding of the majority of physiological processes in the third stage of labour is currently lacking. Primary postpartum haemorrhage (PPH) caused by “uterine atony occurs when the relaxed myometrium fails to contract the blood vessels, resulting in bleeding”. Due to the fact that approximately 20% of the mother's cardiac output (1000 ml/min) goes into the circulation between the uterus and placenta near the end of pregnancy, postpartum haemorrhage can result in a significant and rapid blood loss. “Uterine atony accounts for 75%–90% of primary postpartum haemorrhage (PPH)”, while “traumatic causes, such as obstetric lacerations, uterine inversion, and uterine rupture, contribute to 20% of all primary PPH cases”. Atonic postpartum haemorrhage (PPH) is a well-established complication. Even if a caesarean section is conducted, there is a notable risk of experiencing heavy bleeding during the surgery.

### **THE 4 T'S: TONE, TISSUE, TRAUMA, THROMBIN**<sup>14</sup>

PPH is caused by anomalies in one or more of four fundamental processes. “the four Ts: tone, trauma, tissue, and thrombin”.

#### **“Uterine contraction Tone / abnormalities”**

Uterine atony accounts for 80% of cases of postpartum haemorrhage (PPH), making it the most frequent cause. Patients with an excessively enlarged uterus (due to twins, macrosomia, or hydramnios) are also at risk. Additional factors contributing to this issue include intra-amniotic infection and functional/anatomic abnormalities of uterus.

**“Tissue (retained product of conception)”**

Retained placenta, which refers to the failure of the placenta to be delivered within 30 minutes after childbirth, happens in approximately 3% to 5% of instances. Retained products of conception or invasive attachments of the placenta to the uterine wall, such as accreta, percreta, or increta, can result in severe postpartum haemorrhage (PPH). PPH has also been associated with thrombosis and embolism.

**“Trauma [at genital tract]”**

Approximately 10%–15% of women encounter trauma during childbirth, which can lead to lacerations and hematomas in the cervix, vagina, and perineum, resulting in substantial blood loss. An exhaustive examination of these regions should be conducted, and the necessary measures to address any damage should be taken. PPH has also been linked to uterine rupture and uterine inversion.

**“Thrombin [abnormality of coagulation]”**

Coagulation problems are an uncommon aetiology of postpartum haemorrhage, occurring in approximately 1% to 2% of cases.

**“ACTIVE MANAGEMENT OF THE THIRD STAGE OF LABOR (AMTSL)”<sup>14</sup>**

Following childbirth, it is imperative to regularly monitor blood loss and other clinical factors. There is not enough data to support the recommendation of measuring the amount of blood loss using objective methods instead than relying on clinical judgement. Implementing measures to prevent postpartum haemorrhage (PPH) can significantly decrease the mortality and morbidity rates among women caused by excessive bleeding during pregnancy. The majority of cases of postpartum haemorrhage (PPH) can be avoided. Multiple circumstances can increase a woman's

susceptibility to experiencing haemorrhage. Nevertheless, 90% of women do not possess any risk factors. Consequently, it is imperative that every woman has the opportunity to receive the services of a proficient birth attendant, who possesses the expertise to effectively handle the process of labour and delivery in order to reduce potential hazards. “Active management of the third stage of labour is more effective than expectant care in reducing blood loss”, postpartum haemorrhage, and other significant problems. Active management should be the preferred method of routine management for women anticipating childbirth in a maternity hospital.

Multiple Cochrane studies have provided information on the preventive measures for the third stage of labour in women who give birth vaginally. Based on these review studies, the likelihood of postpartum haemorrhage (PPH) can be diminished by implementing active management techniques and administering preventive uterotonics during the third stage of labour. “AMTSL, or Active Management of the Third Stage of Labour”, is a procedure that involves the use of interventions such as uterotonics, early umbilical cord clamping, and controlled cord traction (CCT). The purpose of AMTSL is to speed up the delivery of the placenta and minimise blood loss. During expectant management, the medical team waits for indicators of placental separation and allows the placenta to be delivered naturally. Based on a Cochrane systematic review, active management was found to decrease the average risk of severe bleeding during childbirth (more than 1000 ml and low maternal haemoglobin levels (less than 9 g/dl) after giving birth for women with varying levels of bleeding risk.

- “All the three steps AMTSL should only be done by SBA/trained staff.
  - i. Administration of uterotonics after delivery of baby
  - ii. Delayed cord clamping
  - iii. Controlled cord traction”

“AMTSL, which stands for Active Management of the Third Stage of Labour, is a preventive measure that is endorsed by the World Health Organisation (WHO)”. Over the years, there has been a focus on preventing postpartum haemorrhage (PPH) through the use of Active Management of the Third Stage of Labour (AMTSL). “The protocol includes three components: 1) Administering uterotonic medication immediately after the infant is delivered, 2) Applying controlled tension to the umbilical cord, and 3) Performing uterine massage”. By administering uterotonics, the three treatments can be consolidated into a single step of care, as it promptly enhances uterine contraction following delivery. Uterotonics should be provided to all women who have given birth, whether through caesarean or vaginal delivery, in order to avoid postpartum haemorrhage (PPH).

- Oxytocin intravenous injection has been the preferred uterotonic agent for “Active Management of the Third Stage of Labour (AMTSL)” over the years. Based on studies examining the safety and efficacy of uterotonics, Oxytocin (10 IU, IM) is the recommended choice for contraction of uterus.

When oxytocin is not accessible, carbetocin (100 mcg IM/IV) that can be stored at room temperature, or “methylergometrine (0.2 mg IV/IM), or misoprostol (800 to 1,000 mcg rectally or 600 to 800 mcg sublingually or orally) should be considered as the initial options”. It is important to be cautious when considering ergot derivatives (methylergometrine) as a preventive measure for postpartum haemorrhage, as these medications are not

recommended for women with hypertensive problems. Therefore, it is advisable to refrain from using ergot derivatives in populations that have not been tested. If there is no skilled attendant present and oxytocin is not accessible, such as in the case of an unattended home birth, administer 600 mcg of oral misoprostol. Women who give birth without a trained professional present should also get uterotonic medication to avoid postpartum haemorrhage. Therefore, it is recommended that a community health worker who is there administer oral misoprostol. Delayed cord clamping, which involves clamping the umbilical cord within 1 to 3 minutes after delivery, is still advised for all deliveries.

- The uterus is examined by pressing on the abdomen, and after it contracts (which typically occurs within 1 to 3 minutes after uterotonics are given), controlled cord traction is used to deliver the placenta. It is not advisable to use Control Cord Traction (CCT) when SBA is unavailable.
- Expeditiously suture any tears in the perineum, labia, or from an episiotomy.
- Continue to regularly palpate the uterus to ensure it remains firm (contracted).
- Assist the mother in nourishing and tending to her infant.

**Table 2 - "OVERVIEW OF UTEROTONICS – POST PARTUM**

**HEMORRHAGE"<sup>14</sup>**

<b>"Drug</b>	<b>Dosage</b>	<b>Action</b>	<b>Side effects</b>	<b>Contraindication</b>
Oxytocin	10U IM/IV	Onset: 1–3 mins lasts: 10–15 mins	Minimal	<ul style="list-style-type: none"> <li>• Allergic to oxytocin</li> <li>• Cardiac dysfunction (to minimize risk of volume overload)</li> <li>• Obstructed labour</li> <li>• Grand-multiparity (relative contraindication)</li> </ul>
Methylergometrine	0.2mg IV/IM	Onset: 2–7 mins lasts: 2–4 hours	Nausea, vomiting, headache, hypertension	<ul style="list-style-type: none"> <li>• Hypertension</li> <li>• Cardiac disease</li> </ul>
Prostaglandin F2a	250mcg IM	Onset: 1–2 mins lasts: 15–20 mins	Vomiting, diarrhea, bronchospasm	<ul style="list-style-type: none"> <li>• Bronchial asthma</li> </ul>
Misoprostol	800 to 1,000 mcg rectally or 600 to 800 mcg sublingu ally or orally	Onset: 3–5 mins Peak: 20–30 mins lasts: <75 mins	Shivering, rise in temperature	<ul style="list-style-type: none"> <li>• Pre-existing cardiovascular disease</li> </ul>
Carbetocin room temperature stable	100mcg IV/IM	<ul style="list-style-type: none"> <li>• Rapid onset of action (within 2 minutes for both IV and IM administration)</li> <li>• long half-life, and prolonged duration of action (60 min for a single IV</li> </ul>	Generally well tolerated, Vomiting, abdominal pain, headache, tremor, dizziness, chest pain	<ul style="list-style-type: none"> <li>• Serious cardiovascular disorders</li> <li>• In women with hepatic or renal disorders</li> <li>• Epilepsy</li> <li>• Hypersensitivity to carbetocin, oxytocin or any of the</li> </ul>

		injection, 120 min for an IM injection)		excipients according to the composition <ul style="list-style-type: none"> <li>• Pregnancy and labour before the delivery of the infant</li> <li>• Must not be used in induction of labour</li> </ul>
Syntometrine	Combina tion of Inj Oxytoci n 5iu IM + Inj Methyl ergometr ine 0.5mg IM	Onset : 2.5 mins  Lasts : 3 hours	Nausea, vomiting, headache, hypertension	<ul style="list-style-type: none"> <li>• Hypertension</li> <li>• Cardiac disease”</li> </ul>

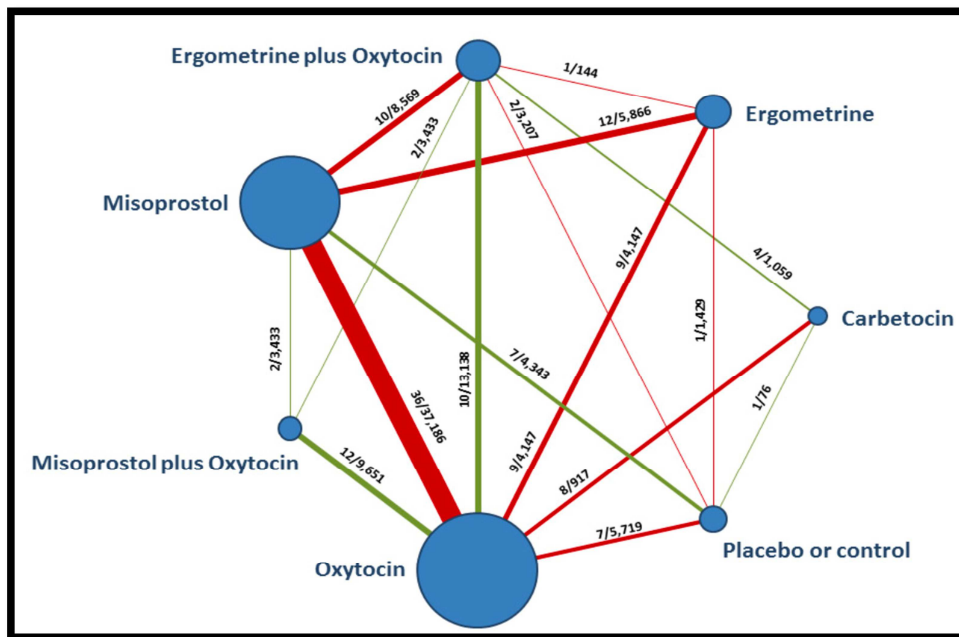


Figure 1 : Network meta-analysis

Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis (Review)

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Network diagram for PPH  $\geq$  500 mL. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green when more than 50% of the trials involved in the specific direct comparison are judged to be at “low risk of bias” if they were double-blinded, and had allocation concealment with little loss to follow-up (less than 10%). The colour is red when less than 50% of the trials are at “low risk of bias”. Multi-arm trials contribute to more than one comparison.<sup>18</sup>

A Cochrane network meta-analysis done by comparing different trial outcomes done between uterotonics and it concludes Ergometrine plus oxytocin combination, carbetocin, and misoprostol plus oxytocin combination were more effective for preventing PPH than the current standard oxytocin alone.<sup>18</sup>

## **OXYTOCIN**

Oxytocin, which is released by the posterior pituitary gland, shares a similar structure with vasopressin. Activation of oxytocin receptors in the myometrium results in contractions of the myometrium<sup>16</sup>. The density of these receptors rises as the pregnancy progresses and during labour, and it is greater in the upper part of the uterus (fundus) compared to the lower part (lower uterine segment)<sup>17</sup>.

**Effectiveness:** A network meta-analysis of randomised studies found that oxytocin was only superior to placebo/no therapy in decreasing postpartum haemorrhage (PPH) of 500 mL or more<sup>18</sup>.

**Administration:** Administering oxytocin intravenously (IV) is more advantageous than administering it intramuscularly (IM) due to its higher effectiveness, more precise dose, and faster beginning of action. However, IM injection is an acceptable alternative for patients who do not have access to IV. A meta-analysis of randomised trials compared the use of prophylactic IV oxytocin, typically administered at varying infusion rates of 10 units in one litre of normal saline, with IM oxytocin, typically administered once at a dose of 10 units, in reducing blood loss during the third stage of labour. The analysis included 7 trials with a total of 7817 participants. The results showed that IV administration of oxytocin reduced the risk of postpartum haemorrhage (PPH) of 500 mL or more (5.6% versus 7.2%) and the need for blood transfusion (0.6% versus 1.3%). There was also a trend towards a reduction in serious maternal morbidity (0.3% versus 0.6%) and PPH of 1000 mL or more (1.5% versus 2.3%). The incidence of side effects was comparable in both groups.<sup>19</sup>

**Intravenous infusion:** There is a lack of sufficient data to provide definite recommendations for the ideal dosage and length of therapy for IV oxytocin infusion as a preventive measure. As a result, different institutions have varying approaches to this treatment.<sup>20</sup> The typical dosage of oxytocin ranges from 10 to 40 units, which is administered in a solution of 500 to 1000 mL of 0.9 percent saline. The infusion rate is regulated based on the contraction strength of the uterus, with a maximum rate of 500 mL per hour<sup>21</sup>. The rate is then reduced (e.g., to 1 to 2.5 units/hour) as long as there is consistent contraction of the uterus and bleeding is not excessive. The treatment plan involves administering 30 units of medication in a 500 mL solution of 0.9 percent saline through intravenous infusion over a period of one hour. This is followed by an additional 30 units of medication in a 500 mL solution, which is infused at a rate of 125 mL per hour (equivalent to 2.5 units per hour) until the entire

solution is infused. According to the CMQCC, one expert organisation, the recommended dosage is 10 to 30 units of crystalloid in 500 mL or 20 to 60 units of crystalloid in 1000 mL<sup>22</sup>. A standard infusion consists of 30 units dissolved in 500 mL of crystalloid solution, which is administered at a rate of 334 mL per hour. This rate ensures that 10 units are delivered during the first 30 minutes, followed by a maintenance rate of 125 mL per hour to supply an additional 7.5 units over the next 60 minutes<sup>22</sup>. Following the facility policy and administering a standardised concentration helps minimise the likelihood of medication errors<sup>23</sup>. Some facilities use the same concentration of oxytocin for both managing the third stage of labour and inducing labour in order to reduce the likelihood of medication errors. If the patient is stable, the IV line is withdrawn at the conclusion of the oxytocin infusion. In patients, when uterine tone and volume of bleeding are normal, the total infusion time typically ranges from two to four hours after birth. However, the duration may vary depending on the specific protocols used<sup>24,25</sup>. Some clinicians prolong the infusion for a maximum of eight hours in patients who are at a heightened risk of haemorrhage. Studies have examined doses greater than about 40 units administered over a period of 60 minutes, but no obvious advantage has been shown. A randomised trial was carried out to compare the effects of three different doses of “oxytocin (80, 40, or 10 units/500 mL normal saline infused over one hour) on nearly 1800 vaginal births. The study discovered that there was no discernible variation in the frequency of atony or haemorrhage requiring treatment (such as uterotonic medications, transfusion, tamponade, embolisation, or surgery) between the groups receiving 80 units versus 10 units or 40 units versus 10 units”. The composite outcome of atony or haemorrhage requiring treatment was observed in 6 or 7 percent of patients in each group<sup>26</sup>. Following the initial hour, the 80 units group had a decreased likelihood of receiving more oxytocin in comparison to the 10 units group. Administration of a

large amount of oxytocin did not result in a higher occurrence of side effects that necessitated the use of additional fluids or medications to address low blood pressure or excessive fluid accumulation. A systematic review and meta-analysis examining several intravenous oxytocin dose regimens for preventing postpartum haemorrhage after caesarean birth did not find any conclusive evidence supporting the superiority of one regimen over another<sup>20</sup>. During a single experiment, a total of 80 units were administered intravenously over a period of 30 minutes to 158 patients. This treatment did not result in any increase in adverse effects. Furthermore, it was seen that the need for further uterotonic medication was less frequent in comparison to the administration of 10 units, with percentages of 19 and 39 respectively<sup>27</sup>.

**Intramuscular administration:** Intramuscular (IM) delivery of 10 units of oxytocin is a viable option when intravenous (IV) infusion is not possible. However, it is somewhat less efficacious than IV oxytocin, as explained earlier<sup>28,29</sup>. The onset of action is comparatively slower when administered through methods other than intravenous (IV) route, taking approximately three to seven minutes. In contrast, the IV route has a faster onset of action, typically less than one minute. However, the clinical effect of non-IV routes lasts longer, likely for at least one hour, whereas the IV route's clinical effect lasts for three to five minutes. The efficacy and safety of repeated intramuscular (IM) dosing has not been investigated. However, according to one monograph, it is advised that the IM dose of 10 units can be repeated every four hours<sup>30</sup>.

**Intravenous bolus:** Administering oxytocin intravenously as a bolus is effective and potentially more effective than intramuscular administration<sup>31</sup>. However, the safety of this method has been called into question due to reported cases of severe low blood pressure resulting from rapid injection. This can potentially cause heart muscle

damage, cardiovascular failure, and even death<sup>32-35</sup>. These incidents occurred in individuals who were undergoing caesarean birth while under neuraxial anaesthesia. It is possible that the cases were, at least partially, caused by the anaesthesia and the underlying cardiovascular illness. In a clinical investigation with more than 1000 individuals who underwent vaginal birth, there were no recorded incidents.<sup>36</sup> While bolus injection may be beneficial for certain people receiving therapy for PPH, it is not required for preventing PPH and should be avoided from in patients with cardiovascular risk factors. The lowest effective bolus dose of oxytocin for a single injection is uncertain, but it seems to be no more than 3 units administered over a period minimum of one minute, and it could be as low as 0.3 units<sup>37,38</sup>. If the starting bolus injection proves ineffective, it might be administered again once or twice before considering an alternative drug. It is recommended to administer the injection slowly over a period of three minutes in order to reduce the cardiovascular effects (such as a fall in blood pressure and systemic vascular resistance index, and an increase in cardiac and left ventricular work indices) that are associated with a quick bolus. The “French College of Gynaecologists and Obstetricians (CNGOF) and French Society of Anesthesiology and Intensive Care have recommended administering 5 to 10 units intravenously (IV) over a minimum of one minute”. However, in patients with obvious cardiovascular risk factors, the administration should be extended to at least five minutes<sup>25</sup>. Following the administration of a concentrated dose of medication, an ongoing delivery of oxytocin is typically started. This continuous infusion has been seen to decrease the amount of blood loss and the requirement for blood transfusion and/or additional drugs that stimulate uterine contractions, in comparison to just a concentrated dose of medication<sup>39,40</sup>. Nevertheless, the administration of both a bolus injection and an infusion does not seem to decrease the requirement for additional

uterotonic drugs when compared to the use of an infusion alone, while initially inducing a more intense uterine contraction<sup>41</sup>.

**Side effects:** The majority of oxytocin's negative effects are directly linked to the dosage and speed at which it is administered. Flushing is linked to the relaxation of vascular smooth muscle cells and the widening of blood vessels in the periphery. Administering a large amount of oxytocin rapidly through an intravenous injection (known as IV bolus) can result in severe adverse effects, such as low blood pressure and raised heart rate, which can potentially lead to chest discomfort, cardiovascular failure, and death. Infrequently, administering high quantities of oxytocin over an extended duration has resulted in fluid retention, resulting in hyponatremia and its subsequent complications. Oxytocin has the potential to lengthen the QT interval, however, it is not necessary to routinely perform an ECG prior to its administration.

### **ERGOT ALKALOIDS**

Ergot alkaloids act as agonists on serotonergic receptors in smooth muscle, weakly antagonise dopaminergic receptors, and function as partial agonists on alpha-adrenergic receptors. They cause rapid and regular contractions of the uterus, resulting in prolonged uterine contraction (spasm, tetany)<sup>42</sup>. The primary ergot alkaloids utilised for the prevention of postpartum haemorrhage (PPH) are ergometrine/ ergonovine, methylergometrine/ methylergonovine, and the combination of ergometrine-oxytocin. Ergometrine-oxytocin capitalises on the swift initiation of oxytocin's effects and the enduring uterotonic properties of an ergot alkaloid (with a half-life ranging from 30 to 120 minutes).

**Effectiveness:** Based on a network meta-analysis of randomised trials, ergometrine alone shown greater efficacy than placebo or no therapy in decreasing postpartum

haemorrhage (PPH) of 500 mL or more<sup>18</sup>. When comparing oxytocin alone with another treatment, there was a tendency towards reduced effectiveness.

The combination of oxytocin and ergometrine, marketed under the brand name Syntometrine. In the context of network analysis, the combination of ergometrine and oxytocin was found to be more efficacious than placebo or no treatment in reducing postpartum haemorrhage (PPH) of 500 millilitres or more.

**Administration:** Ergot alkaloids are typically administered via intramuscular injection. Ergot alkaloids should not be used in individuals with hypertension, Raynaud phenomenon, known coronary artery disease, or hypersensitivity to the medicine due to their vasoconstrictive properties. The typical dosage for Methylergonovine (methylergometrine) or ergonovine (ergometrine) is 0.2 mg injected intramuscularly. The time it takes for the effects to start is between two to five minutes. Alternatively, the medicine can be administered via direct injection into the myometrium. While it is technically possible to inject medication slowly into the blood vessels, it is not advisable since it can lead to severe negative effects on the heart or brain<sup>43</sup>. While oral administration is technically an option, it is not advisable due to the fact that it takes 20 to 30 minutes for the drug to have an impact on the uterine muscle, and the effectiveness of the drug can vary due to inconsistent absorption into the bloodstream<sup>16,44</sup>. The combination of oxytocin-ergometrine is composed of 5 units of oxytocin and 0.5 mg of ergometrine. It is delivered intramuscularly.

**Side effects:** One significant drawback of ergot alkaloids, in comparison to oxytocin, is that they are linked to a higher occurrence of side effects, namely an elevated risk of raised blood pressure and its subsequent consequences. Headache, a rise in

postpartum abdominal pain necessitating analgesia, and vomiting are further side effects.<sup>45</sup>

### **CARBETOCIN**

Carbetocin, a synthetic analogue of oxytocin, has pharmacologic qualities that closely resemble those of natural oxytocin. However, its half-life is significantly longer, ranging from 4 to 10 times that of natural oxytocin, lasting approximately 40 minutes<sup>46</sup>. It attaches to receptors in the smooth muscles of the uterus and has been shown to cause a strong and sustained contraction of the uterus within two minutes. This contraction typically lasts for about six minutes, followed by rhythmic contractions for one hour<sup>47</sup>.

The potential benefits of carbetocin include its extended duration of effectiveness and the availability of a formulation that remains stable under high temperatures.

**Effectiveness:** Carbetocin shown superior efficacy compared to placebo/no therapy in decreasing postpartum haemorrhage (PPH) of 500 mL or more, according to a network meta-analysis of randomised studies<sup>18</sup>. Additionally, it showed greater efficacy compared to oxytocin administered alone.

A network meta-analysis of randomised trials specifically focused on caesarean births found that “carbetocin was more effective than oxytocin in reducing estimated blood loss, although the difference in volume (55 mL) was not clinically significant”. Carbetocin also resulted in a lower need for additional uterotonic medications, with 68 cases per 1000 cases compared to 253 instances with oxytocin<sup>48</sup>.

**Administration:** Carbetocin, at a dosage of 100 mcg, is given intravenously (IV) during a time frame of 30 to 60 seconds<sup>46,49</sup>. Alternatively, the identical dosage can be administered via intramuscular injection, which may yield greater efficacy<sup>31</sup>. The

dosage remains consistent during vaginal birth, planned caesarean birth, and intrapartum caesarean birth. Smaller amounts of the medication may be enough, and can be given again if needed, but the total amount should not exceed 100 mcg. The extended duration of action obviates the necessity for an infusion subsequent to the initial dosage.<sup>49</sup>

**Side effects:** Although there is a lack of data, carbetocin's profile of side effect is comparable to that of oxytocin, including QT prolongation<sup>18</sup>.

### **SYNTOMETRINE**<sup>50</sup>

Syntometrine is a mixture of oxytocin and ergotamine, and 1 ml of syntometrine contains 5 IU oxytocin and 0.5 mg ergometrine. This mixture combines the rapid onset of action of oxytocin and the sustained effect of ergometrine and is one of the most popular uterotonic agents used in the third stage of labour. The UK practice guidelines presently prescribe Syntometrine for patients with active postpartum hemorrhage (PPH). Compared to oxytocin, syntometrine appears to lower the risk of postpartum hemorrhage (PPH) in women who are not at high risk of PPH (> 500–1000 ml) after vaginal delivery. There was no discernible difference between syntometrine and oxytocin in big PPH cases (> 1000 ml). Side effects like nausea and vomiting (which can occur in as many as 46%) and hypertension (which is contraindicated if pre-existing) are often reported side effects of syntometrine administration, despite the medication's positive benefits on lowering PPH and the decreased need for further uterotonics.

**MISOPROSTOL**<sup>18</sup>

Uterine contractions are brought on by the synthetic prostaglandin E1 analog misoprostol. When compared to oxytocin and ergot alkaloids, it is more favorable due to its thermal stability and simplicity of administration in low-resource settings where refrigeration and clean needles are not available.

**Effectiveness:** Misoprostol was found to be more efficacious than placebo or no treatment in decreasing PPH  $\geq 500$  mL in a network meta-analysis of randomized trials. Outcomes compared with oxytocin alone were mixed.

**Administration:** It is possible to administer misoprostol buccally, rectally, sublingually, or orally. Postpartum vaginal administration is not practicable due to the possibility of uterine hemorrhage obstructing the medication's absorption. The oral, sublingual, and buccal routes have a relatively rapid onset of action (within 10 to 15 minutes) and more rapid onset than rectal administration. The half-life is 20 to 40 minutes. Hypersensitivity to the drug is a contraindication. The International Federation of Obstetrics and Gynecology and the World Health Organization (WHO) recommend administration of misoprostol 600 mcg orally when injectable uterotonics are not available.

**Side effects:** Frequent adverse effects include fever and shivering. Shivering is typically present prior to misoprostol-related fever, which starts after 20 minutes of administration, peaks after one to two hours, and then naturally reduces over the course of three hours. The incidence of fever varies by dose and route of administration and is most common in patients receiving high doses sublingually. In a single small pharmacodynamic research, 8 percent of patients receiving 200 or 400

mcg sublingual misoprostol experienced fever over 39°C, whereas 45 percent of those receiving 600 mcg became febrile.

### **TRANEXAMIC ACID**<sup>18</sup>

Tranexamic acid is an antifibrinolytic medication that has been useful for both prevention and treatment of bleeding in various clinical settings. Its mechanisms of action have not been elucidated completely and may extend beyond anti fibrinolysis. Its use has become a standard of care in the treatment of patients with PPH; the author of this topic uses it prophylactically as well.

**Administration:** Tranexamic acid 1 g is administered intravenously (IV) over 10 minutes.

**Side effects:** Thrombosis and thromboembolism (venous and arterial, including central retinal artery/vein obstruction) are theoretic concerns, but a statistically significant increase in such events compared with controls was not reported in a meta-analysis of randomized trials in patients of all ages, sexes, and medical/surgical disciplines (216 trials, >125,000 patients, thrombotic events 2.1 versus 2.0 percent in the control group, risk difference 0.001; 95% CI -0.001 to 0.002).

### **CARBOPROST**<sup>51</sup>

A prostaglandin analogue called carboprost (15-methyl prostaglandin F2 $\alpha$ ) is used to treat postpartum hemorrhage (PPH) brought on by uterine atony. Hemabate-Upjohn's is administered via deep intramuscular injection and includes 250 $\mu$ g of carboprost per milliliter. It is intended only as a backup medication in cases where oxytocin and ergot derivatives have proven ineffective in halting bleeding. In the few clinical trials that were conducted, it was able to control bleeding in almost 90% of

patients when traditional treatments failed. The likelihood of carboprost treatment failure increases in the presence of reasons other than uterine atony, such as residual placental materials. Fever, vomiting, diarrhea, and elevated blood pressure each impact roughly 10% of individuals. The medication is only safe to use when there is no risk of pulmonary oedema or asthma, which are rare but dangerous side effects in units with 24 hour medical cover.

### **Blood loss measurement**

After delivery, there is always some blood loss; however, when there is excessive maternal blood loss, PPH is to be considered.

Early detection of excessive blood loss allows for quicker implementation which benefits the mother's health. Therefore, finding the optimal method to assess post-partum blood loss is crucial<sup>61</sup>.

The birth attendant frequently measures blood loss by observing the volume of blood lost and calculating it (visual estimation) quantitatively or semi-quantitatively. Even though this method is not extremely precise, it is accessible in all birth environments.<sup>62</sup>

Another technique involves the delivery attendant placing a shallow bedpan beneath the mother's buttocks and weighing the blood that has been gathered and blood that has flowed into any pads or other materials. It is known as an indirect method<sup>63</sup>.

One direct approach that has been developed involves placing a "calibrated delivery drape" (Excellent BRASSSV Drape™) under the mother's buttocks, tying it around her waist, and hanging the calibrated funnel portion of the drape between her legs to show how much blood is lost<sup>64</sup>.



**Figure 2: BRASS V drape**

Two evaluation methods are available once the bleeding stops: either the bag can be calibrated so that a direct measurement can be made, or it can be weighed (a process known as the gravimetric technique)<sup>65</sup>.

Hemoglobin concentration (Hb) in venous blood sampling and spectrophotometry provides a more accurate way to assess blood loss.

## **MATERIALS AND METHODS**

The present study was conducted, in the labour room, Department of Obstetrics & Gynaecology, KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre.

**STUDY DESIGN:** A Randomized Controlled Trial.

**STUDY POPULATION:** Pregnant women in labour admitted in labour room, KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, meeting the selection criteria.

**STUDY PERIOD:** April 2023 to March 2024.

### **SELECTION CRITERIA -**

#### **INCLUSION CRITERIA**

- Women with age  $\geq 18$  years
- Singleton live gestation
- Gestational age between 37 weeks to 41 weeks
- Women willing to provide informed consent
- Women admitted in labour (< 6cm cervical dilatation – as per WHO criteria)

#### **EXCLUSION CRITERIA**

- Hypertensive disorders of pregnancy
- Known medical disorders like Cardiac diseases, Bronchial asthma, Epilepsy etc.
- Antepartum hemorrhage

- Known coagulopathies – ITP, hemophilia, von Willebrand disease, clotting factor deficiencies, DVT, DIC
- Known hemoglobinopathies
- Diagnosed placental abnormalities

**ETHICAL CLEARANCE:** The study was approved by JNMC institutional Ethics & Research committee, Belagavi (vide. 7/11/22 Ref no. MDC/JNMCIEC/251)

**CTRI REGISTRATION:** The study trial was also registered with Central Trial registry of India. (vide. 24/05/2023 Reg no. CTRI/2023/05/053086)

**SAMPLE SIZE:**

- The following formula was used for calculating sample size,

$$n = \frac{2 \left( Z_{1-\frac{\alpha}{2*k}} + Z_{1-\beta} \right)^2}{f^2}$$

$$\text{where, } f = \left( \frac{\min(|\mu_i - \mu_j|)}{\sigma} \right)$$

- where,  $\mu_i$  is mean of  $i^{\text{th}}$  group,  $\mu_j$  is mean of  $j^{\text{th}}$  group,  $\sigma$  is the common error variance,  $Z_{1-\frac{\alpha}{2*k}}$  is Z score adjusted for  $\alpha$  level of significance (Bonferroni Correction),  $k$  is the number of pairwise comparisons and  $Z_{1-\beta}$  value is Z score for  $(1-\beta)$  % power.

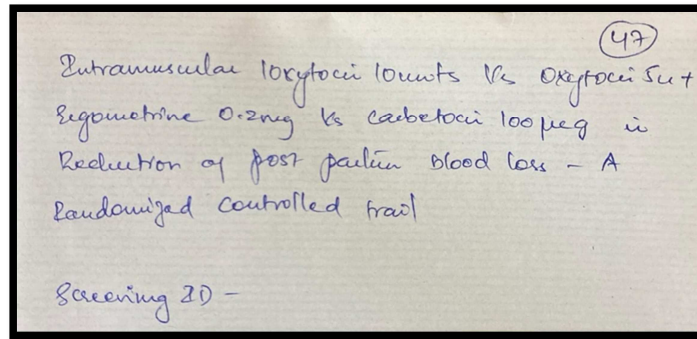
- The current study has 3 groups i.e.,

- Group A –Inj Oxytocin 10 IU IM
- Group B - Inj Oxytocin 10 IU IM + Inj Methyl Ergometrine 0.2mg IM
- Group C –Inj Carbetocin HS 100mcg IM.

- ▶ Assuming that the blood loss has between group effect size to be 0.4, at 5% level of significance, and 80% power, the sample size is obtained to be 44 subjects per group. Hence, total sample size per group required was  $44 \times 3 = 132$  subjects with **20% additional**.
  
- ▶ The accuracy of the result increases with an increase in sample size.

**PROCEDURE:**

- ▶ All pregnant women in labour admitted to labour room for delivery, who fulfil the selection criteria were screened, eligible consented women were enrolled into the study.
  
- ▶ The details of each participant were recorded using a “pre-approved data collection instrument (study related proforma)” Annexure (no.)
  
- ▶ Participants were randomized by SNOSE method (Sequentially Numbered Opaque Sealed Envelope – done by the study pharmacist and randomization list was kept with the pharmacist) , randomization was done when the participant was in active labour (> 6cm dilated)
  
- ▶ Participants were randomized into either of 3 groups -
  - Group A - Inj Oxytocin 10 IU IM
  - Group B - Inj Oxytocin 5 IU IM + Inj Methyl Ergometrine 0.2mg IM
  - Group C - Inj Carbetocin HS 100 mcg IM



**Figure 3 – Sealed envelop (SNOSE Method)**

- As per the randomization, the particular drug was administered within 1 minute of delivery of the fetus to the mother, by intramuscular route as a component of AMTSL
- Estimation of maternal blood loss – Blood loss was measured by calculating the blood collected in BRASSS V DRAPE (calibrated), which is placed under the buttocks of the women, after delivery of the fetus and wet gauze and pads used during delivery were weighed on a digital scale, by subtracting their dry weights of gauze and pad used during delivery (1g = 1ml).



**Figure 4 – Calibrated BRASSS V drape, soaked gauze and pad**

- Pre-delivery Hemoglobin and Hematocrit (at the time of admission ) and post-delivery Hemoglobin and Hematocrit ( $60 \pm 12$  hours after the delivery of the fetus) were compared.

**DATA PROCESSING AND ANALYSIS/ STATISTICAL ANALYSIS:**

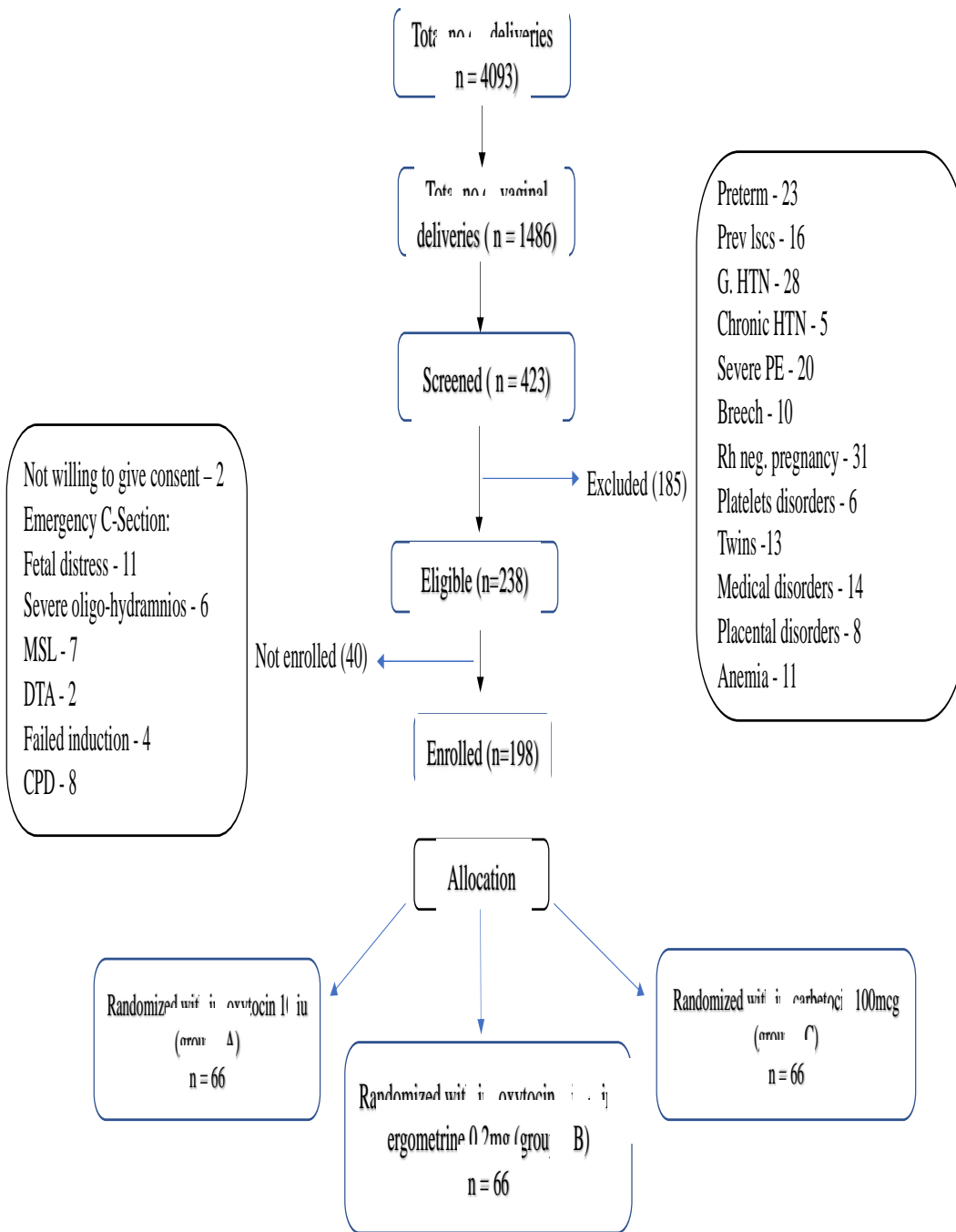
“Data was entered into M.S. Excel sheet and was statistically analysed using Statistical package for social sciences (SPSS Version 16) for M.S Windows.

Descriptive statistical analysis was carried out to explore the distribution of several categorical and quantitative variables. Categorical variables were summarized with n (%), while quantitative variables were summarized by mean  $\pm$  S.D. All results were presented in tabular form and are also shown graphically using bar diagram or pie diagram as appropriate. The difference in the two groups was tested for Statistical Significance using Parametric tests such as t-test, ANOVA (Analysis of Variance) was used to compare the means of continuous variables and categorical variables tested by chi square test. P-value  $<0.05$  was considered statistically significant after assuming all the rules of statistical tests”.

## **RESULTS**

The present study, was conducted in the “Department of Obstetrics & Gynaecology at KLE’s Dr. Prabhakar Kore Hospital and Medical Research Centre”, amongst the labouring women, admitted in labour room for safe confinement, aimed to compare the effectiveness of Intramuscular Inj Oxytocin 10IU, Oxytocin 5IU plus Methyl Ergometrine 0.2mg, and Carbetocin (100 mcg) in reducing postpartum blood loss. [Group A: Inj Oxytocin 10IU IM; Group B: Inj Oxytocin 5IU IM + Inj Methyl Ergometrine 0.2mg IM; Group C: Inj Carbetocin 100 mcg IM (heat stable)]

CONSORT diagram (Consolidated Standards of Reporting Trials)



**Table 3 – Comparison of baseline demographic characters between 3 participant groups**

Variables	Sub Category	Intervention group			Total N= 198	p-value
		Group A N=66	Group B N=66	Group C N=66		
Mean Age	Mean $\pm$ SD	24.79 $\pm$ 3.05	25.49 $\pm$ 3.36	25.25 $\pm$ 3.35	25.18 $\pm$ 3.26	0.4199 <sup>K</sup>
Gravida	Primigravida	32 (32.7%)	32 (32.7%)	34(34.7%)	98	0.92
	Multigravida	34 (34%)	34 (34%)	32 (32%)	100	
Gestation age at delivery	Mean $\pm$ SD	38.71 $\pm$ 0.96	38.76 $\pm$ 1.03	38.92 $\pm$ 1.07	38.8 $\pm$ 1.02	0.4953 <sup>K</sup>
BMI	Normal (18.5-24.9)	4 (28.6%)	4 (28.6%)	6 (42.9%)	14	0.82
	Over weight (25-29.9)	58 (33.3%)	60 (34.5%)	56 (32.2%)	174	
	Obesity(>30)	4 (40%)	2 (20%)	4 (40%)	10	

All 3 groups demographic characters are well matched, as they show no statistical significance.

#### Age Group Distribution

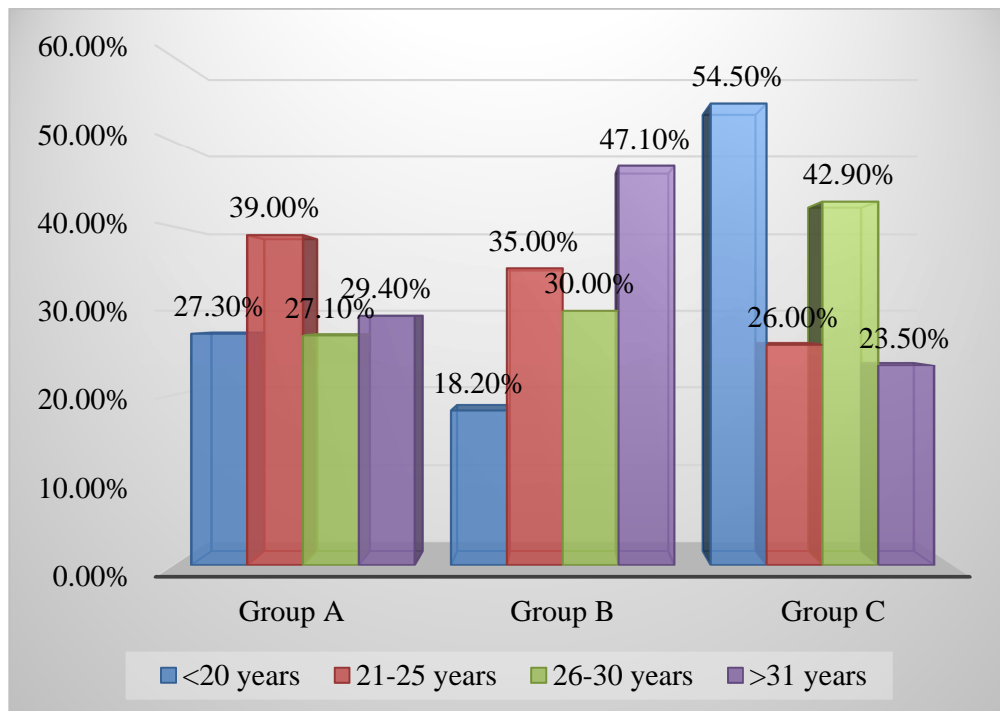
Group A vs B: p=0.75

Group A vs C: p=0.10

Group B vs C: p=0.10

Group A vs B vs C: p=0.14

The age groups are categorized as <20 years, 21-25 years, 26-30 years, and >31 years. In the <20 years category, there are 3 participants (27.3%) in Group A, 2 participants (18.2%) in Group B, and 6 participants (54.5%) in Group C. For the 21-25 years category, Group A has 39 participants (39.0%), Group B has 35 participants (35.0%), and Group C has 26 participants (26.0%). In the 26-30 years category, Group A includes 19 participants (27.1%), Group B includes 21 participants (30.0%), and Group C includes 30 participants (42.9%). For those aged >31 years, Group A has 5 participants (29.4%), Group B has 8 participants (47.1%), and Group C has 4 participants (23.5%).



**Graph 1: Age Group Distribution**

BMI Category Distribution

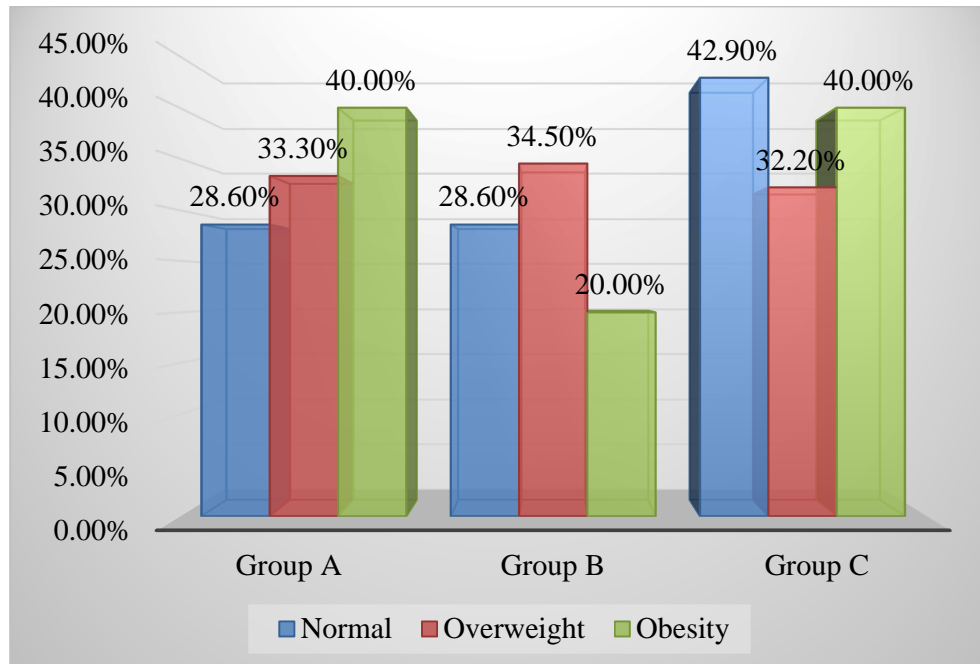
Group A vs B:  $p=0.74$

Group A vs C:  $p=0.80$

Group B vs C:  $p=0.54$

Group A vs B vs C:  $p=0.82$

In the Normal category, Group A and Group B each have 4 participants (28.6%), while Group C has 6 participants (42.9%). For the Overweight category, Group A includes 58 participants (33.3%), Group B includes 60 participants (34.5%), and Group C includes 56 participants (32.2%). In the Obesity category, Group A and Group C each have 4 participants (40.0%), while Group B has 2 participants (20.0%).



**Graph 2: BMI Category Distribution**

Gravida Status Distribution

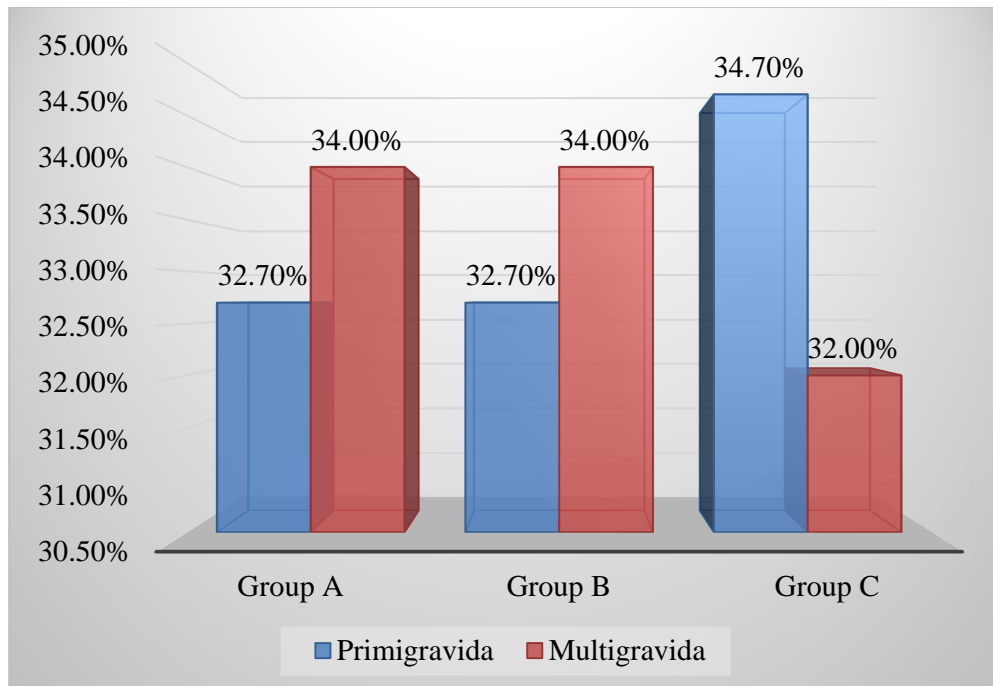
Group A vs B:  $p=0.56$

Group A vs C:  $p=0.43$

Group B vs C:  $p=0.43$

Group A vs B vs C:  $p=0.92$

In the Primigravida category, Group A and Group B each have 32 participants (32.7%), while Group C has 34 participants (34.7%). For the Multigravida category, Group A and Group B each include 34 participants (34.0%), and Group C includes 32 participants (32.0%).



**Graph 3: Gravida Status Distribution**

**Table 4 : Distribution of participants based mean blood loss.**

Mean blood loss		Mean	SD	P Value
Brass V drape (ml)	Group A	227.42	102.34	A vs B: <b>0.008 (&lt;0.01)</b>
	Group B	186.52	67.08	A vs C: <b>0.009 (&lt;0.01)</b>
	Group C	186.52	70.74	B vs C: 1.00
	Total	200.15	83.46	A vs B vs C: <b>0.005 (&lt;0.01)</b>

Group A has a mean blood loss of 227.42 ml (SD = 102.34) and median is 200 (100, 700), Group B has a mean blood loss of 186.52 ml (SD = 67.08) median 200 (50, 400), and Group C has a mean blood loss of 186.52 ml (SD = 70.74) median 200 (50, 400). The overall mean blood loss across all groups is 200.15 ml (SD = 83.46) median 200 (50, 700).

There is **significant differences in mean blood loss** among the groups: Group A vs B (0.008), Group A vs C (0.009), and Group A vs B vs C (0.005). There is no significant difference between Group B and Group C (P = 1.00)". This data suggests that participants in Group A experienced significantly higher blood loss compared to those in Groups B and C. The similarity in blood loss between Groups B and C indicates that these treatments are similarly effective in reducing blood loss, while the treatment in Group A is less effective in this regard.

**Table 5: Distribution of participants based on blood loss**

Variables	Sub category	Group A (66)	Group B (66)	Group C (66)	Total (198)	pValue
Blood loss	<300 ml	51 (29.65%)	62 (36.05%)	59 (34.3%)	172 (100%)	<b>0.03</b>
	300-500 ml	14 (58.3%)	3 (12.5%)	7 (29.2%)	24 (100%)	<b>0.02</b>
	>500 ml Post partum hemorrhage	1 (50%)	1 (50%)	0	2 (100%)	0.60

Table states that blood loss among the 3 groups is significant, and B group has an upper hand in better control of postpartum blood loss, and on pair wise comparison, both B and C groups have similar and better effects on the control of postpartum blood loss when compared to group A.

Distribution of participants based on Postpartum Haemorrhage (Blood loss >500ml)

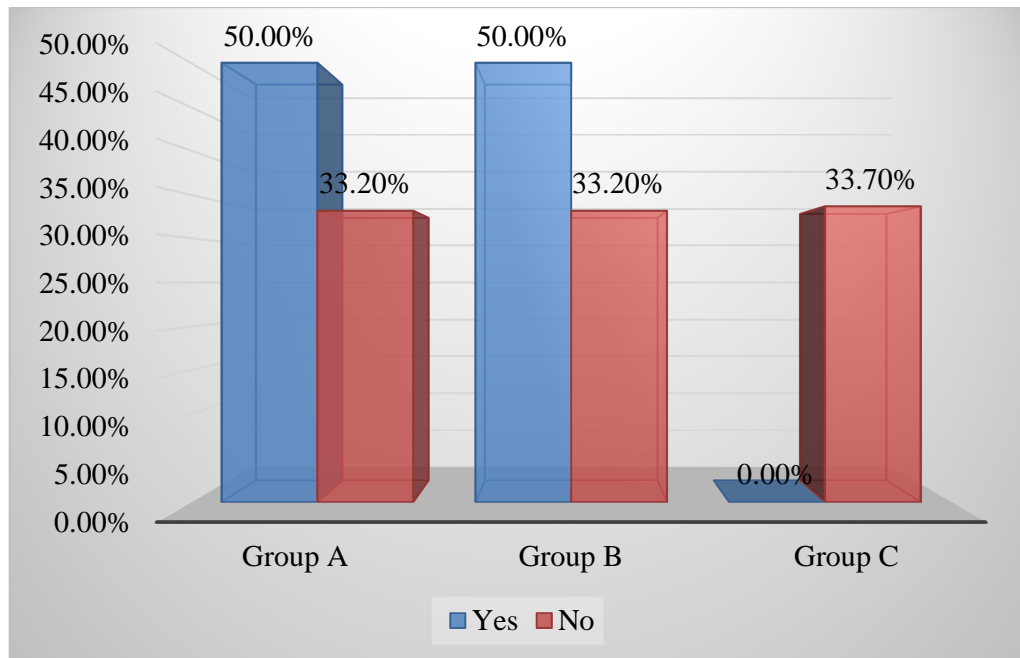
Group A vs B:  $p=0.75$

Group A vs C:  $p=0.50$

Group B vs C:  $p=0.50$

Group A vs B vs C:  $p=0.60$

In participants with PPH, Group A and Group B each have 1 participant (50.0%), while Group C has no participants (0.0%). In patients without PPH, Group A and Group B each include 65 participants (33.2%), and Group C includes 66 participants (33.7%). “There is no significant differences in the incidence of PPH among the groups”.



**Graph 4: Distribution of patients based on Postpartum Haemorrhage  
(Blood loss >500ml)**

**Table 6: Distribution of participants based on Use of Additional Uterotonics**

Variables			Group			Total 198
			Group A (66)	Group B (66)	Group C (66)	
Use of additional uterotonics	Yes	n	18	5	6	29
		%	62.1%	17.2%	20.7%	100.0%
	No	n	48	61	60	169
		%	28.4%	36.1%	35.5%	100.0%

Group A vs B:  $p=0.003$

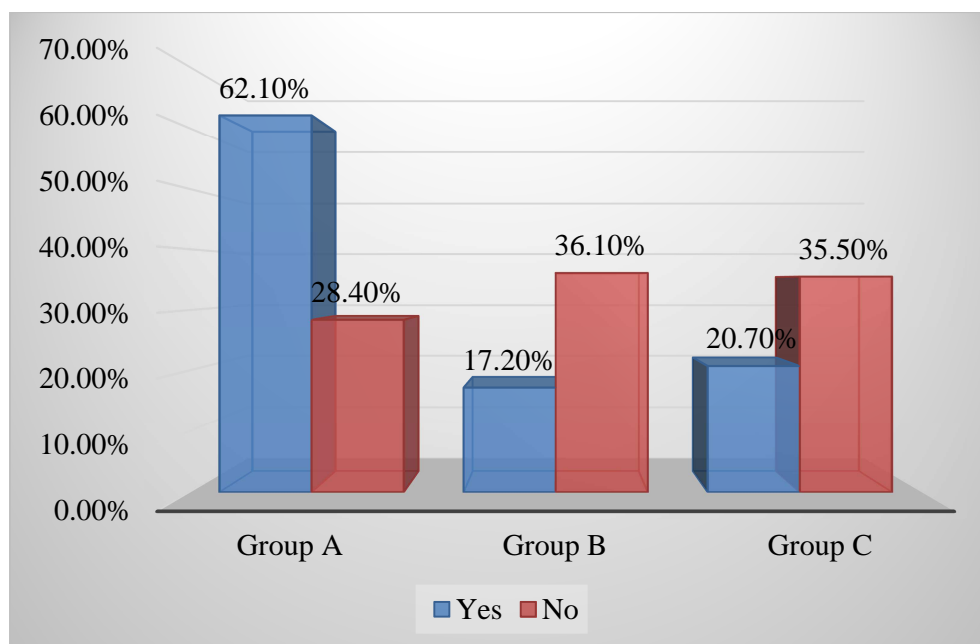
Group A vs C:  $p=0.006$

Group B vs C:  $p=0.50$

Group A vs B vs C:  $p=0.002$

In patients with use of additional uterotonics, Group A has 18 participants (62.1%), Group B has 5 participants (17.2%), and Group C has 6 participants (20.7%). In patients without use of additional uterotonics, Group A includes 48 participants (28.4%), Group B includes 61 participants (36.1%), and Group C includes 60 participants (35.5%). Compared all 3 groups P value  $<0.05$ .

Pairwise comparison states group B and C has no statistical significant with each other but has significance when compared with group A



**Graph 5: Distribution of patients based on Use of Additional Uterotonics**

**Table 7: Distribution of participants based on Postpartum side Effects**

			Group			Total
			Group A	Group B	Group C	
Side effects (post partum)	Yes	n	2	2	0	4
		%	50.0%	50.0%	0.0%	100.0%
	No	n	64	64	66	194
		%	33.0%	33.0%	34.0%	100.0%
Total		n	66	66	66	198
		%	33.3%	33.3%	33.3%	100.0%

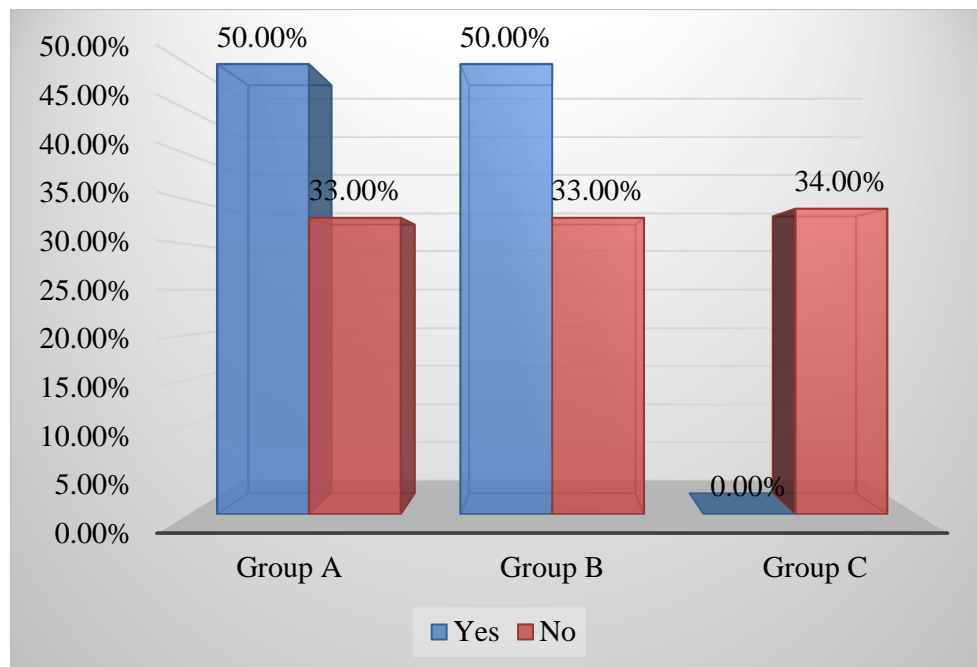
Group A vs B:  $p=0.69$

Group A vs C:  $p=0.24$

Group B vs C:  $p=0.24$

Group A vs B vs C:  $p=0.36$

In patients with postpartum side effects, Group A have 2 participants (50.0%) who experienced hypotension and dizziness and Group B have 2 participants (50.0%) who experienced headache and nausea, while Group C has no participants (0.0%). In patients without postpartum side effects Group A and Group B each include 64 participants (33.0%), and Group C includes 66 participants (34.0%). There is no significant differences in the incidence of postpartum side effects among the groups”.



**Graph 6: Distribution of patients based on Side Effects (Postpartum)**

**Table 8: Distribution of participants based on Pre delivery & Post delivery****Hemoglobin**

		Mean	SD	pValue
Pre delivery HB (mg/dl)	Group A	11.75	1.20	A vs B: 0.14
	Group B	12.02	0.93	A vs C: 0.85
	Group C	11.78	1.03	B vs C: 0.16
	Total	11.85	1.06	A vs B vs C: 0.27
Post delivery HB (mg/dl)	Group A	10.49	1.21	A vs B: <b>0.008</b>
	Group B	11.03	1.03	A vs C: <b>0.04</b>
	Group C	10.90	1.06	B vs C: 0.47
	Total	10.81	1.12	A vs B vs C: <b>0.01</b>

The mean pre-delivery Hemoglobin levels are similar across all groups with no significant difference.

For pre delivery HB levels, Group A has a mean Hb of 11.75 mg/dl (SD = 1.20), Group B has a mean HB of 12.02 mg/dl (SD = 0.93), and Group C has a mean Hb of 11.78 mg/dl (SD = 1.03). The overall mean preoperative Hb across all groups is 11.85 mg/dl (SD = 1.06).

For post delivery Hb levels, Group A has a mean Hb of 10.49 mg/dl (SD = 1.21), Group B has a mean Hb of 11.03 mg/dl (SD = 1.03), and Group C has a mean Hb of 10.90 mg/dl (SD = 1.06). The overall mean post delivery Hb across all groups is 10.81 mg/dl (SD = 1.12). There is significant differences in postoperative Hb levels among the groups: Group A vs B (0.008), Group A vs C (0.04), and Group A vs B vs C (0.01), while there is no significant difference between Group B and Group C (p= 0.47)”.’

**Table 9: Distribution of participants based on Pre delivery & Post delivery Hematocrit**

		Mean	SD	pValue
Pre delivery hematocrit	Group A	35.01	3.49	A vs B: 0.11
	Group B	35.89	2.65	A vs C: 0.77
	Group C	35.18	2.93	B vs C: 0.15
	Total	35.36	3.05	A vs B vs C: 0.22
Post delivery hematocrit	Group A	31.93	3.61	A vs B: <b>0.03</b>
	Group B	33.14	2.77	A vs C: 0.60
	Group C	32.27	3.91	B vs C: 0.15
	Total	32.45	3.48	A vs B vs C: 0.12

The mean pre-delivery Hematocrit levels are similar across all groups with no significant difference.

For pre delivery hematocrit levels, Group A has a mean hematocrit of 35.01 (SD = 3.49), Group B has a mean hematocrit of 35.89 (SD = 2.65), and Group C has a mean hematocrit of 35.18 (SD = 2.93). The overall mean preoperative hematocrit across all groups is 35.36 (SD = 3.05).

For post delivery hematocrit levels, Group A has a mean hematocrit of 31.93 (SD = 3.61), Group B has a mean hematocrit of 33.14 (SD = 2.77), and Group C has a mean hematocrit of 32.27 (SD = 3.91). The overall mean post delivery hematocrit across all groups is 32.45 (SD = 3.48). There is significant differences in post delivery hematocrit levels among the groups: Group A vs B (0.03), while Group A vs C (0.60), Group B vs C (0.15), and Group A vs B vs C (0.12) are not significant”.

**Table 10: Distribution of participants based on Hemoglobin Correction post delivery**

			Group			Total (198)
			Group A (66)	Group B (66)	Group C (66)	
Hemoglobin correction	Yes	n	15	8	9	32
		%	46.9%	25.0%	28.1%	100.0%
	No	n	51	58	57	166
		%	30.7%	34.9%	34.3%	100.0%

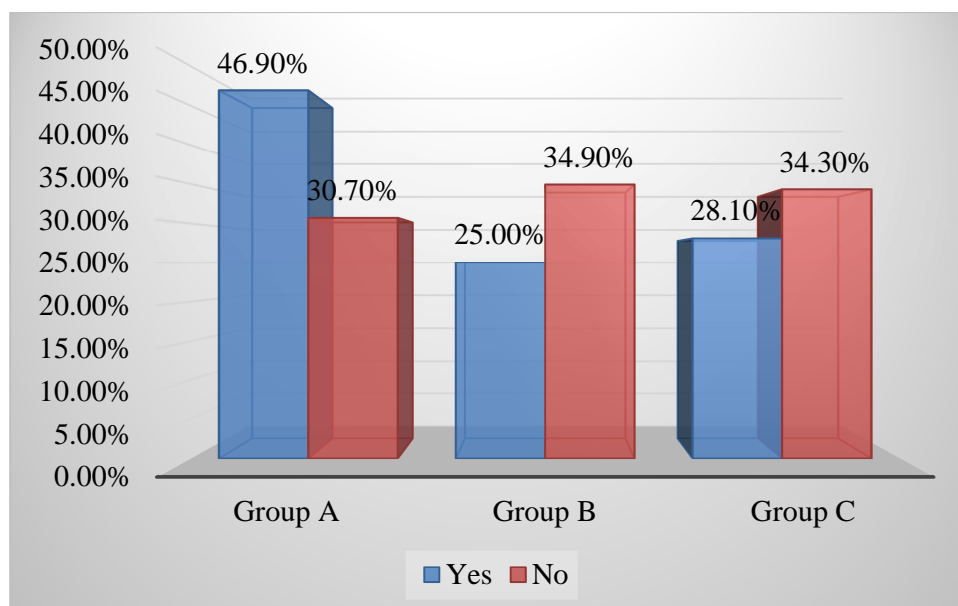
Group A vs B:  $p=0.08$

Group A vs C:  $p=0.12$

Group B vs C:  $p=0.50$

Group A vs B vs C:  $p=0.20$

In patients with anemia correction, Group A has 15 participants (46.9%), Group B has 8 participants (25.0%), and Group C has 9 participants (28.1%). In patients without anemia correction, Group A includes 51 participants (30.7%), Group B includes 58 participants (34.9%), and Group C includes 57 participants (34.3%). There is no significant differences in the need for Hemoglobin correction among the groups.



**Graph 7: Distribution of patients based on hemoglobin Correction**

**Table 11: Comparison of different variables of participants over the intervention groups**

Variables			Groups			Total 198
			Group A (66)	Group B (66)	Group C (66)	
Baby delivery (Easy / difficult)	Yes- Easy	n	66	66	66	198
		%	33.3%	33.3%	33.3%	100.0%
Baby cried immediately after birth	Yes	n	66	66	66	198
		%	33.3%	33.3%	33.3%	100.0%

1. Each group shows that 33.3% of the total participants had their baby delivery easy, no statistical significance
2. For each group, all 66 participants recorded that their baby cried immediately after birth, no statistical significance.

**Table 12: Distribution of participants based on duration of third stage of labour.**

Variables		Groups			Total 198	pValue
		Group A (66)	Group B (66)	Group C (66)		
Duration of third stage of labour (in minutes)	Mean	0.96	0.97	0.95	0.96	A vs B: 0.78
	SD	0.13	0.19	0.14	0.15	A vs C: 0.77 B vs C: 0.61 A vs B vs C: 0.86

Group A has a mean duration of 0.96 minutes (SD = 0.13), Group B has a mean duration of 0.97 minutes (SD = 0.19), and Group C has a mean duration of 0.95 minutes (SD = 0.14). The overall mean duration across all groups is 0.96 minutes (SD = 0.15). No significant differences in the mean duration of the third stage of labour among the groups.

**Table 13: Distribution of participants based on Mean Age & mean BMI**

		Mean	SD	pValue
AGE (years)	Group A	24.79	3.051	A vs B: 0.23
	Group B	25.46	3.376	A vs C: 0.47
	Group C	25.18	3.323	B vs C: 0.63
	Total	25.14	3.24	A vs B vs C: 0.49
BMI	Group A	27.13	1.59	A vs B: 0.72
	Group B	27.23	1.55	A vs C: 0.85
	Group C	27.18	1.57	B vs C: 0.85
	Total	27.18	1.56	A vs B vs C: 0.93

Group A has a mean age of 24.79 years (SD = 3.051), Group B has a mean age of 25.46 years (SD = 3.376), and Group C has a mean age of 25.18 years (SD = 3.323). The overall mean age across all groups is 25.14 years (SD = 3.24). There is no significant differences in mean age among the groups: Group A vs B (0.23), Group A vs C (0.47), Group B vs C (0.63), and Group A vs B vs C (0.49)". This data suggests that the ages of participants are similarly distributed across the three treatment groups, with no significant differences. The slight variations in mean age and standard deviation are not statistically significant, indicating that age is not a confounding factor affecting the outcomes of this study.

Group A has a mean BMI of 27.13 (SD = 1.59), Group B has a mean BMI of 27.23 (SD = 1.55), and Group C has a mean BMI of 27.18 (SD = 1.57). The overall mean BMI across all groups is 27.18 (SD = 1.56). There is no significant differences in mean BMI among the groups: Group A vs B (0.72), Group A vs C (0.85), Group B vs C (0.85), and Group A vs B vs C (0.93)". This data suggests that the BMI of participants is similarly distributed across the three treatment groups, with no significant differences. The slight variations in mean BMI and standard deviation are not statistically significant, indicating that BMI is not a confounding factor affecting the outcomes of this study.

**Table 14: Distribution of participants based on Dry Gauze Weight & Soaked gauze weight**

		Mean	SD	pValue
Dry gauze weight	Group A	0.01	0.001	A vs B: 0.93
	Group B	0.01	0.001	A vs C: 0.93
	Group C	0.01	0.001	B vs C: 1.00
	Total	0.01	0.001	A vs B vs C: 1.00
Soaked gauze weight	Group A	0.72	0.57	A vs B: <b>0.002</b>
	Group B	0.43	0.45	A vs C: <b>0.001</b>
	Group C	0.42	0.45	B vs C: 0.86
	Total	0.52	0.51	A vs B vs C: <b>0.001</b>

For the dry gauze weight, Group A, Group B, and Group C each have a mean weight of 0.01 grams (SD = 0.001). There is no significant differences among the groups for dry gauze weight

For the soaked gauze weight, Group A has a mean weight of 0.72 grams (SD = 0.57), Group B has a mean weight of 0.43 grams (SD = 0.45), and Group C has a mean weight of 0.42 grams (SD = 0.45). The overall mean soaked gauze weight across all groups is 0.52 grams (SD = 0.51). There is significant differences in the soaked gauze weight among the groups: Group A vs B (0.002), Group A vs C (0.001), and Group A vs B vs C (0.001), while there is no significant difference between Group B and Group C (P = 0.86)<sup>2</sup>.

**Table 15: Distribution of participants based on Dry pad weight & Wet pad weight**

		Mean	SD	pValue
Dry pad weight	Group A	0.45	1.24	A vs B: 0.31
	Group B	0.30	0.001	A vs C: 0.31
	Group C	0.30	0.001	B vs C: 1.00
	Total	0.35	0.71	A vs B vs C: 0.36
Wet pad weight (in gm) 1g = 1ml	Group A	0.88	0.34	A vs B: <b>0.009</b>
	Group B	0.74	0.24	A vs C: <b>0.001</b>
	Group C	0.70	0.22	B vs C: 0.34
	Total	0.78	0.28	A vs B vs C: <b>0.001</b>

For the dry pad weight, Group A, Group B, and Group C each have a mean weight of 0.01 grams (SD = 0.001). There is no significant differences among the groups for dry pad weight

For the wet pad weight, Group A has a mean weight of 0.88 grams (SD = 0.34), Group B has a mean weight of 0.74 grams (SD = 0.24), and Group C has a mean weight of 0.70 grams (SD = 0.22). The overall mean wet pad weight across all groups is 0.78 grams (SD = 0.28). There is significant differences in wet pad weight among the groups: Group A vs B (0.009), Group A vs C (0.001), and Group A vs B vs C (0.001), while there is no significant difference between Group B and Group C (P = 0.34)”.

Cost effective analysis –

On an average,

Group A Inj.Oxytocin 10IU costs Rs 38/- (10.8%)

Group B Inj.Oxytocin 5IU + Inj.MethylErgometrine 0.2mg costs Rs 35/- (10%)

Group C Inj.Carbetocin HS 100mcg costs Rs 350/- (100%)

It is evident that there is disparity in cost of approximately 90% in range between group C and other 2 groups

## **DISCUSSION**

The current study was conducted on pregnant women undergoing vaginal delivery in labour room of the study hospital. The purpose of the study is to compare the effectiveness of three different uterotonics in reducing postpartum blood loss: Group A received Inj Oxytocin 10 IU IM , Group B received Inj Oxytocin 5 IU IM + Inj Methyl Ergometrine 0.2mg IM, and Group C received Inj Carbetocin HS 100 mcg IM. Total number of deliveries conducted during study period were 4,093 in which total 1,486 were vaginal deliveries, convenient sampling done in which 423 participants were screened, 238 participants were eligible and 40 participants were excluded after screening as they underwent emergency caesarean section and total 198 participants were randomized into three equal groups containing 66 participants each.

**Post partum Blood loss –****Table 16 - Comparison of mean blood loss among the different uterotonics with current study vs other studies in vaginal deliveries.**

Mean blood loss	Group A (Inj Oxytocin 10IU IM)	Group B (Inj Oxytocin 5IU+ Inj Ergometrine 0.2mg)	Group C (Inj Carbetocin 100mcg IM)	Syntometrine (Oxytocin 5IU+ Ergometrine 0.5mg)	Sublingual misoprostol 400mcg	Misoprostol		
						400 mcg	600 mcg	800 mcg
Current study	227.42±102.34	186.52±67.08	186.52±70.74	NA	NA	NA		
Van der Nelson et al <sup>66</sup>	500	NA	500	298	NA	NA		
Maged AM et al <sup>60</sup>	378.73	NA	337.73	NA	NA	NA		
Bellad et al <sup>71</sup>	366 ± 136	NA	NA	NA	192 ± 124	NA		
Shringam wong et al	NA	NA	NA	NA	NA	509.1	465.7	441.1
Prasad A et al <sup>67</sup>	226.13±98.44	NA	NA	NA	293.75±125.8	NA		
Centin C et al <sup>69</sup>	294.13 ± 198.64	NA	277.19±208.10	NA	NA	NA		
Paweena et al <sup>70</sup>	146.7 ± 90.4	NA	195.1±146.2	NA	NA	NA		

**Table 17 – Comparison of the blood loss among the different uterotonics with studies in caesarean sections.**

Mean blood loss	Group A (Inj Oxytocin 10IU IM)	Group B (Inj Oxytocin 5IU+ Inj Ergometrine 0.2mg)	Group C (Inj Carbetocin 100mcg IM)	Syntometrine (Oxytocin 5IU+ Ergometrine 0.5mg)	Sublingual misoprostol 400mcg	Misoprostol		
						400 mcg	600 mcg	800 mcg
Ahmed Md. Maged <sup>60</sup>	1010±525	NA	811±389	NA	NA	NA		
Algazarib Md et al <sup>68</sup>	NA	NA	688±58	1026±65	NA	NA		

In the current study, with findings of blood loss < 300ml; blood loss of 300ml – 500ml suggests that Group B is more effective than Group A and Group C in case of PPH (blood loss >500ml) there were only 2 participants noted one participant in Group A and B, and zero participants in group C, with only 2 cases reported across all groups. The variations in blood loss (>500ml) between the groups do not reach statistical significance, suggesting that the treatments have similar effectiveness in cases of PPH.

In similar study by Maged AM et al, there was significant difference between the carbetocin and oxytocin groups with blood loss of < 500ml and >500ml<sup>60</sup>.

In similar study 3 arm study by H Van der Nelson et al, there was no significant blood loss between the 3 different groups. It was noted that use of additional uterotonics was significantly reduced with group using syntometrine as compared to those using oxytocin and carbetocin group alone<sup>66</sup>

**Use of additional uterotonics :****Table 18 – Comparison of use of additional uterotonics with current study vs various similar studies**

	Group A	Group B	Group C	Syntometrine	Misoprostol
Current study	(n=66) 18	(n=66) 5	(n=66) 6	NA	NA
H Van der Nelson et al <sup>66</sup>	(n=1894) 359	NA	(n=1909) 364	(n=1914) 293	NA
Maged AM et al <sup>60</sup>	(n=100) 37	NA	(n=100) 23	NA	NA
Bellad et al <sup>71</sup>	(n=331) 8	NA	NA	NA	(n=321) 1
Widmer et al <sup>58</sup>	(n=14768) 1533	NA	(n=14,771) 1528	NA	NA

This current study suggests that a greater number of participants in Group A required additional uterotonics when compared to Groups B and C. The however difference between the use of additional uterotonics between Groups B and C are not significant.

In the large, multi-centric study where they compared between 3 groups, van der et al - study showed that the use of additional uterotonics was significantly reduced in the group receiving syntometrine when compared with those receiving Oxytocin and carbetocin alone<sup>66</sup>.

However, In Maged AM et al.,<sup>60</sup> and Widmer et al.,<sup>58</sup> also showed that blood loss and need for additional uterotonics were significantly lower in group receiving carbetocin alone<sup>60</sup>

**Hemoglobin & Hematocrit -**

The table below shows pre-delivery and post-delivery mean hemoglobin and mean hematocrit levels in various studies.

**Table 19 – Comparison of Pre-delivery and post-delivery hemoglobin and hematocrit values with current study and other similar studies**

	Group A (Inj Oxytocin 10 IU IM)				Group B (Inj Oxytocin 5IU +Inj.Methylergometrine 0.2mg)				Group C (Inj Carbetocin 100mcg )			
	Pre delivery		Post delivery		Pre delivery		Post delivery		Pre delivery		Post delivery	
	Hb	Hct	Hb	Hct	Hb	Hct	Hb	Hct	Hb	Hct	Hb	Hct
Current study	11.75	35.01	10.49	31.93	12.02	35.89	11.03	33.14	11.78	35.18	10.9	32.27
Maged AM et al <sup>60</sup>	11.11	NA	10.53	NA	NA	NA	NA	NA	11.01	NA	10.51	NA
Larciprete G et al <sup>59</sup>	11.8	34	10	32.1	NA	NA	NA	NA	11.4	34.6	10	33.2

The mean difference of Hemoglobin levels done post-delivery was higher in group A (1.26) and whereas Group B (0.99) and C (0.88) showed similar results, it suggests that Groups B and C are equally effective in maintaining HB levels post-delivery.

The mean difference of Hematocrit levels done post-delivery was lower in Group B (2.75) compared to group A (3.08) and group C (2.91), it suggests that Group B is more effective in maintaining post-delivery hematocrit

Similar studies showed no significant difference between oxytocin and carbetocin groups and in other investigations that similarly used the change in Hb as an endpoint.<sup>55,56</sup> The most objective way to correctly assess blood loss is to compare pre-delivery and post-delivery hemoglobin concentrations; this approach has been used extensively to assess blood loss following PPH.<sup>53,54</sup>

Delorme et al. reported similar findings, with a trend towards lower rates of hemoglobin decline in Carbetocin group, though their primary measure was hemoglobin decline rather than direct blood loss measurement.<sup>52</sup>

In Maged AM et al.,<sup>60</sup> “the mean difference between blood haemoglobin levels before delivery and 24 h after delivery were higher for Oxytocin (0.58) compared to those receiving Carbetocin (0.5)

Similar findings noted in study conducted by Larciprete G et al.,<sup>59</sup> in patients undergoing caesarean sections.

**Demographic characters-**

The table below is description of comparison of demographic characters of the current study vs various similar studies, A- Inj Oxytocin 10 IU IM; B – Inj Oxytocin 5 IU + Inj Methyl ergometrine 0.2mg IM; C – Inj Carbetocin HS 100mcg IM; D – Inj Syntometrine

**Table 20 - Comparison of demographic characteristics - current study with other similar studies**

	Current study	Van der Nelson et al <sup>66</sup>	Maged AM et al <sup>60</sup>
Mean age	A- 24.79 B- 25.46 C- 25.18 D- NA	A- 30 B- NA C- 30 D- 30	A- 33.8 B- NA C- 32.8 D- NA
Mean BMI	A- 27.13 B- 22.23 C- 27.18 D- NA	A- 25 B- NA C- 25 D- 25	A- 27.22 B- NA C- 28.7 D- NA
Gravida	No significance, similar across all the groups	No significance, similar across all the groups	No significance, similar across all the groups

**Age-**

In current study, the age distribution among the three treatment groups is relatively balanced with no statistical significance, the majority of participants falling within the 21-25 years age group.

The study conducted by H Van der Nelson et al., it is found that there is no difference in age distribution among their 3 groups.<sup>66</sup>

**BMI -**

In current study, the distribution of participants across BMI categories is relatively balanced,. The differences in BMI distribution among the three treatment groups are not statistically significant.

The study conducted by Delorme et al., data, it is found “no significant difference in BMI distribution between their study periods.”<sup>52</sup>

**Gravida -**

In current study, the distribution of participants based on their gravida status is balanced across the three groups and no statistical significance, with an almost equal split between Primigravida and Multigravida participants.

The study data it is significant that, “75% of their participants in Period A were nulliparous, compared to 74% in Period B (p = 0.66), showing a similar balance in parity status”.<sup>52</sup>

**Duration of third stage of labour-**

The current study data suggests, that time period of the third stage of labour is similarly distributed across the three treatment groups, with no significant differences. The slight variations in mean duration and standard deviation are not statistically significant, indicating that the treatment type does not significantly impact the time period of the third stage of labour in this study.

### **Side effects (postpartum)**

This suggests that the incidence of postpartum side effects is low and does not significantly vary among the treatment groups. The majority of participants in each group did not experience any side effects, indicating that the treatments are similarly safe in terms of postpartum side effects.

Delorme et al.,<sup>52</sup> did not report on side effects.

In Maged AM et al.,<sup>60</sup> history was taken in the occurrence of nausea, vomiting, tachycardia, flushing, dizziness, headache, shivering, metallic taste, dyspnea, palpitations and itching, there was no significant difference between the 2 groups.

### **STRENGTHS**

- Heat stable carbetocin is used in the study.
- Three Arm Randomized controlled trial.
- This Study contributes to our understanding of the new combination (Inj Oxytocin 5u + Inj Methyl ergometrine 0.2mg ) being utilized and how well it helps in controlling the post-partum blood loss.

### **LIMITATIONS**

- A larger sample size yields more better outcomes.
- A comparison between Inj Oxytocin 5u + Inj Methyl ergometrine 0.2mg and Syntometrine in this study, would have provided a much better understanding of this novel combination's actions and side effects .
- As the combination is not readily available, 2 separate intra muscular injections had to be given to the participants.

- Inj Oxytocin and Inj Methyl ergometrine needed the use of cold chain storage.
- The validity of this study would have been much higher, if double blinding was done.
- Convenient sampling

## **CONCLUSION**

It is evident from this study that combination (Inj Oxytocin 5IU IM + Inj Methyl Ergometrine 0.2mg IM) has lower mean blood loss compared group A (Inj Oxytocin 10IU IM) and comparable to group C ( Inj Carbetocin 100mcg IM). The participants with lower blood loss (less than 300 ml) were more in group B and blood loss of 300-500 ml were less in group B compared to other two groups (group A - Inj Oxytocin 10IU IM; group C - Inj Carbetocin 100mcg IM ). Indicating the superiority over other two uterotonics of the study. This is proved by pre and post delivery Hemoglobin and Hematocrit.

The additional use of uterotonics was also less in Group B ((Inj Oxytocin 5IU IM + Inj Methyl Ergometrine 0.2mg IM) and this combination was also found to be cost effective based on the analysis.

However this combination needs cold chain maintenance like Oxytocin hence to be used only where 24/7/365 refrigeration facility is available.

## **RECOMMENDATIONS**

The findings of this study need to be confirmed by a large multicentre double blinded trial with larger sample is recommended.

## **SUMMARY**

The study compared the effectiveness of three uterotonic regimens in reducing postpartum blood loss among women in labour undergoing vaginal deliveries. The participants were randomized into three groups: Group A (Inj Oxytocin 10 units IM), Group B (Inj Oxytocin 5 units IM + Inj Methyl Ergometrine 0.2mg IM), and Group C (Inj Carbetocin 100 mcg IM, heat stable).

- Blood Loss Measurements:
  - Group A exhibited considerably higher mean blood loss measured by BRASS V drape ( $p < 0.01$ ) and greater soaked gauze and pad weight ( $p < 0.01$ ) in contrast to Groups B and C.
  - The participants of PPH ( $>500$  ml blood loss) was low, with only 2 cases in total, and There were no considerable variations between the groups. ( $p > 0.05$ ).
- Use of Additional Uterotonics: Group A had a significantly higher need for additional uterotonics compared to Groups B and C ( $p < 0.01$ ), indicating lower effectiveness in Group A.
- Hemoglobin (HB) and Hematocrit Levels:
  - Post-delivery hemoglobin and hematocrit levels were considerably lower in Group A compared to Groups B and C ( $p < 0.05$ ), indicating greater blood loss in Group A.
- Age and BMI Distribution: The age and BMI distributions were similar across the three groups, with no significant differences ( $p > 0.05$ ), indicating balanced demographics among the groups.

- Gravida Status: The distribution of primigravida and multigravida participants was also balanced across the groups, with no significant differences ( $p > 0.05$ ).
- Side Effects: The occurrence of postpartum side effects was minimal and showed no significant variation among the groups ( $p > 0.05$ ).
- While Group A had a higher percentage of participants requiring anemia correction compared to group B and C, there was no statistically significance noted between three groups with regard to anemia correction ( $p > 0.05$ ).

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**ANNEXURE – I - INFORMED CONSENT FORM**

**“INJ.OXYTOCIN 10 IU IM VS INJ. OXYTOCIN 5 IU IM + INJ.METHYL  
ERGOMETRINE 0.2 MG IM VS INJ.CARBETOCIN 100 MCG IM DURING  
AMTSL IN VAGINAL DELIVERIES – A RANDOMIZED CONTROLLED  
TRIAL”**

Principal investigator:

Guide:

**Reg No: BJ0121016**

**Dr.**

**Post Graduate,**

**Professor,**

Department of OBG

Department of OBG

J.N. Medical College, KAHER, Belagavi.      J.N. Medical College, KAHER,Belagavi.

**Purpose of the study:** According to the World Health Organisation (WHO), postpartum haemorrhage is a leading cause of maternal mortality, accounting for 35% of maternal deaths worldwide. At least half of all maternal deaths occur within 24 hours of giving birth, most commonly from excessive blood loss (WHO 2012). Around 54-93% of maternal deaths owing to PPH may be preventable. Given that nearly 40% of PPH occurs in low risk women, every parturient is at risk. The network analysis proved Syntometrine as the most potent uterotonic but with more side effects reported due to its dosage of methyl ergometrine 0.5mg. This study aims to reduce standard dose of Inj Methyl Ergometrine from 0.5mg to 0.2mg and to see if this novel combination is superior to or equally as effective as Inj Syntometrine, as well as to assess if there is a reduction in side effects with lowering the dosage of methyl ergometrine.

**Explanation of procedure:** The enrolled subjects after getting informed consent will be randomized into either of 3 groups. Group A receiving Inj Oxytocin 10 IU IM, Group B receiving Inj Oxytocin 5 IU IM + Inj Methyl Ergometrine 0.2mg and Group C receiving Inj Carbetocin HS 100mcg, administered during AMTSL. After the delivery patient will be observed for the amount of blood loss occurred by calculating the blood collected in calibrated BRASSS V drape. Blood samples are taken from the women at the time of admission and  $60 \pm 12$  hours post-delivery to estimate hemoglobin and hematocrit by cyanmethemoglobin method.

**Withdrawal from participation in the study:** Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

**Possible benefits from participating in the study:** The uterotonic drugs administered post-delivery will help in reduction of postpartum blood loss without affecting the quality of life.

**Possible risks from participating in the study:** No noted risks.

**Privacy and confidentiality:** Your confidentiality will be respected. The information collected from you will be coded, to prevent any person from identifying you. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

**Financial incentives:** You will not receive any payment for participating in this study.

**Authorization for publication of aggregated data:** Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups.

However, your identity will never be revealed.

**Whom to contact with questions about the study :** We have given you information about the study called “Inj Oxytocin 10 Units IM Vs Inj Oxytocin 5U IM + Inj Methyl Ergometrine 0.2mg Vs Inj Carbetocin 100mcg in reduction of Post-Partum Blood loss– A Randomized Controlled Trial”

We have discussed about the study and you understand that you do not have to agree to be in the study or may decide later not to be part of the study. This will not affect your or your baby’s care in any way.

If you have any questions,

If you have any question or complaints with regard to your right as study participant you may contact Dr. Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

**Legal rights:** By signing this consent form, we are not waving any of your legal rights.

**CONSENT STATEMENT**

I am making a voluntary decision to participate in the study: **“INJ.OXYTOCIN 10 IU IM VS INJ. OXYTOCIN 5 IU IM + INJ.METHYL ERGOMETRINE 0.2 MG IM VS INJ.CARBETOCIN 100 MCG IM DURING AMTSL IN VAGINAL DELIVERIES – A RANDOMIZED CONTROLLED TRIAL”** My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

**ANNEXURE – II - SCREENING FORM**

Participant information:

Screening number:

IP number:

Date of screening (dd-mm-yyyy):

First name:

Middle name:

Last name:

Husband's name:

Age (years). :

Address: H.no. -

Street -

Taluka-

District-

Phone number 1:

Phone number 2:

Eligibility –

Yes- 1, No - 2

Screening form

Date of screening –

(dd/mm/yyyy)

1) Term pregnancy? Yes  No

LMP –

EDD -

USG 1<sup>st</sup> trimester EDD –

Actual gestational age –

2) Inclusion criteria:

1. Singleton Live Gestation.

2. Gestational age (37 0/7 to 41 6/7 weeks) of pregnancy

3. Maternal Hb: >9.9mg/dl.

4. Multiple Gestation.

5. Women in labor (< 6 cm cervical dilatation).

Is she eligible?

If eligible, consent to be taken.

**Consent:**

a. Does the woman assent to participate?

b. Has the study consent form been signed?

3) Exclusion criteria :

• Hypertensive disorders in pregnancy Yes.  No

• Antepartum haemorrhage Yes.  No

• Known Epilepsy Yes.  No

- Placental abnormalities Yes  No
- IUGR Yes  No
- known medical abnormalities Yes  No
- known contraindications to drugs which are included in the study. Yes.  No
- Known coagulopathies Yes  No
- Known hemoglobinopathies Yes  No
- Women who are not willing to consent for the study. Yes  No
- Rh negative pregnancy Yes  No

Randomization form:

Eligibility

Is the eligible for the study? Yes  No

Did women give consent for the study? Yes  No

Enrollment:

Was women enrolled in the study? Yes.  No

Was women randomized? Yes  No

If not randomized, reason?

1. Withdrawal from the study
2. Others

Date of Randomization:

--	--	--	--	--	--	--	--

(dd/mm/yyyy)

Time of randomization (hh:mm) :

--	--	--	--	--

Participant number:

--	--	--	--	--	--	--	--

(See sealed envelope)

**Data collection instrumentation**

Study ID :

Date of admission -   Date of delivery –   Time of delivery –  Date of discharge -   

Mode of delivery -

**Obstetric history:**Married Life (years) : Consanguinity :  (YES - 1, NO - 2)

If yes,

Degree of consanguinity: Obstetric score : Gravida  Para  Live  Abortion **Past History : YES – 1 , NO – 2**a. Known case of Diabetes mellitus : If yes, Duration (in years) : Treatment received : b. Known case of Hypertension : If yes, Duration (in years) :

Treatment received :

c. H/O recurrent blood transfusions :

If yes, Duration (in years) :

d. Known case of Cardiac disorder :

If yes, Duration (in years) :

Treatment received :

e. Known case of Hypothyroidism. :

If yes, Duration (in years) :

Treatment received :

f. H/O any surgery in past :

g. H/O any Drug allergy :

If Yes, Name of the drug. :

### General physical examination- at admission

Height (in centimetres)

Weight (in kilogram)

BMI

Pallor  (Yes – 1, No – 2)

Icterus

Pedal Oedema



VDRL :  (Negative – 1, Positive – 2)

Platelets (lakhs) :

S. TSH (mu IU/ml) :

DIPSI :

Urine R &M :

**Provisional diagnosis:**

**LABOUR ROOM DETAILS:**

a. Place : Labour room

b. History of EROM :  (Yes-1, No-2)

c. Mode of delivery:

Term :

Vaginal :

d. Liquor :

Clear :

Meconium stained :

e. Baby cried immediately after birth :

f. baby cord clamping time :

f. Baby birth time:

g. Time of administration study medication :

h. Use of additional uterotonics :

specify –

i. Use of additional procedures :

Specify -

j. Placental delivery by CCT :

k. Duration of third stage of labour :  minutes

l. Maternal blood loss :

vaginal delivery : Brass V Drape :  ml

Mops – Dry mop weight :

Soaked mop weight :

Pads – Dry pad weight :

Wet pad weight :

(weight 1gm = 1ml )

**Maternal Outcomes:**

1. Estimated Maternal Blood Loss In:

A. Vaginal Delivery:(ml)

Before Delivery

After Delivery

2.Haemoglobin: (gm/dl)

(Cyanmethemoglobin)

3.Packed Cell Volume: (%)

4.Duration Of Third Stage :  minutes

**ANEXURE: III**  
**MASTER CHART**

Screening no	Enrolled and randomised	Allocated and intervention done	BMI	AGE(years)	High risk	SCORE	Gestational age AT DELIVERY(weeks and days)	Intervention group	mode of delivery	BABY EXTRACTION easy / difficult (1 - yes/2- no)	Baby cried immediately after birth (1 - yes/2- no)	Baby birth time	Time of administration study medication	Duration of third stage of labour (in minutes)	Brass V drape ( ml)	Dry gauze weight	Soaked gauze weight	Dry pad weight	Wet pad weight (in gm) Ig = 1ml	Pre op HB (mg/dl)	Pre op hematocrit	post op HB (mg/dl)	Post op hematocrit	POST PARTUM HEMORRHAGE )BLOOD LOSS > 500 ML	Use of additional uterotonics ( 1=yes/ 2-no)	side effects (post partum)	anemia correction	
1	1	yes/yes	26.6	22	post datism	primi	40.1	A	NVD	1	1	17:50	17:51	1	150 ml	0.01	0.08	0.3	0.5	12.4	37.2	12	36.4	no	no	no	no	
2	2	yes/yes	29.2	26	post datism	primi	40	C	NVD	1	1	13:44	13:45	1	100ml	0.01	0.08	0.3	0.5	12.7	37.6	11.5	34.2	no	no	no	no	
3	3	yes/yes	29.5	24		primi	38.5	C	NVD	1	1	20:16	20:17	1	250ml	0.01	0.08	0.3	0.6	11.4	34.2	10.9	31	no	no	no	no	
4	4	yes/yes	26	25		multi	37.6	B	NVD	1	1	02:06	02:06	1	120ml	0.01	0.08	0.3	0.6	12	37	11.5	34.2	no	no	no	no	
5	5	yes/yes	28.3	24	IGT	multi	39.4	B	NVD	1	1	20:32	20:33	1	200ml	0.01	0.08	0.3	0.6	11.5	34.2	10.9	31	no	no	no	no	
6	6	yes/yes	28.1	22		multi	39	A	NVD	1	1	07:12	07:13	1	150ml	0.01	0.08	0.3	0.6	12.6	37.4	12.1	36.8	no	no	no	no	
7	7	yes/yes	27.9	24		primi	37.6	B	NVD	1	1	10:47	10:48	1	100ml	0.01	0.08	0.3	1	13.2	39.6	12.8	38	no	no	no	no	
8	8	yes/yes	26.9	24	post datism	multi	40.2	B	NVD	1	1	11:44	11:45	1	100ml	0.01	0.08	0.3	1	13	39.2	12.6	37.8	no	no	no	no	
9	9	yes/yes	30.2	32		primi	39.3	B	NVD	1	1	18:04	18:04	1	500ml	0.01	0.08	0.3	1	11.8	35.4	10.8	32.4	yes	yes	no	yes	
10	10	yes/yes	30.9	28	ov. Ind	primi	38	A	NVD	1	1	12:30	12:31	1	200ml	0.01	0.08	0.3	1	13.3	39.6	12.7	37.8	no	no	no	no	
12	11	yes/yes	25.8	21		primi	39	A	NVD	1	1	10:10	10:11	1	150ml	0.01	0.08	0.3	1	12	37	10	31	no	no	no	no	
13	12	yes/yes	25.8	28	post datism	primi	40.1	C	NVD	1	1	10:56	10:57	1	200ml	0.01	0.08	0.3	1	12.1	37	11.6	35.6	no	no	no	no	
14	13	yes/yes	27.8	26		primi	38.6	C	NVD	1	1	20:28	20:28	1	200ml	0.01	0.08	0.3	0.6	12	37	11.6	34.2	no	no	no	no	
15	14	yes/yes	27.8	22		primi	38.6	A	NVD	1	1	12:26	12:27	1	400ml	0.01	2	0.3	2	11.3		9.8			no	yes	no	yes
16	15	yes/yes	27.5	31		multi	38.4	B	NVD	1	1	13:02	13:03	1	140ml	0.01	0.08	0.3	0.3	11.5	34.6	10.3	32.8	no	no	no	no	
17	16	yes/yes	28.1	25		multi	38.2	C	NVD	1	1	09:42	09:42	1	100ml	0.01	0.08	0.3	0.6	10.8		10			no	no	no	no
18	17	yes/yes	25.3	26	post datism	multi	40.1	A	NVD	1	1	12:59	13:00	1	100ml	0.01	0.08	0.3	0.3	10.3	33.2	10	33	no	no	no	no	
19	18	yes/yes	25.3	25	post datism	primi	40.2	B	NVD	1	1	05:37	05:38	1	280ml	0.01	1.2	0.3	1	11.4	34.2	10	31	no	no	no	no	
20	19	yes/yes	27.5	23	post datism	multi	40.3	C	NVD	1	1	18:04	18:04	1	200ml	0.01	1	0.3	1	11.8		10.8			no	no	no	no
26	20	yes/yes	24.4	21		multi	38.4	A	NVD	1	1	17:48	17:49	1	100ml	0.01	0.08	0.3	0.6	10.2	33.2	9.4	32.8	no	no	no	no	
40	21	yes/yes	29.1	24		multi	39.3	B	NVD	1	1	17:38	17:38	1	210ml	0.01	0.9	0.3	0.6	13.1		11.9			no	no	no	no
41	22	yes/yes	27.3	26		primi	38.3	C	NVD	1	1	19:12	19:12	1	300ml	0.01	1.4	0.3	0.6	12.7	37.8	9.4	30.2	no	yes	no	yes	
42	23	yes/yes	29	26		primi	37.1	C	NVD	1	1	05:31	05:32	1	100ml	0.01	0.08	0.3	0.6	13.4		13			no	no	no	no
48	24	yes/yes	28.1	21		primi	38.2	C	NVD	1	1	08:32	08:32	1	50ml	0.01	0.06	0.3	0.3	12.3	36.4	12	35.8	no	no	no	no	
51	25	yes/yes	27.9	24		primi	38	A	NVD	1	1	07:17	07:18	1	200ml	0.01	0.9	0.3	0.6	12.4	38.6	11	34.8	no	no	no	no	
52	26	yes/yes	26	28.1		multi	39.5	B	NVD	1	1	10:14	10:15	2	300ml	0.01	1.6	0.3	1.4	12.1	36.3	9	28	no	yes	no	yes	
54	27	yes/yes	25.8	22		multi	37.6	C	NVD	1	1	11:56	11:56	1	100ml	0.01	0.08	0.3	0.6	12.4	36.8	12	35.8	no	no	no	no	
55	28	yes/yes	28.1	21		primi	38.3	B	NVD	1	1	19:56	19:56	1	120ml	0.01	0.08	0.3	0.6	12	36	11.2	33.8	no	no	no	no	
56	29	yes/yes	27.3	24		multi	37.2	B	NVD	1	1	23:43	23:44	1	180ml	0.01	0.08	0.3	1	12		10.4			no	no	no	no
60	30	yes/yes	26	22		multi	38.1	A	NVD	1	1	06:34	06:34	1	100ml	0.01	0.08	0.3	0.6	12		11.5			no	no	no	no
61	31	yes/yes	28.5	23		primi	37	A	NVD	1	1	01:25	01:26	1	200ml	0.01	1.2	0.3	1	11.1	33.2	10	30.4	no	no	no	no	
62	32	yes/yes	26	25		primi	39.2	C	NVD	1	1	04:36	04:36	30 sec	200ml	0.01	0.08	0.3	1	11	32.8	10.6	32	no	no	no	no	
64	33	yes/yes	26.4	25		multi	39.1	A	NVD	1	1	07:24	07:25	1	180ml	0.01	0.08	0.3	0.6	10.8	32	10	31	no	no	no	no	

67	34	yes/yes	26.6	26	PROM	multi	39	C	NVD	1	1	13:55	13:56	1	200 ml	0.01	1	0.3	1	10.5	33.5	9.8	32	no	no	no	yes
68	35	yes/yes	29.5	31	post datism	multi	40	B	NVD	1	1	14:15	14:16	1	200ml	0.01	0.8	0.3	1	10.6	32.8	9.4	30.2	no	no	no	no
70	36	yes/yes	26.6	23		primi	39.6	B	NVD	1	1	00:35	00:36	1	150ml	0.01	0.08	0.3	0.6	12.5	34.6	11.6	33.2	no	no	no	no
71	37	yes/yes	28.4	23		primi	39.4	B	NVD	1	1	07:08	07:09	1	200ml	0.01	0.08	0.3	0.8	10	32.8	9.4	31.2	no	no	no	yes
72	38	yes/yes	28.1	22		primi	39	A	NVD	1	1	10:11	10:12	1	260ml	0.01	1	0.3	1	12.1	34.2	11	33	no	no	no	no
73	39	yes/yes	29.4	23		multi	39.3	B	NVD	1	1	21:19	21:20	1	240ml	0.01	0.6	0.3	1	12.7	34.2	10	30.1	no	yes	no	no
74	40	yes/yes	29	21		primi	37.5	A	NVD	1	1	01:19	01:20	1	200ml	0.01	0.6	0.3	1	10.1	32	9.6	31.6	no	no	no	yes
75	41	yes/yes	28	32		multi	39.3	C	NVD	1	1	21:19	21:20	1	180ml	0.01	0.08	0.3	0.6	12.7	35	12	34	no	no	no	no
76	42	yes/yes	30.04	21		primi	37.5	C	NVD	1	1	01:19	01:20	1	200ml	0.01	0.08	0.3	1	10.1	32	9.4	31	no	no	no	no
77	43	yes/yes	24.2	28	polyhydramnios	multi	37.5	B	NVD	1	1	01:21	01:22	1	250ml	0.01	1	0.3	1	11.4	35	10.6	34.2	no	no	no	no
78	44	yes/yes	24.8	22		primi	39.6	C	NVD	1	1	11:09	11:09	30 sec	200ml	0.01	0.08	0.3	0.6	12.1	35	11.8	34	no	no	no	no
80	45	yes/yes	29	27	post datism	multi	40	C	NVD	1	1	12:04	12:05	1	200ml	0.01	0.6	0.3	0.8	9.9	28	8.7	25.8	no	no	no	yes
81	46	yes/yes	31	25	oligohydramnios	primi	37.3	A	NVD	1	1	12:29	12:30	1	280ml	0.01	1.2	0.3	1	9.9	28.9	8.4	26	no	yes	no	yes
82	47	yes/yes	29.4	23	hypothyroidism	multi	37.2	A	NVD	1	1	21:01	21:02	1	200ml	0.01	0.6	0.3	1	11.6	34.8	10.4	34.2	no	no	no	no
85	48	yes/yes	32.9	32		multi	39	B	NVD	1	1	00:30	00:31	1	240ml	0.01	0.6	0.3	0.6	11	32.8	10.4	32	no	no	no	no
86	49	yes/yes	30.2	24	GDM	primi	38.6	A	NVD	1	1	02:29	02:29	30 sec	200ml	0.01	1	0.3	0.6	14.9	40	12	36	no	no	no	no
87	50	yes/yes	25.9	24		multi	37.6	A	NVD	1	1	05:36	05:37	1	150ml	0.01	0.08	0.3	1	11	33	10.7	32	no	no	no	no
88	51	yes/yes	26.1	27	PROM	primi	37.6	A	NVD	1	1	06:49	06:50	1	350ml	0.01	1	0.3	1	13	38	11.8	34	no	no	no	no
89	52	yes/yes	24.6	28		multi	37.6	B	NVD	1	1	11:09	11:10	1	240ml	0.01	0.6	0.3	0.6	12.9	36	11.8	34.2	no	no	no	no
91	53	yes/yes	26.3	27		multi	39.1	C	NVD	1	1	09:26	09:27	1	200ml	0.01	0.08	0.3	0.6	12.1	34	11	32	no	no	no	no
92	54	yes/yes	27.6	31		multi	38.2	B	NVD	1	1	10:16	10:17	1	70ml	0.01	0.08	0.3	0.6	13.1	38	12.6	37.8	no	no	no	no
93	55	yes/yes	30.2	26		primi	37.4	C	NVD	1	1	18:44	18:45	1	300ml	0.01	1	0.3	0.6	13.5	38	12	36	no	no	no	no
95	56	yes/yes	26.4	28		primi	38.6	A	NVD	1	1	06:11	06:11	30 sec	260ml	0.01	1	0.3	0.6	12.1	36	11.2	34	no	no	no	no
96	57	yes/yes	28.8	25	hypothyroidism	multi	39.4	C	NVD	1	1	06:22	06:23	1	240ml	0.01	0.08	0.3	0.6	11.1	33.2	10.5	31.6	no	no	no	no
98	58	yes/yes	24.8	24	post datism	primi	40	C	NVD	1	1	14:55	14:56	1	250ml	0.01	0.08	0.3	0.6	13	35.4	12.1	33.3	no	no	no	no
100	59	yes/yes	26	20		primi	39.6	C	NVD	1	1	16:02	16:03	1	200ml	0.01	0.6	0.3	0.6	12.5	36.7	11	33	no	no	no	no
103	60	yes/yes	28.8	23		primi	39.4	C	NVD	1	1	23:32	23:33	1	200ml	0.01	0.08	0.3	0.6	10.5	34	9.4	32.1	no	no	no	yes
104	61	yes/yes	28.6	23	hypothyroidism	multi	40	A	NVD	1	1	03:57	03:58	00:00	280ml									no	no	no	no
106	62	yes/yes	27.4	26	VDRL, oligo	multi	37.2	B	NVD	1	1	01:14	01:15	1	150ml	0.01	0.08	0.3	0.6	12	35	11.5	34.2	no	no	no	no
107	63	yes/yes	28.4	21		primi	40	A	NVD	1	1	21:46	21:46	30 sec	120ml	0.01	0.08	0.3	0.6	16.1	46	15	45	no	no	no	no
109	64	yes/yes	26.6	22	PROM	multi	39.5	A	NVD	1	1	08:44	08:44	1	150ml	0.01	0.08	0.3	0.8	12.9	38	12	36	no	no	no	no
114	65	yes/yes	26.1	30		multi	38.1	B	NVD	1	1	18:47	18:47	30 sec	100ml	0.01	0.08	0.3	0.6	10.9	32.7	10	32	no	no	no	no
115	66	yes/yes	28	25	post datism	primi	40	B	NVD	1	1	09:40	09:41	1	100ml	0.01	0.08	0.3	1	10.7	32.1	10	30.8	no	no	no	no
116	67	yes/yes	28.2	25	oligohydramnios	multi	38.1	A	NVD	1	1	10:49	10:49	1	150ml	0.01	0.6	0.3	0.6	10.4	32.2	10	31	no	no	no	no
117	68	yes/yes	28.4	22		primi	38.6	B	NVD	1	1	19:38	19:39	1	200ml	0.01	0.08	0.3	0.8	13.5	38.8	12	36	no	no	no	no
119	69	yes/yes	25.8	27	EROM	multi	38.5	B	NVD	1	1	02:33	02:34	1	150ml	0.01	0.6	0.3	1	11.5	33.5	10.8	32.4	no	no	no	no
120	70	yes/yes	28	26		primi	37.4	A	NVD	1	1	02:36	02:37	1	300ml	0.01	1.2	0.3	1	12.3	36.9	10	30	no	yes	no	no
121	71	yes/yes	29.5	20		primi	37.1	A	NVD	1	1	07:00	07:01	1	120ml	0.01	0.8	0.3	0.6	12.2	36.6	11.4	34.2	no	no	no	no
122	72	yes/yes	25.5	20	hypothyroidism	primi	37.3	C	NVD	1	1	13:24	13:25	1	180ml	0.01	0.6	0.3	1	11.6	34.8	11	33	no	no	no	no
123	73	yes/yes	27.9	24	ov. Ind	primi	39.6	A	NVD	1	1	18:21	18:22	1	200ml	0.01	0.6	0.3	0.8	12	36	11	33.4	no	no	no	no
124	74	yes/yes	23.7	20	post datism	primi	40	C	NVD	1	1	22:22	22:22	30 sec	120ml	0.01	0.6	0.3	0.6	12.3	36.6	11.8	34.6	no	no	no	no
127	75	yes/yes	26.4	21		primi	38.4	B	NVD	1	1	01:11	01:12	1	150ml	0.01	0.08	0.3	0.6	12.2	36.6	11.4	34.2	no	no	no	no
128	76	yes/yes	29	28	post datism	multi	40.2	C	NVD	1	1	04:42	04:42	1	120ml	0.01	0.08	0.3	1	11.6	34.2	10.8	31.6	no	no	no	no
129	77	yes/yes	27.5	26		multi	37	A	NVD	1	1	16:25	16:26	1	350ml	0.01	1.4	0.3	1.6	10.8	32.4	9	28.2	no	yes	no	yes

131	78	yes/yes	26.4	27	post datism	multi	40.1	C	NVD	1	1	09:54	09:55	1	150ml	0.01	0.08	0.3	0.6	12.1	36.3	11.7	34.1	no	no	no	no
132	79	yes/yes	24.6	30	post datism	multi	40.3	B	NVD	1	1	10:14	10:15	1	150ml	0.01	0.08	0.3	0.6	13.1	39.3	12.2	36.6	no	no	no	no
135	80	yes/yes	27.3	26	post datism	primi	40.1	C	NVD	1	1	10:19	10:20	1	200ml	0.01	0.08	0.3	0.6	10.7	32.1	9.6	28.8	no	no	no	yes
136	81	yes/yes	26.4	23	post datism	primi	40	A	NVD	1	1	12:58	12:59	1	200ml	0.01	0.6	0.3	0.6	12.1	36.3	11.2	33.4	no	no	no	no
137	82	yes/yes	31	20	PROM	primi	38.4	A	NVD	1	1	00:10	00:11	1	180ml	0.01	1	0.3	0.8	14	42	13.2	39.6	no	no	no	no
138	83	yes/yes	26.4	22	post datism	primi	40.1	B	NVD	1	1	03:46	03:47	1	250ml	0.01	0.08	0.3	0.6	11.9	35.7	9.8	29.4	no	no	no	yes
139	84	yes/yes	27.8	29		multi	39.5	C	NVD	1	1	04:40	04:41	1	100ml	0.01	0.08	0.3	0.6	12.2	36.6	11.8	34.4	no	no	no	no
140	85	yes/yes	27	23	post datism	primi	40.1	B	NVD	1	1	10:04	10:05	1	200ml	0.01	0.08	0.3	1	12.3	36.9	10.9	32.7	no	no	no	no
141	86	yes/yes	27.2	30	FGR	primi	40.2	B	NVD	1	1	07:51	07:51	30 sec	180ml	0.01	0.08	0.3	0.6	11.7	35.1	10.9	32.7	no	no	no	no
143	87	yes/yes	26	25	FGR	multi	38.6	A	NVD	1	1	02:42	02:43	1	220ml	0.01	1	0.3	1	12.9	38.7	11.2	34.6	no	no	no	no
145	88	yes/yes	28.4	21	EROM	primi	37.1	B	NVD	1	1	07:29	07:30	1	150ml	0.01	0.6	0.3	0.6	13.2	39.6	12.7	37.1	no	no	no	no
148	89	yes/yes	26.8	27	hyperthyroidism	primi	38.5	C	NVD	1	1	14:51	14:52	1	350ml	0.01	1.2	0.3	1	11.7	35.1	10	32	no	yes	no	no
149	90	yes/yes	28	25		primi	37.3	B	NVD	1	1	14:56	14:57	1	150ml	0.01	0.08	0.3	0.6	11.1	33.3	10.7	32.1	no	no	no	no
151	91	yes/yes	27.4	19	FGR	primi	38.5	B	NVD	1	1	09:07	09:08	1	200ml	0.01	0.6	0.3	0.6	12.7	38.1	11.9	35.1	no	no	no	no
153	92	yes/yes	26.6	21	gest thrombocytopenia	multi	37.1	C	NVD	1	1	23:22	23:22	30 sec	180ml	0.01	0.08	0.3	0.6	13.2	39.6	12.6	35.8	no	no	no	no
156	93	yes/yes	25.8	23	PROM	primi	38.3	A	NVD	1	1	09:33	09:33	30 sec	180ml	0.01	0.6	0.3	0.6	11.2	33.6	10.4	31.2	no	no	no	no
161	94	yes/yes	27.2	27		multi	37.6	C	NVD	1	1	09:53	09:54	1	100ml	0.01	0.6	0.3	0.6	11.6	34.8	11	33	no	no	no	no
163	95	yes/yes	29.4	26	FGR	multi	37.5	C	NVD	1	1	12:06	12:07	1	100ml	0.01	0.08	0.3	0.6	10	30.4	9.6	28	no	no	no	yes
166	96	yes/yes	30.1	26	hypothyroidism	multi	38	C	NVD	1	1	01:18	01:19	1	260ml	0.01	1	0.3	1.2	12.5	37.5	11	33	no	no	no	no
170	97	yes/yes	27.2	25		multi	39.5	A	NVD	1	1	02:58	02:59	1	380ml	0.01	1.8	0.3	1.6	12	36	9.4	28.2	no	yes	no	yes
172	98	yes/yes	28.6	26	post datism	multi	40	C	NVD	1	1	06:22	06:23	1	300ml	0.01	1	0.3	0.6	9.9	30	9	27	no	yes	no	yes
173	99	yes/yes	25.8	26		multi	38.6	B	NVD	1	1	08:32	08:33	1	100ml	0.01	0.08	0.3	0.6	12.9	38.4	12.4	37.2	no	no	no	no
175	100	yes/yes	26.4	26		primi	40.1	B	NVD	1	1	17:18	17:18	30 sec	400ml	0.01	1.8	0.3	1.4	12.1	36.3	9.8	29.4	no	yes	heada	no
176	101	yes/yes	27	28	post datism	multi	40.2	C	NVD	1	1	04:29	04:30	1	100ml	0.01	0.08	0.3	0.6	12	36	11.2	33.6	no	no	no	no
179	102	yes/yes	28.2	26		multi	39.2	A	NVD	1	1	03:19	03:20	1	190ml	0.01	0.08	0.3	0.6	11.8	35.4	11	33	no	no	no	no
182	103	yes/yes	29.4	34	hypothyroidism	multi	39	B	NVD	1	1	01:33	01:34	1	150ml	0.01	0.08	0.3	0.6	11.1	33.3	11	33	no	no	no	no
188	104	yes/yes	25.9	26	GDM	multi	38.6	A	NVD	1	1	07:41	07:42	1	160ml	0.01	1	0.3	0.6	11.1	33	10	30	no	no	no	no
191	105	yes/yes	27.4	24		primi	38.6	B	NVD	1	1	06:29	06:30	1	200ml	0.01	0.6	0.3	0.6	12	36	11.2	33.6	no	no	no	no
192	106	yes/yes	25.4	28		multi	39.4	A	NVD	1	1	11:25	11:25	30 sec	250ml	0.01	1	0.3	1	11.8	35.4	10.4	34.2	no	no	no	no
194	107	yes/yes	26.2	21	PROM	primi	38.3	C	NVD	1	1	17:55	17:56	1	180ml	0.01	0.08	0.3	0.6	10.7	32.1	10	30	no	no	no	no
195	108	yes/yes	27.8	25		multi	38	A	NVD	1	1	18:11	18:12	1	150ml	0.01	0.6	0.3	0.6	12	36	11.4	34.2	no	no	no	no
197	109	yes/yes	26	27	macrosomia	multi	39.3	C	NVD	1	1	01:44	01:45	1	150ml	0.01	0.08	0.3	0.6	11	33.4	10.4	32.2	no	no	no	no
202	110	yes/yes	28.4	32	FGR	multi	38.1	A	NVD	1	1	11:52	11:53	1	340ml	0.01	1.2	0.3	1	12.8	38.4	10	34	no	yes	no	yes
204	111	yes/yes	26.8	27		multi	39.5	B	NVD	1	1	16:51	16:52	1	250ml	0.01	0.06	0.3	0.6	13	39	11.2	34	no	no	no	no
207	112	yes/yes	24.8	23		primi	38.4	A	NVD	1	1	17:50	17:51	1	700ml	0.01	2.4	0.3	2	10.3	30.9	7.9	23.7	yes	yes	hypoter	yes
211	113	yes/yes	28.9	24		multi	40.1	B	NVD	1	1	07:58	07:59	1	150ml	0.01	0.06	0.3	0.6	12	36	11.2	33.6	no	no	no	no
213	114	yes/yes	24	20	FGR	primi	37.6	B	NVD	1	1	10:33	10:34	1	200ml	0.01	1	0.3	0.6	11.8	35.4	10.2	31.4	no	no	no	no
215	115	yes/yes	29	30		multi	38.4	C	NVD	1	1	12:30	12:31	1	50ml	0.01	0.08	0.3	0.3	12.1	36.3	11.8	35.4	no	no	no	no
219	116	yes/yes	27.5	25	post datism	multi	40	A	NVD	1	1	09:40	09:41	1	180ml	0.01	0.6	0.3	0.6	9.9	29.7	9	27	no	no	no	yes
221	117	yes/yes	28.2	31	grand multi	multi	40.2	A	NVD	1	1	14:00	14:01	1	250ml	0.01	0.8	0.3	1	10	30	9	27	no	yes	no	yes
223	118	yes/yes	25.6	22		primi	39.4	B	NVD	1	1	12:18	12:19	1	200ml	0.01	1	0.3	1	12.1	36.3	11	33	no	no	no	no
225	119	yes/yes	29	32	post datism	multi	40.2	B	NVD	1	1	16:32	16:33	1	180ml	0.01	0.08	0.3	0.6	12.7	38.1	11.9	35.7	no	no	no	no
228	120	yes/yes	30	27	GDM	primi	39.6	C	NVD	1	1	20:15	20:16	1	200ml	0.01	0.6	0.3	0.6	13.7	41.1	12.1	36.3	no	no	no	no

230	121	yes/yes	26.8	24		multi	39.2	C	NVD	1	1	18:36	18:37	1	250ml	0.01	0.8	0.3	0.6	12.6	37.8	11	34	no	no	no	no
233	122	yes/yes	28.6	28	FGR	multi	38.4	B	NVD	1	1	02:47	02:48	1	250ml	0.01	1	0.3	1	13.7	41.1	12.9	38.1	no	no	no	no
236	123	yes/yes	25.4	20	FGR	primi	37.6	A	NVD	1	1	20:18	20:19	1	180ml	0.01	0.08	0.3	0.6	12.6	37	11.2	33.6	no	no	no	no
237	124	yes/yes	28	26	hypothyroidism	multi	38.4	B	NVD	1	1	02:42	02:43	1	250ml	0.01	1	0.3	0.6	12.1	36.3	11	33	no	no	no	no
240	125	yes/yes	27	27		multi	37.3	C	NVD	1	1	08:16	08:16	30 sec	250ml	0.01	0.9	0.3	1.2	11.8	35.4	10	31	no	no	no	no
244	126	yes/yes	26.8	21	post datism	multi	40.3	A	NVD	1	1	16:13	16:14	1	100ml	0.01	0.08	0.3	0.6	11.2	33.6	10.6	31.8	no	no	no	no
246	127	yes/yes	28	28	GDM	primi	40.5	A	NVD	1	1	18:09	18:10	1	150ml	0.01	0.08	0.3	0.6	9.9	28	8.9	26.7	no	no	no	yes
247	128	yes/yes	24.8	24		primi	38.6	C	NVD	1	1	19:38	19:39	1	180ml	0.01	0.08	0.3	0.6	11.4	34.2	10.7	32.1	no	no	no	no
251	129	yes/yes	26.2	34	FGR	multi	39.2	C	NVD	1	1	23:13	23:14	1	150ml	0.01	0.6	0.3	0.6	13.4	41.2	12.6	37.8	no	no	no	no
254	130	yes/yes	27.8	28	FGR	primi	37.5	B	NVD	1	1	15:15	15:15	30 sec	250ml	0.01	1	0.3	1	12.2	36.6	11	33	no	no	diziti	no
256	131	yes/yes	28	27	PROM	multi	38.4	A	NVD	1	1	20:10	20:11	1	200ml	0.01	0.08	0.3	1	11.6	34.8	10.2	31.2	no	no	no	no
257	132	yes/yes	26.4	29	PROM	primi	37.6	C	NVD	1	1	22:03	22:04	1	240ml	0.01	0.6	0.3	0.6	10.6	31.8	9.8	29.4	no	no	no	yes
260	133	yes/yes	24	29	UTI	primi	38	A	NVD	1	1	01:59	02:00	1	300ml	0.01	1	0.3	1.2	9.9	29	8.8	26.4	no	yes	no	yes
262	134	yes/yes	26.8	23		primi	38.3	C	NVD	1	1	05:44	05:45	1	280ml	0.01	1.8	0.3	1.4	12.4	37.2	10	30	no	yes	no	no
266	135	yes/yes	26	20	hypothyroidism	multi	41.1	C	NVD	1	1	13:28	13:29	1	150ml	0.01	0.08	0.3	0.6	11.7	35.1	11	33	no	no	no	no
266	136	yes/yes	25	24	oligohydramnios	multi	38.5	A	NVD	1	1	13:40	13:41	1	180ml	0.01	0.6	0.3	0.6	11	33	10.6	31.8	no	no	no	no
267	137	yes/yes	28.4	33	grand multi	multi	40	A	NVD	1	1	07:03	07:04	1	320ml	0.01	1.2	0.3	1	12.4	27	10	30	no	yes	no	no
269	138	yes/yes	26	24	PROM	multi	39	B	NVD	1	1	16:21	16:22	1	280ml	0.01	0.6	0.3	1	10.2	30.6	9.4	28.2	no	no	no	yes
271	139	yes/yes	29	22	hypothyroidism	primi	38.5	B	NVD	1	1	19:58	19:59	1	100ml	0.01	0.08	0.3	0.6	13.1	39.3	12.7	35.1	no	no	no	no
273	140	yes/yes	26.8	22		multi	38	C	NVD	1	1	09:14	09:15	1	200ml	0.01	0.6	0.3	0.6	11.1	33.3	10.7	31.1	no	no	no	no
275	141	yes/yes	26.4	30		primi	38.5	A	NVD	1	1	01:20	01:21	1	460ml	0.01	1.6	0.3	1	10	30	8.5	25.5	no	yes	yes	yes
277	142	yes/yes	28	24		multi	39.4	C	NVD	1	1	09:05	09:06	1	100ml	0.01	1.2	0.3	0.6	11	33.2	10.6	31.8	no	no	no	no
279	143	yes/yes	27	26		multi	37.3	B	NVD	1	1	11:31	11:32	1	150ml	0.01	1	0.3	0.6	13.1	39.3	12.7	37	no	no	no	no
283	144	yes/yes	29	28	IGT	primi	40.2	C	NVD	1	1	13:38	13:39	1	300ml	0.01	1	0.3	1.2	11.3	33.9	9.8	29.4	no	no	no	no
285	145	yes/yes	26.4	22	polyhydramnios	multi	40	A	NVD	1	1	18:42	18:43	1	300ml	0.01	1	0.3	1	12.7	38	10	30.5	no	yes	no	no
286	146	yes/yes	27.9	27	IGT	primi	38.4	C	NVD	1	1	08:34	08:35	1	300ml	0.01	1.2	0.3	1	13	39	11	33	no	yes	no	no
287	147	yes/yes	26.8	25		primi	38.1	B	NVD	1	1	23:25	23:25	30 sec	200ml	0.01	0.08	0.3	0.6	11.9	35.7	10.9	32.7	no	no	no	no
291	148	yes/yes	26.4	26		primi	38.5	B	NVD	1	1	10:27	10:28	1	300ml	0.01	1	0.3	1.2	11.9	35.7	10	30	no	yes	no	no
292	149	yes/yes	29	26	GDM	multi	38.4	B	NVD	1	1	13:37	13:38	1	160ml	0.01	0.08	0.3	0.6	10.2	30.6	9.6	28.6	no	no	no	yes
294	150	yes/yes	28	24	hypothyroidism	primi	38	A	NVD	1	1	16:16	16:17	1	200ml	0.01	0.08	0.3	1	11.7	35.1	10.9	32.7	no	no	no	no
296	151	yes/yes	28.5	23	hypothyroidism	primi	37.3	C	NVD	1	1	00:20	00:21	1	400ml	0.01	1.2	0.3	1.2	10	30	8.8	26.4	no	yes	no	yes
298	152	yes/yes	26.4	22	FGR	multi	40.2	B	NVD	1	1	16:59	17:00	1	150ml	0.01	0.08	0.3	0.6	10	30	9.6	28.6	no	no	no	yes
301	153	yes/yes	27.6	26		primi	39.4	B	NVD	1	1	21:20	21:21	1	250ml	0.01	1	0.3	1	12.4	37.2	11	33	no	no	no	no
302	154	yes/yes	25.4	27	FGR	multi	38.5	A	NVD	1	1	00:05	00:06	1	200ml	0.01	0.6	0.3	0.6	12.9	39.7	11.7	35.1	no	no	no	no
305	155	yes/yes	26	22		primi	40.3	B	NVD	1	1	13:05	13:06	1	250ml	0.01	0.6	0.3	0.6	11.5	34.5	10	30	no	no	no	no
305	156	yes/yes	25.6	22		primi	39.6	C	NVD	1	1	13:20	13:21	1	150ml	0.01	0.08	0.3	0.6	11	33	10.4	31.2	no	no	no	no
306	157	yes/yes	28	27	hypothyroidism	multi	37.3	C	NVD	1	1	05:04	05:05	1	100ml	0.01	0.08	0.3	0.6	9.9	29.7	9	27	no	no	no	no
307	158	yes/yes	26.4	23	post datism	multi	40.4	B	NVD	1	1	07:13	07:13	1	200ml	0.01	0.6	0.3	0.6	12.5	37.5	11.7	35.1	no	no	no	no
308	159	yes/yes	25.4	25	PROM	multi	39.3	C	NVD	1	1	17:58	17:59	1	250ml	0.01	1	0.3	1	12.2	36.6	11.3	33.9	no	no	no	no
309	160	yes/yes	26.4	23	post datism	primi	37.5	A	NVD	1	1	19:46	19:47	1	200ml	0.01	1	0.3	1	11	33	10	30	no	no	no	no
310	161	yes/yes	24.2	26		multi	40	A	NVD	1	1	20:22	20:23	1	300ml	0.01	1.4	0.3	1.2	10.8	32.4	9	27	no	yes	no	yes
311	162	yes/yes	26.4	24		multi	38.2	A	NVD	1	1	16:44	16:45	1	280ml	0.01	1	0.3	1	13.1	39.3	11.4	34.2	no	no	no	no
312	163	yes/yes	26.4	25		multi	38.3	C	NVD	1	1	23:11	23:12	1	200ml	0.01	0.08	0.3	0.6	10.6	31.8	10	30	no	no	no	no
313	164	yes/yes	27	26	FGR	primi	39.1	B	NVD	1	1	02:40	02:41	1	200ml	0.01	0.08	0.3	0.6	13.3	39.9	12.6	37.8	no	no	no	no

314	165	yes/yes	25.6	24		primi	38.5	B	NVD	1	1	08:07	08:08	1	250ml	0.01	0.6	0.3	0.6	10.9	32.7	9.9	29.7	no	no	no	no
317	166	yes/yes	28.5	22	GDM, polyhydramnios	multi	37	A	NVD	1	1	18:06	18:07	1	280ml	0.01	1	0.3	1	11	33	9.8	29.4	no	yes	no	no
319	167	yes/yes	29	26	post datism	multi	40.2	C	NVD	1	1	03:47	03:48	1	200ml	0.01	0.6	0.3	0.6	11.7	34.1	10.5	31.5	no	no	no	no
320	168	yes/yes	29	31	hypothyroidism, GDM, Polyhydramnios	multi	38.5	A	NVD	1	1	23:20	23:21	1	450ml	0.01	1.8	0.3	1.6	13.5	40.5	10	30	no	yes	no	yes
321	169	yes/yes	26.4	29	FGR	primi	39.6	A	NVD	1	1	07:16	07:17	1	150ml	0.01	0.08	0.3	0.6	11.6	34.8	11	33	no	no	no	no
326	170	yes/yes	26	20		primi	38.2	C	NVD	1	1	03:30	03:31	1	200ml	0.01	0.08	0.3	0.6	11.4	34.2	10.6	31.8	no	no	no	no
332	171	yes/yes	25.4	21	fetus having single UA	primi	40	C	NVD	1	1	#####	21:17	1	200ml	0.01	0.6	0.3	0.6	13.3	39.3	12.8	37.4	no	no	no	no
333	172	yes/yes	26	31		multi	38.2	A	NVD	1	1	22:14	22:15	1	200ml	0.01	0.08	0.3	0.6	12.2	36.6	11.7	34.1	no	no	no	no
334	173	yes/yes	25.6	19		primi	40.5	C	NVD	1	1	01:17	01:18	1	180ml	0.01	0.08	0.3	0.6	10.2	30.6	9.9	30	no	no	no	no
335	174	yes/yes	26	23	PROM	primi	37.4	B	NVD	1	1	02:55	02:56	1	150ml	0.01	0.08	0.3	0.6	12.4	37.2	11.9	35.7	no	no	no	no
336	175	yes/yes	26.5	23	hypothyroidism	primi	40.4	B	NVD	1	1	04:03	04:04	1	250ml	0.01	1	0.3	1.2	12.5	37.5	11	33	no	no	no	no
342	176	yes/yes	26	26	FGR	primi	38.1	A	NVD	1	1	23:20	23:21	1	280ml	0.01	00:00	10.3	1.4	12	36	9.6	28.8	no	yes	no	no
346	177	yes/yes	26.5	24	macrosomia	multi	37	B	NVD	1	1	08:54	08:55	1	200ml	0.01	0.06	0.3	0.6	11.6	34.8	10.8	32.4	no	no	no	no
353	178	yes/yes	28	23		primi	39.2	B	NVD	1	1	05:30	05:31	1	150ml	0.01	0.06	0.3	0.6	13	39	12.6	37.8	no	no	no	no
358	179	yes/yes	26	24	EROM	primi	38.6	A	NVD	1	1	17:56	17:57	1	200ml	0.01	0.6	0.3	1	11	33	10	30	no	no	no	no
360	180	yes/yes	24.8	24		multi	37.4	C	NVD	1	1	02:39	02:39	30 sec	150ml	0.01	0.08	0.3	0.6	12.5	37.5	12	36	no	no	no	no
368	181	yes/yes	28	27	hypothyroidism, mod anemia	multi	38.3	B	NVD	1	1	21:21	21:22	1	60ml	0.01	0.06	0.3	0.3	9.9	29.7	9.2	27.6	no	no	no	yes
374	182	yes/yes	26	22	oligohydramnios	primi	37.1	B	NVD	1	1	10:09	10:09	30 sec	260ml	0.01	1	0.3	1.2	13.1	39.3	12	36	no	no	no	no
378	183	yes/yes	29.7	24	overt DM	multi	37.6	B	NVD	1	1	11:12	11:13	1	250ml	0.01	1	0.3	1	12.2	36.6	10.8	32.4	no	no	no	no
380	184	yes/yes	27	28	hypothyroidism	multi	38	B	NVD	1	1	00:54	00:55	1	200ml	0.01	1	0.3	0.6	13	39	10.4	31.2	no	no	no	no
385	185	yes/yes	28.4	32	post datism	multi	40	C	NVD	1	1	22:13	22:14	1	150ml	0.01	0.08	0.3	0.6	13.2	39.6	12.6	37.8	no	no	no	no
388	186	yes/yes	28	23	hypothyroidism	primi	39.5	A	NVD	1	1	17:17	17:18	1	100ml	0.01	0.08	0.3	0.6	12	36	11.4	34.2	no	no	no	no
390	187	yes/yes	26.4	23	FGR	primi	37.3	B	NVD	1	1	22:17	22:18	1	50ml	0.01	0.08	0.3	0.6	12.2	36.6	12	36	no	no	no	no
392	188	yes/yes	26	24	oligohydramnios	multi	39	A	NVD	1	1	03:13	03:14	1	300ml	0.01	1.4	0.3	1.2	10.7	32.1	9	27	no	yes	no	yes
393	189	yes/yes	25.4	28	post datism	primi	40.2	C	NVD	1	1	09:30	09:31	1	200ml	0.01	1	0.3	1	12.2	36.6	11	11	no	no	no	no
396	190	yes/yes	26	26	PROM	primi	39.5	A	NVD	1	1	03:09	03:10	1	250ml	0.01	1.4	0.3	1	11.8	35.4	10	30	no	no	no	no
400	191	yes/yes	26	21	post datism	primi	40.1	C	NVD	1	1	02:54	02:55	1	150ml	0.01	0.06	0.3	0.6	11.3	33.9	10.7	32.1	no	no	no	no
404	192	yes/yes	25.4	32	BOA	multi	39.2	B	NVD	1	1	10:01	10:02	1	50ml	0.01	0.08	0.3	0.3	10.7	32.1	10.4	31.2	no	no	no	no
407	193	yes/yes	27	26	post datism	primi	40	A	NVD	1	1	18:05	18:06	1	200ml	0.01	0.08	0.3	0.6	12	36	11	33	no	no	no	no
408	194	yes/yes	27.8	33		multi	38.4	C	NVD	1	1	23:15	23:16	1	150ml	0.01	0.08	0.3	0.6	14	42	13	39	no	no	no	no
409	195	yes/yes	26	23	PROM	multi	39.1	A	NVD	1	1	23:41	23:42	1	250ml	0.01	1	0.3	1	12	36	10	30	no	yes	no	no
410	196	yes/yes	27.4	25	oligohydramnios	primi	40	C	NVD	1	1	00:03	00:04	1	100ml	0.01	0.08	0.3	0.6	12.7	38.1	11.9	35.7	no	no	no	no
411	197	yes/yes	24.6	28	oligohydramnios	primi	37.4	C	NVD	1	1	05:21	05:22	1	120ml	0.01	0.6	0.3	0.6	12	36	11.2	33.6	no	no	no	no
421	198	yes/yes	26	24		multi	39.3	A	NVD	1	1	04:46	04:47	1	100ml	0.01	0.08	0.3	0.6	11.6	34.8	11	33	no	no	no	no