ROLE OF TRANEXAMIC ACID IN REDUCING BLOOD LOSS IN NORMAL LABOUR

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The Tamilnadu Dr. M.G.R. Medical University

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OBSTETRICS AND GYNAECOLOGY

K.A.P. Viswanathan Government Medical College

Tiruchirappalli

The Tamilnadu Dr. M.G.R. Medical University

Chennai

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CERTIFICATE

This is certify that the dissertation entitled **"ROLE OF TRANEXAMIC ACID IN REDUCING BLOOD LOSS IN NORMAL LABOUR"** is a bonafide work done by **Dr. B. SOWMYA** at K.A.P. Viswanathan Government Medical College, Trichy. This dissertation is submitted to Tamilnadu Dr. M.G.R. Medical University in partial fulfillment of University rules and regulations for the award of M.D. degree in Obstetrics and Gynaecology.

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ABBREVIATIONS

PR	PULSE RATE
SBP	SYSTOLIC BLOOD PRESSURE
DBP	DIASTOLIC BLOOD PRESSURE
RR	RESPIRATORY RATE
HT	HEIGHT
WT	WEIGHT
BMI	BODY MASS INDEX
PPH	POST PARTUM HAEMORRHAGE
HB	HAEMOGLOBIN
POD	POST OPERATIVE DAY
NICU	NEONATAL INTENSIVE CARE UNIT
LFT	LIVER FUNCTION TEST
RFT	RENAL FUNCTION TEST
IUD	INTRA UTERINE FETAL DEATH
AMTSL	ACTIVE MANAGEMENT OF THIRD STAGE OF LABOUR
VWD	VON WILLEBRAND'S DISEASE
ITP	IDIOPATHIC THROMBOCYTOPENIC PURPURA
TTP	THROMBOTIC THROMBOCYTOPENIC PURPURA
DIC	DISSEMINATED INTRA VASCULAR COAGULATION
DUB	DYSFUNCTIONAL UTERINE BLEEDING
TXA	TRANEXAMIC ACID
CVS	CARDIO VASCULAR SYSTEM
RS	RESPIRATORY SYSTEM
HELLP	HEMOLYSIS, ELEVATED LIVER ENZYMES, LOW PLATELETS
CT	CLOTTING TIME
BT	BLEEDING TIME
CBC	COMPLETE BLOOD COUNT
CVP	CENTRAL VENOUS PRESSURE
PCV	PACKED CELL VOLUME
TD	TIME OF DELIVERY

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INTRODUCTION

INTRODUCTION

Gods interest in the human race is nowhere better evinced than in obstetrics – **Martin H. Fischer**.

Child birth is one of the most marvelous and memorable segment in a woman's life. The art of vaginal birth is a unique experience and calls for a celebration. Although the incidence of caesarean section is increasing throughout the world, the art of vaginal birth has not lost its charm. Birth is a life changing event. The care given to woman during labour has the potential to affect her both physically and emotionally in the short and long term.

Though labour is a physiological process, it is often associated with morbidity and mortality. The most common cause being blood loss. Life threatening obstetric hemorrhage occurs in approximately 1 per 1000 deliveries. The most recent Practice Bulletin from the American College of Obstetrics and Gynaecology places the estimate at 1,40,000 maternal deaths per year or 1 woman every 4 minutes. There are a number of drugs available for the management of PPH. The recent ones being the anti fibrinolytics and recombinant factor VII_a.

Postpartum haemorrhage (PPH) remains a leading cause of maternal mortality, especially in developing countries (**Ronsmons 2006**). In confidential enquiries into maternal deaths in South Africa (2005 to 2007) (**Confidential enquiries 2006**), 383 maternal deaths due to PPH were reported and the majority of these were considered to be preventable. Of these deaths, 67

(17.5%) were caused by uterine atony, where uterotonics were required to control the bleeding. Other cases of maternal death from PPH were due to uterine rupture (37 in women with previous caesarean sections and 43 in women without previous caesarean sections), retained placenta (88), inverted uterus (seven), and other genital tract trauma including caesarean section (141). The great majority were thus not due to uterine atony, and attempts to address the problem need to go beyond the use of uterotonic drugs. Because of the difficulty of randomised trials in women presenting with PPH, the use of tranexamic acid for preventing PPH in high-risk women could be regarded as a proxy for assessing its use for treating PPH. In particular, high-risk factors which may not be responsive to uterotonics, such as placenta praevia and lacerations from instrumental delivery, may respond to tranexamic acid. If tranexamic acid is found to be effective in the prevention of PPH in such high-risk women, its use could be extrapolated to the treatment of PPH (as has been the case for most treatments for PPH, such as oxytocin and ergometrine).

The changes in the fibrinolytic components during and immediately after placental delivery are consistent with fibrinolysis occurring as a response to local fibrin deposition. The plasma fibrinogen level decreases during the 3rd stage of labour and after placental delivery, and the level of fibrin/ fibrinogen degradation products in the serum increases 1 hour after child birth and remains raised in the early puerperium.

Hence antifibrinolytics will be effective in reducing blood loss by interacting with the fibrinolytic mechanism.

This study observes the blood loss reduced by Tranexamic Acid, an antifibrinolytic agent during 3rd stage.

AIM OF THE STUDY

1. To evaluate the efficacy of parenteral Tranexamic Acid in reducing blood loss during normal labour.
2. To compare it with the amount of blood loss in patients who did not receive Tranexamic Acid in the 3rd stage.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Post partum hemorrhage is the leading cause of maternal mortality. All woman who carry a pregnancy beyond 20 weeks gestation are at risk of PPH and its sequelae. In the developing world, several countries have maternal mortality rates in excess of 1000 women per 100,000 live births and WHO statistics suggest that 25% of maternal deaths are due to PPH, accounting for more than 100,000 maternal deaths per year.

The leading causes of pregnancy related death are hemorrhage, embolism and hypertensive disorders of pregnancy **– Berg CJ et al 1996.**

Prendiville et al. in Bristol Third Stage Trial found an incidence of postpartum bleeding of 5.9% in actively managed group and 17.9% in physiologically managed group. They concluded that intervention in third stage of labour reduces the risk of PPH by 30 – 40%.

MrCormick et al. published a systematic review of studies that assessed the efficacy of intervention in 3rd stage – concluded that intervention reduced the incidence of PPH, decreased the need for blood transfusion and decreased the need for additional uterotonic drugs.

Malcolm Potts 2006 – Darwinian evolution is not about what is nice, safe or aesthetic, but about what works. Human beings are burdened with a highly invasive trophoblast and at delivery, the human placenta leaves a huge, 20cm diameter wound on the inside of the uterus. The potential of catastrophically heavy bleeding can be avoided only by powerful uterine contractions and a good coagulation mechanism.

Idara Udofia et al. 2008 – Any intervention aimed at preventing PPH will reduce maternal mortality by more than one quarter.

Blood loss during normal labour

Normal pregnancy is accompanied by changes in the haemostatic mechanisms, particularly increase in the levels of factor VII, VIII, X and fibrinogen and a pronounced decrease in fibrinolytic activity. Parturition presents a serious challenge to the vascular compartment, but it has been generally held **(Taylor, 1966; Donald, 1969)** that contraction of the myometrium “the living ligatures” of the uterus - is the mechanism which, mainly controls blood loss at delivery. In the other situations where there is injury to the vascular tree an efficient blood coagulation system plays a vital part in achieving effective haemostasis and preserving the blood volume.

The coagulation and fibrinolytic mechanisms may be in a state of dynamic equilibrium which keeps the vascular compartment intact and patent, the coagulation system laying down fibrin to seal any gaps in the vascular endothelium and the fibrinolytic mechanism removing the deposits of fibrin after they have served their haemostatic function. Fibrinolytic activity is known to be decreased in the late pregnancy and labour and to return to normal in early puerperium.

Physiological adaptations in pregnancy

Antepartum adaptations for physiological blood loss at delivery include a 42% increase in plasma volume and a 24% increase in red blood cell volume by the third trimester. Progressively complicated deliveries are accompanied by greater degrees of blood loss.

Vaginal delivery – 500ml

Caesarean section – 1000ml

Caesarean hysterectomy – 1500ml

Emergency hysterectomy – 3500ml

However, these thresholds do not take into account the pre-existing health status and blood loss of as little as 200ml can be life threatening for a woman with severe anemia or cardiac disease **(Kongnyuy et al., 2009)**.

GREENTOP GUIDELINES (RCOG 2007) – defines PPH as

- 1 blood volume loss / 24 hrs
- 150 ml / minute blood loss
- 50% blood volume loss / 3 hrs

Some of the factors leading to increased blood loss in the third stage labour are as follows:

- Mean vaginal blood loss is higher in multiparae than in primiparae
- In primiparae, forceps delivery is associated with greater blood loss than spontaneous delivery; this is related to the episiotomies and other injuries to the genital tract.

- Patients with an episiotomy and a laceration lose significantly more blood than those without such insult. Episiotomies contribute to 154 ml to the average blood loss.

Incidence of PPH

2% to 11% - when blood loss is estimated visually **(Brent et al., 1967)**

20% - when blood loss is estimated by quantitative methods **(Newton et al., 1961)**

Types of PPH

- 1° PPH / early PPH – which occurs within 24 hrs of delivery
- 2° PPH / late PPH – which occurs 24 hrs to 6 weeks after delivery

Most cases of PPH almost 99% are due to 1° PPH

Pathophysiology

At term the uterus and placenta receive 500 – 800 ml of blood per minute through their low resistance network of vessels. This high flow predisposes a gravid uterus to significant bleeding if not well physiologically or medically controlled. By the third trimester, maternal blood volume increases by 40% - 50%, which increases the body's tolerance of blood loss during delivery. Following delivery of the fetus, the gravid uterus is able to contract down significantly given the reduction in volume. This allows the placenta to separate from the uterine interface, exposing maternal blood vessels that interface with the placental surface. After separation and delivery of the

placenta, the uterus initiates a process of contraction and retraction, shortening its fiber and kinking the supplying blood vessels, like physiologic sutures or "living ligatures."

If the uterus fails to contract, or the placenta fails to separate or deliver, then significant hemorrhage may ensue. Uterine atony, or diminished myometrial contractility, accounts for 80% of postpartum hemorrhage. The other major causes include abnormal placental attachment or retained placental tissue, laceration of tissues or blood vessels in the pelvis and genital tract, and maternal coagulopathies. An additional, though uncommon, cause is inversion of the uterus during placental delivery.

Potential causes for increased blood loss during labour:

1. Tone loss
2. Trauma
3. Tissue retention
4. Thrombotic defect

Of these, tone loss is the commonest and thrombotic defect is the most difficult to treat.

1. TONE LOSS : 80%, the following are the predisposing factors

- Multiparity
- Uterine overdistension – multiple pregnancy, hydramnios, macrosomia
- Prolonged labour
- Precipitate labour

- Anemia
- Chorioamnionitis
- Uterine abnormalities or fibroids
- Previous H/O PPH
- Induced labour
- Inadvertent use of oxytocics
- Drugs – halogenated anaesthetics, $MgSO_4$, nifidepine, beta agonists, diazoxide
- Placenta – accreta, praevia, abruption

2. TRAUMA : 20%

Lacerations and haematomas resulting from birth trauma can cause significant blood loss that can be lessened by haemostasis and timely repair. Factors causing increased blood loss are:

- Obstructed labour
- Big baby
- Pfannensteil incision
- Transverse lie
- Classical caesarean section
- Poor obstetrician's skill

3. TISSUE RETENSION : 10%

Placenta, accreta, increta, percreta, missed cotyledons and succenturiate placental lobe.

Risk factors

- Advanced maternal age
- High parity
- Previous invasive placenta
- Previous caesarean section
- Placenta praevia
- Previous H/O manual removal of placenta

4. THROMBOTIC DEFECT: 5%

- Coagulopathies – ITP, TTP, VWD, hemophilia
- Acquired – HELLP, abruption, IUD, DIC, septicemia

PPH is a potentially life threatening complication of both vaginal and caesarean delivery. Associated morbidity is related to the direct consequences of blood loss as well as the potential complications of haemostatic and resuscitative interventions.

Consequence of uncontrolled haemorrhage include

- Hypovolemic shock and associated organ failure including renal failure, stroke, myocardial infarction
- Postpartum hypopituitarism (Sheehan syndrome): Acute blood loss and / or hypovolemic shock during and after childbirth can lead to hypoperfusion of the pituitary and subsequent necrosis. Although often asymptomatic, it may present with an inability to breastfeed, fatigue, hypogonadism, amenorrhea, and hypotension.
- Death secondary to hypovolemic shock

Consequences of fluid resuscitation

- Fluid overload can lead to extremity edema and pulmonary edema. The latter is less common in young healthy women, but it should be suspected in the setting of large fluid and blood product resuscitation.
- Dilutional coagulopathy occurs when crystalloids and/or serum-poor blood products are given in large volume.

Risks from exposure to blood products

- Allergic or febrile reactions have an incidence of about 1 case per 333 population.
- Anaphylactic reactions occur in 1 in 20,000 to 1 in 47,000 blood products transfused.
- Transfusion-related acute lung injury (TRALI) occurs in 1 out of every 5,000 transfusions, but more often with high plasma containing products like fresh frozen plasma (FFP) and platelets. It often starts within 1-2 hours of the transfusion, but it can happen anytime up to 6 hours after a transfusion. The symptom complex includes severe bilateral pulmonary edema, severe hypoxemia, tachycardia, cyanosis, hypotension, and fever.
- Acute immune hemolytic reaction, though rare, is the most serious type of transfusion reaction. Symptoms are associated with red blood cell hemolysis. Patients may have fevers, chills, chest and lower back pain, nausea, renal failure, and death if the transfusion is not stopped.

- Delayed hemolytic reaction: This type of reaction happens when the body slowly attacks antigens (other than ABO antigens) on the transfused blood cells. Symptoms occur days to weeks after a transfusion. Affected patients are either asymptomatic or have mild symptoms, which may include jaundice, low-grade fever, and a low hemoglobin or hematocrit

Infection

Hepatitis is the most common disease transmitted by blood transfusions.

According to the American Red Cross, about 1 blood transfusion in 205,000 transmits a hepatitis B infection, and 1 blood transfusion in about 2 million transmits hepatitis C.

Other rare but potential infections include HIV (risk of 1 in 2.5 million), Lyme disease, babesiosis, and malaria. Donors are screened for potential exposure so transmission is very rare. Rarely, blood may be contaminated with tiny amounts of skin bacteria during donation. Platelets are the most likely blood product to be affected by contamination from skin flora.

- Metabolic reactions: With large volume and rapid transfusions, patients are at risk of encountering 3 metabolic reactions: hypothermia, hyperkalemia, and citrate toxicity.
- Hypothermia results from the transfusion of unwarmed crystalloid or colloid that drops the body temperature. Hypothermia inhibits coagulation and can worsen postpartum hemorrhage. Citrate is a blood

product additive that binds serum calcium and can cause hypocalcemia with large-volume transfusions. Hemolysis occurs with red blood cell storage releasing increasing amounts of intracellular potassium with time. Transfusions of older red blood cells increase the risk of hyperkalemia.

Risks associated with surgical intervention

- Intubation and anesthesia complications: Pregnant women have an increased risk for aspiration, failed intubation, and death from failed ventilation when compared with nonpregnant patients. Respiratory injury or infection, myocardial infarction, myocardial arrhythmia, stroke, or allergic reactions to anesthetic medications may also rarely occur.

Bleeding: Continued bleeding from the genital tract or a bleeding complication from the surgery may occur.

Infection: Sepsis, wound infection, or pneumonia is possible.

- Deep venous thrombosis and/or pulmonary embolism: Risk is increased due to postpartum and postoperative associated hypercoagulability as well as from relative immobility in the operative and postoperative period.

If the bleeding cannot be controlled conservatively (removal of products of conception, suturing disrupted tissues, application of pressure) then surgical intervention may be necessary. In severe cases, the following may occur:

- Hysterectomy
- Asherman syndrome, which is secondary (non-hormone mediated) amenorrhea due to uterine scarring that develops after infection and/or curettage performed to remove placental fragments

BLOOD LOSS ASSESSMENT

In order to assess the efficiency of the drug, the blood loss assessment has to be standardized.

Clinical methods

1. By subjective characters
2. Visual estimation

1. Estimation by subjective characters

- **Shock index**

SI = HEART RATE / SYSTOLIC BP

NORMAL = 0.5 – 0.7, with significant hemorrhage, it increases to 0.9 – 1.1

- **Rule of 30**

1. If systolic BP falls by 30 mmHg
2. Heart rate rises by 30 bpm
3. Respiratory rate rises by 30 breaths per minute
4. Hb or Hct drops by 30%
5. Urine output < 30 ml per hour

Patient is said to have lost atleast 30% of blood volume if all the above exists.

- **Measurement of CVP**

Normal : 8 – 14 cm of water. If CVP is low 0-6 cm of water, it means the blood volume is low in relation to cardiac capacity. If CVP is high > 15 cm of water, it means the blood volume is high in relation to cardiac capacity.

- **Classification of haemorrhage**

PARAMETER	CLASS I	CLASS II	CLASS III	CLASS IV
Blood loss (ml)	< 750	750 – 1500	1500 - 2000	> 2000
Blood loss (%)	< 15	15 – 30	30 – 40	> 40
Pulse rate/min	< 100	> 100	> 120	> 140
Blood pressure	N	↓	↓	↓
Respiratory rate/min	14 – 20	20 – 30	30 – 40	> 40
Urine output (ml/hr)	> 30	20 – 30	5 – 15	Negligible
CNS symptoms	Normal	Anxious	Confused	Lethargic

2. Visual estimation

This is the most frequently practiced method. The incidence of PPH is underestimated in the visual estimation by 89% - **Brant & Duthie et al.**

Budny et al. reported a strong positive association between calculated blood loss and blood loss estimated by junior and senior surgeons. It is inconsistent.

Dr. P. Bore et al. 2006

- 10 × 10 cm swab = 60 ml
- 30 × 30 cm swab = 140 ml
- 45 × 45 cm swab = 350 ml
- 1 kg soaked swabs = 1000 ml
- 50 cm diameter floor spill = 500 ml
- 75 cm diameter floor spill = 1000 ml
- 100 cm diameter floor spill = 1500 ml

Gravimetric methods

- Patient weighing method
- Swab weighing method

By measuring the weight of the patient or swabs prior to and after delivery.

- Patient weighing method: allowance must be made for drain, dressings, infection, tissue removal and insensible water loss.
- Swab weighing method: 1 gm of weight gain = 1 ml of blood loss

(Bonica and Lyter et al. in 1951, Harding 1984). Swabs must be weighed immediately to avoid the loss due to evaporation. Inter observer variation or inconsistency can be avoided in this method.

Calibrated obstetric drape

This comes in sterile packing and fold out to a 1 × 1 metre sterile area for a woman to give birth. At the bottom of the sterile area is a pouch that holds more than 2500 ml of fluid, allowing for accurate measurement of postpartum blood loss. The pouch itself also includes a flexible plastic filter to 'catch' material that is not liquid. The pouch includes a wire around its 'mouth' that keeps the pouch open.

Colorimetric method: (Roe et al., 1962, Thornton et al., 1963, Rustad et al., 1963)

The washing of the blood contaminated swabs is carried out in a known volume of tap water to which has been added sufficient amount of ammonium hydroxide to give a 1 in 1000 dilution as a defoaming agent. The blood collected in the suction container has to be added to the water and the concentration of the resultant solution has to be determined.

$$\text{Blood loss in ml} = \frac{\text{Hb\% of washing fluid} \times \text{volume of washing fluid}}{\text{Hb\% of patient's blood} \times \text{dilution factor of patient's Hb}}$$

Measurement of blood in the suction apparatus

Blood in the suction container can be measured. Inaccuracy in this method can be reduced by having measuring cylinder in the suction line and adding defoaming agent to the container.

Electrolyte conductivity method : (Leveen and Rubricius et al., 1958)

Using automated blood loss meter based on electrolyte conductivity.

Radioactivity method : (Murray and Dott's et al., 1960)

Intravenous injection of small but known amount of radio isotope should be followed by measuring the radioactivity of blood on swabs collected during delivery.

Blood volume measurements

- Dye method: using evans blue dye which must neither be catabolised nor rapidly lost from the circulation
- Radio isotopes like I_{131} labelled albumin or Cr_{51} labelled RBC can be used before delivery and measuring the post delivery radio activity by Geiger – Muller counter. (**Mollison ans Veall et al., 1955**).

Among the above mentioned methods swab weighing method and blood collected in the calibrated obstetric drape measurement are practically possible and feasible methods that were used in our study.

REDUCING BLOOD LOSS

Done by the following measures

- Antenatal care
- First and Second stage measures
- Third stage measures
- Postpartum measures

Antenatal care

1. Develop a birth preparedness plan : women should plan to give birth with a skilled attendant who can provide interventions to prevent, identify and manage PPH.
2. Routinely screen to prevent and treat anemia during preconceptional, antenatal, postpartum visits.
3. Blood grouping and Rh typing to be done.
4. Correction of coagulation abnormality in case of abruption, IUD, HELLP syndrome.

During first and second stage

1. A woman in established labour should receive supportive one to one care
2. Limit induction and augmentation use for medical and obstetric reasons
3. Do not encourage pushing before cervix is fully dilated
4. Do not apply fundal pressure to assist the birth of the baby
5. Perineal massage should not be performed by healthcare professionals

6. Encourage the woman to keep her bladder empty
7. Do not perform routine episiotomy
8. Either “hands on” or the “hands poised’ techniques can be used to facilitate spontaneous birth

During third stage : provide Active Management Of Third Stage Of Labour

Postpartum measures

It has been suggested that drainage of blood from the placenta would reduce its bulkiness, allowing the uterus to contract and retract and thus aiding delivery **(Roger et al., 1988)**.

Placental cord drainage may be used in conjunction with other interventions such as routine administration of oxytocics, controlled cord traction or maternal effort (**Hinchongbrooks RCT Lancet, 1998)**.

Placental cord drainage with or without prophylactic oxytocics is effective in reducing the blood loss in third stage thus preventing PPH (**Keirse, 1998)**.

Timing at cord clamping is also an important factor in the management of third stage of labour, influences the duration of third stage **(McDonald, 2003).**

These are evidences to indicate that there are benefits in active management of third stage of labour, but it may be associated with increased nausea, vomiting and raised blood pressure **(Prendiville et al., 2003)**.

The overall meta – analysis results of **Cochrane database systematic reviews 2004**, showed that there was a tendency for the active management group to have higher incidence of these complications. But this did not reach statistical significance. There was no statistically significant difference in neonatal outcome or breast feeding rates and no difference in long term maternal outcome.

TREATMENT

Most maternal deaths in PPH are due to the 3 delays:

1. Delay in recognition of complications
2. Delay in institution of definitive management
3. Delay in referral / accessing transportation

MANAGEMENT

General

Specific

i) medical

ii) surgical

General Management

- Assessment of general condition of the patient, the amount of blood loss and degree of hypoxemia
- Vital parameters should be recorded
- 100 % oxygen by face mask should be given
- 2 large bore iv cannula should be secured

- Blood should be sent for cross matching, CBC, RFT
- Cyrstalloids and colloids should be rushed in the mean time. It enhances the critical filling and improves the cardiac output. 250 – 500 ml of either a crystalloid or a colloid is administered over a period of 10 – 20 minutes as the urgency indicates. Cyrstalloids are preferred over colloids as they quickly become distributed throughout the extracellular space, they are cheap, easily available and there is no risk of anaphylaxis
- Replace blood by blood
- Invasive hemodynamic monitoring by CVP measurement
- BT, CT should be measured and when it is prolonged FFP and cryoprecipitate should be given
- The **Non-Pneumatic Anti-Shock Garment (NASG)** is a low-technology first-aid device used to treat hypovolemic shock. It's efficacy for reducing maternal deaths due to obstetrical hemorrhage is being researched. When in shock, the brain, heart and lungs are deprived of oxygen because blood accumulates in the lower abdomen and legs. The NASG reverses shock by returning blood to the heart, lungs and brain. This restores the woman's consciousness, pulse and blood pressure. Additionally, the NASG decreases bleeding from the parts of the body compressed under it.

Medical management

UTEROTONICS

i) **Oxytocin –** 10 units im / iv followed by 20 units iv infusion in 500 ml RL / NS

ii) **Methylergometrine –** 0.2 mg im / iv repeated for every 15 minutes to a maximum of 5 doses

iii) **15 methyl PG $F2_{\alpha}$ -** 250 µgm im repeated every 15 minutes to a maximum of 8 doses

iv) **Misoprostol –** 400 - 1000 µgm vaginal, oral, rectal

v) **Recombinant factor VII_a –** 60 – 120 µgm / kg iv

vi) **Tranexamic acid** – 1gm iv 8^{th} hourly

- Oxytocin stimulates the upper segment of the myometrium to contract rhythmically, which constricts the blood vessels and reduces blood flow through the uterus (**Dreyfus M et al., 2004**). Produces rhythmic uterine contractions, can stimulate the gravid uterus, and has vasopressive and antidiuretic effects. Can be used to control postpartum bleeding or hemorrhage. Some suggest its prophylactic use in the third stage of labor; one study of 1000 deliveries revealed a 32% reduction in the rate of PPH. **Pierre F, Mesnard L, Body G *Eur J Obstet Gynecol Reprod Biol*. 1992**. Side effects – hypotension if given by rapid iv bolus. Water intoxication with larger volumes.

- Methylergometrine – ergot alkaloids cause generalized smooth muscle contraction in which both upper and lower segments of the uterus. Side effects – hypertension, nausea, vomiting, headache.
- Syntometrine – 5 units oxytocin + 0.5 mg ergometrine.
- 15 methyl PG $F2_{\alpha}$ - enhances uterine contractility and causes vasoconstriction. It has been shown to control PPH in upto 81% of patients. Side effects – nausea, vomiting, diarrhea, hypertension, headache, flushing, pyrexia. Contraindications – hypersensitivity, bronchial asthma.
- Misoprostol – it increases uterine tone. Side effects – hyperpyrexia, diarrhea, shivering.
- Recombinant factor VII_a – it is an enzyme of the serine protease class. It initiates the process of coagulation in conjunction with tissue factor. (**Ahonen et al., 2007)**. It induces haemostasis at the site of vascular injury independent of the presence of factors VIII and IX by forming complexes with exposed tissue factor (TF). Administration of high-dose rFVIIa results in a huge increase in factor VIIa, well above that of the normal physiological levels, leading to faster and greater thrombin generation.
- **Anti fibrinolytics – Tranexamic acid** potentates the blood clotting system and is used to treat and prevent bleeding. The mechanism of action of tranexamic acid is related to its antifibrinolytic effect, which makes this drug potentially very effective in the third stage of labour. During placental delivery, rapid degradation of fibrinogen and fibrin occurs, as well as an

increase in the activation of plasminogen activators and fibrin degradation products due to activation of the fibrinolytic system. This activation can last up to six to 10 hours postpartum, which may cause more haemorrhage. The antifibrinolytic effect of tranexamic acid in the third stage of labour could make it a safe and effective alternative or adjunct to other regimens currently used in the third stage of labour for prevention of PPH. Tranexamic acid could reduce blood loss associated with complications such as placenta praevia and lower genital tract trauma, as well as bleeding from the upper segment placental site. Therefore, it may be particularly useful in preventing cases of PPH due to factors other than uterine atony, where uterotonics will not be effective. Tranexamic acid is an effective agent for the reduction of blood loss, which has been widely used in various areas of medicine. It is an inhibitor of fibrinolysis that blocks the lysine-binding site of plasminogen to fibrin **(Astedt 1987; Longstaff, 1994)**.

It has been used to decrease blood loss for many years in cases of haemorrhage, and is reported to reduce intraoperative and postoperative blood loss **(Boylan, 1996; Karski, 1995; Katsaros, 1996; Reid, 1997; Vacharaksa, 2002)**.

The side effects described with the use of tranexamic acid include gastrointestinal symptoms such as diarrhoea, nausea and vomiting that occur in about 10% of patients. Rare complications include hypotension, thrombosis, blurred vision, renal cortical necrosis and retinal artery obstruction **(Astedt, 1987)**.

However, another study reported no side effects associated with tranexamic acid **(Bekassy, 1990)**.

A Cochrane review on the use of antifibrinolytics for heavy menstrual bleeding reported no rise in side effects with tranexamic acid in comparison to placebo, NSAIDS, oral luteal phase progestagens or ethamsylate **(Lethaby, 2000)**.

There are concerns about the risk of thromboembolic events associated with the use of tranexamic acid; however, there are no data available from randomised controlled trials (RCTs) which record the frequency of thromboembolic events **(Lethaby, 2000)** as the fibrinolytic system gets activated after placental delivery and in menorrhagia, antifibrinolytics are useful in treating PPH and DUB.

Single dose of 1 gm of tranexamic acid given intravenously reduces the mean blood loss within 2 hours of delivery (**Pili ferrer et al., 2009)**.

Tranexamic acid significantly reduces the mean blood loss by 92 ml compared to no treatment (**Gohel et al., 2007)**.

Tranexamic acid reduces blood loss without any side effects or complications like thrombosis (**Gai et al., 2004)**.

When tranexamic acid is used the need for additional uterotonic drugs is reduced (**Gakhan Yildirim et al., 2011)**.

Tranexamic acid given at a dose of 10 mg / kg iv immediately after delivery of baby, reduces blood loss **(Astedt et al., 1987)**.

Tranexamic acid acts immediately after iv administration **(Jurema et al., 2008)**.

Use of tranexamic acid could potentially have prevented some PPH cases, as reported in the Cochrane review in treatment of PPH (**Mousa 2007)**

Tranexamic acid is associated with a significant reduction in objective measurement of heavy menstrual bleeding when compared to placebo or other medical therapies **(Lethaby et al., 2000)**.

Tranexamic acid is a cost effective drug. A study on total hip arthroplasty reported saving blood transfusion and money in cases where Tranexamic acid was used prophylactically prior to surgery **(Johansson, 2005)**.

Blood loss of greater than 400 ml is not reported when Tranexamic acid is used during vaginal birth **(Yang et al., 2001)**.

Tranexamic acid is used safely and effectively to reduce bleeding resulting from caesarean section **(Gai et al., 2004)**.

Tranexamic acid statistically reduces the extent of bleeding from placental delivery to 2 hrs post partum during caesarean section and its use was not associated any side effects **(Ming - Ying Gai et al., 2003)**.

Tranexamic acid reduces blood loss and maternal morbidity in ongoing PPH **(Anne – Sophie Ducloy et al., 2011)**.

Tranexamic acid significantly reduces the amount of blood loss during and after caesarean section **(Patel Purvi et al., 2007)**.

Tranexamic acid reduces post partum blood loss after vaginal birth and after caesarean section **(Novikova N. et al., 2010)**.

Tranexamic acid can be given antenatally by oral route for one week to treat women with history of recurrent abruption – to get successful neonatal outcome **(B Astedt et al., 1978)**.

Prophylactic tranexamic acid before surgery reduces allogenic blood transfusion **(Cochrane database, 2001)**.

Tranexamic acid can be used to decrease bleeding from menorrhagia and conisation of cervix **(Dunn CJ et al., 1999)**.

Tranexamic acid reduces mean blood loss after oral surgery in patients with hemophilia and it is effective as a mouth wash in dental patients receiving oral anti coagulants **(Mairangi Bay et al., 1999)**.

Tranexamic acid when given with in 3 hrs of trauma, mortality is reduced in trauma patients **(Russel L Gruen et al., 2010)**.

Tranexamic acid is an effective and safe option in DUB and operative interference is reduced **(Kriplani A. et al., 2006)**.

If bleeding persists even after removal of retained products of conception in missed abortion and secondary PPH, a fibrinolytic inhibitor such as tranexamic acid can be given to counteract fibrinolysis in uterus (**J Bonner et al., 2011)**.

Using tranexamic acid before caesarean section may reduce the blood loss as well. Use of tranexamic acid for preventing PPH may contribute to

reduction in blood product use, which is associated with multiple risks (transfusion reactions, transmission of blood-borne viruses), is expensive and may be not available when it is needed. In South Africa, most of the maternal deaths due to PPH occur in level one hospitals which do not have emergency access to formal blood transfusion services.

WOMAN Trial

The WOMAN Trial (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind placebo controlled trial. This is an ongoing trial. The results of which are expected in February 2015.

Haleema Shakur[1*], **Diana Elbourne**[4], **Metin Gülmezoglu**[2], **Zarko Alfirevic**[3], **Carine Ronsmans**[5], **Elizabeth Allen**[4] and **Ian Roberts**[1]

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This trial is a large, pragmatic, randomised, double blind, placebo controlled trial among 15,000 women with a clinical diagnosis of postpartum haemorrhage. All legally adult women with clinically diagnosed postpartum haemorrhage following vaginal delivery of a baby or caesarean section are eligible. The fundamental eligibility criterion is the responsible clinician's 'uncertainty' as to whether or not to use an antifibrinolytic agent in a particular woman with postpartum haemorrhage. Treatment entails a dose of tranexamic acid (1 gram by intravenous injection) or placebo (sodium chloride 0.9%) given as soon as possible after randomisation. A second dose may be given if after 30 minutes bleeding continues, or if it stops and restarts within 24 hours after the first dose.

Cost savings could also be gained from avoiding the use of expensive haematological agents such as Factor VIIa, which is establishing its place in the treatment of massive PPH in modern obstetrics despite the extreme cost **(Welsh, 2008)**.

SURGICAL MANAGEMENT

- Bimanual compression
- Uterine balloon tamponade
- Compression sutures
- Arterial ligation
- Aortic clamping
- Total / subtotal hysterectomy

A patient who fails to respond to uterotonic agents and continues to bleed will quickly become haemodynamically unstable and develop a cascade of clotting abnormalities. The spectre of maternal mortality can then only be prevented by initiating surgical haemostasis sooner rather than later. The nature, timing and extent of these invasive interventions will depend on the sophistication of the health facility which handles this medical crisis. The fate of such a woman will therefore vary widely, depending not only on where she lives in the world but also on where she lives in her own country.

INTERVENTIONAL RADIOLOGY

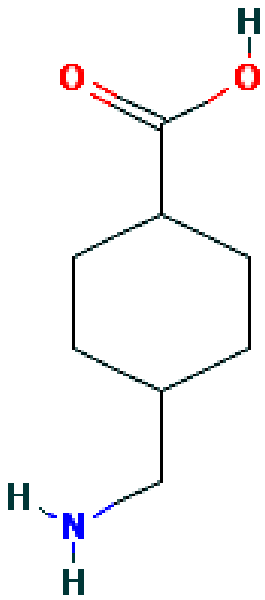
- Consider on stable patient with continued bleeding (**Clinical textbook of obstetric and gynaecology 2010)**.
- Evidence is equivocal (**Greentop guidelines 2009)**.

Pelvic arterial embolsisation is a minimally invasive life-saving therapy that preserves patient quality of life and speeds recovery for patients with PPH.

PHARMACOLOGY OF TRANEXAMIC ACID

Tranexamic acid is an antifibrinolytic drug. It is a synthetic derivative of the amino acid lysine that exerts its anti fibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules.

CHEMICAL STRUCTURE



Molecular formula : $C_8H_{15}NO_2$

It is a trans-4 aminomethyl cyclohexane 1-carboxylate

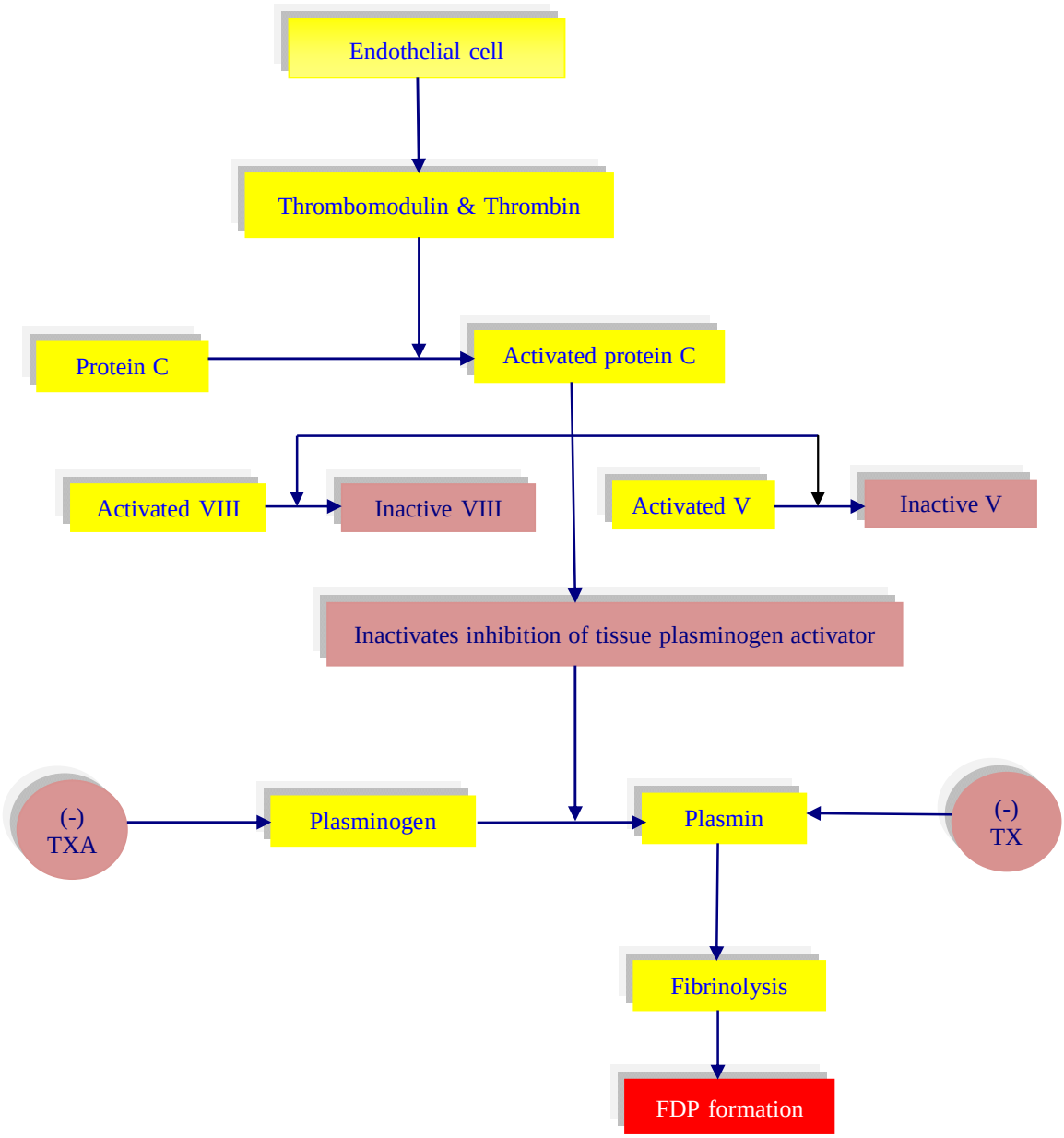
Molecular weight : 157.21

Melting point : 300^{o}c

Water solubility : 1 gm / 6 ml

Pharmacodynamics

Fibrin is the basic framework for clot formation to maintain haemostasis. This clot has to be lysed after a particular period of time by fibrinolysis by the following way.



Tranexamic acid acts as an antifibrinolytic agent by the following 2 ways:

1. Reversible, competitive blockage of lysine binding sites on plasminogen, so that plasminogen activator cannot bind with plasminogen at lower doses.
2. Non competitive inhibition of proteolytic action of plasmin similar to EACA. 8-10 times more potent than EACA as it binds strongly with both strong and weak receptors.

At therapeutic concentration (1mg/ml) it will not cause platelet aggregation.

Pharmacokinetics

- Oral absorption is 30-50%. It is not affected by food
- 100 % bioavailability with iv administration
- Only 3% is plasma protein (globulin) bound. Remaining binds with plasminogen. It will not bind with serum albumin
- Only 5% will be metabolized in liver. Remaining 95% of the drug will be excreted via urine unchanged
- T ½ is 2- 10 hours. 90% of the drug is excreted in urine within 24 hours of administration. Duration of action in iv route is 7 – 8hrs
- Rapidly enter into joint fluid
- Crosses the placenta and blood brain barrier
- 1% of serum level will be achieved in breast milk.

Indications

This antifibrinolytic agent can be used in all types of bleeding especially coagulopathic bleeding. It can also be used prophylactically before surgical procedures where excess bleeding will be expected.

1. HELLP, DIC, Thrombaesthenia related bleeding
2. Postpartum haemorrhage
3. Dental extraction in haemophilia patients
4. Orthopaedic surgeries like spine surgery and total knee / hip replacement
5. Caesarean section
6. Cardiac surgeries
7. Trans urethral resection of prostate
8. Epistaxis
9. Liver transplantation surgery
10. First line nonhormonal treatment for menorrhagia in DUB / fibroid
11. Hereditary angioneurotic oedema where it decreases the attacks by decreasing plasmin induced complement activation.

Contraindications

1. Previous H/O thromboembolism or active intravascular clotting or patients with inherited or acquired thrombophiliac states.
2. Renal failure
3. Liver failure

4. Patients with defective colour vision
5. Subarachnoid haemorrhage – because cerebral oedema and infarction may occur rarely.

Side effects

1. Nausea, vomiting, diarrhoea – commonest side effect, occurs in > 10% cases
2. Giddiness and hypotension – if given by sudden rapid iv occurs in 1-10% of cases
3. Defective colour vision – if used for long time
4. Thromboembolism – rare
5. Drug allergy – rare

Monitoring

LFT, RFT and colour vision should be checked periodically if used for long time.

Should be used with caution in,

1. Drug allergy patients
2. Renal / liver disease patients
3. Elderly individuals with impaired renal function
4. Pregnancy – as this is a category B drug, Tranexamic acid can be safely used in lactating mothers, because
    - 1% of maternal serum level will be reached in breast milk
    - Only 30-50% absorption occur orally

PREPARATIONS AND DOSAGE

1. Oral - 500 mg tablets available

   - 25 mg / kg thrice daily for one week

2. Intravenous

   - Available preparations contain 100 mg / ml (5ml and 10ml ampoules)
   - Dose – 10 mg /kg either direct slow IV or after diluting with 20 ml of 5% dextrose at a rate not more than 1 ml / min. This loading dose can be followed by 1mg / kg / hour IV infusion or 10 mg / kg – thrice daily IV.
   - It can be mixed with aminoacids, electrolytes or carbohydrate solution but not with blood or solutions having penicillin.

3. Mouthwashes containing tranexamic acid are also available and used for haemophilia patients before and after dental extraction because oral mucosa and saliva are rich in plasminogen activator.

* Dose should be adjusted according to creatinine clearance, creative clearance

50 – 80 ml / min - 50% of total dose

10-50 ml/min - 25% of total dose

< 10 ml / min - 10% of total dose

Storage

Should be stored at 25^{o}C (Room temperature) in a cool, dry place and should be kept away from heat or sunlight.

Drug Interactions

1. Chlorpromazine increases cerebral vasospasm when combined with Tranexamic Acid, so it should not be combined.
2. Factor IX when given along with Tranexamic Acid there will be increased thrombosis risk. So it should not be combined.

MATERIALS AND METHODS

MATERIALS AND METHODS

The subjects of this prospective randomised placebo controlled study were 200 pregnant women who were admitted in the labour ward of Annal Gandhi Memorial Government Hospital – Trichy, in the time period from July 2010 to July 2011.

In all patients detailed history – medical history, obstetric history were taken. Vital parameters checked and basic investigations done. Weight of the patient checked. Detailed general examination and obstetric examination done. Gestational age confirmed by USG. 100 patients were placed in study group and 100 patients were placed in control group. All patients were counselled and informed consent obtained.

Study group received

1. Oxytocin 10 units im within 1 minute of delivery.
2. Inj. Tranexamic acid 10 mg / kg slow direct iv over 5 minutes period at delivery of anterior shoulder.

Control group received

1. Oxytocin 10 units im within 1 minute of delivery.
2. Placebo injection of normal saline 5 ml slow direct iv over 5 minutes period at delivery of anterior shoulder.

Inclusion Criteria

1. Primi and 2nd gravida
2. More than 38 weeks of gestation.
3. spontaneous / induced labour

Exclusion Criteria

Women with risk factors for PPH were not included in this study.

1. Haemoglobin < 8gm%
2. Twin pregnancy
3. Polyhydramnios
4. EFW > 4 kg
5. Previous H/O PPH
6. Fibroid complicating pregnancy
7. Preeclampsia
8. Placenta previa
9. Abruptio placenta
10. Prolonged and obstructed labour
11. Heart disease complicating pregnancy
12. Renal / liver disease patients
13. Patients on anticoagulants
14. Previous H/O thromboembolism
15. Gravidity ≥ 3

Methods

Study group and Control group patients received the injections as above mentioned. In each case the following parameters were noted.

1. Predelivery PR, BP, RR, SpO_2, urine output in ml / hr, Hb gm%, PCV% was noted.
2. Blood loss from delivery of the baby to 2hrs post partum was noted.
3. The Apgar scores was noted
4. Side effects of the drug was noted
5. Post partum PR, BP, RR, SpO_2, urine output in ml / hr, Hb gm%, PCV% was noted
6. Maternal needs for blood transfusion was noted.
7. Maternal outcome till discharge was noted.

Measurement of Blood loss

Immediately after delivery of the baby, when all the liquor was drained, the patient was brought to the edge of the table. The patient was placed over a blood drape, a disposable, conical, graduated plastic collection bag.

The amount of blood collected in the blood drape is measured. Then the patient was given pre-weighed pads, which was weighed 2 hrs postpartum. In our study blood loss was measured by measuring the blood collected in the drape and by weighing the swabs before and after delivery.

Total blood loss (ml) = blood in the drape (ml)
+
(swab weight postdelivery in gms – swab weight predelivery in gms)

After collecting all the data, the data were tabulated in a master chart and analysed. The collected questionnaire from the respondents was analysed by using the Statistical Package for Social Sciences (SPSS) ver 13.0. Using this software frequencies, percentage, mean, Standard Deviation, chi square and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

Standard Deviation

Standard deviation is defined as the square root of the arithmetic mean of the squared deviations of the various items from arithmetic mean.

$$\text{Standard Deviation, } \sigma = \sqrt{\frac{\Sigma d^2}{N}}$$

where,

X - variable

σ - standard deviation

$\bar{X}$ - mean of the variable $X = \frac{X_i}{n}$

d_i - $X - \bar{X}$

Pearson's Correlation Coefficient

$$p = \frac{\Sigma (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\Sigma (x_i - \bar{x})^2 (y_i - \bar{y})^2}}$$

where

p - correlation coefficient

x_i - value of i^{th} item of variable x

$\overline{x}$ - mean of variable x

y_i - value of i^{th} item of variable y

$\overline{y}$ - mean of variable y

Σ - sum

RESULTS AND ANALYSIS

RESULTS AND ANALYSIS

TABLE - 1

AGE

Age in Years	Number of Cases			
	Study Group		Control Group	
	Number	%	Number	%
< 20	06	6%	06	6%
20 – 24	48	48%	52	52%
25 – 29	40	40%	36	26%
≥ 30	06	6%	06	6%
Mean	24.60		24.10	
SD	3.43		3.44	
P	0.5890 (P > 0.05) (NS)			

The mean age of the cases in both the groups doesn't differ significantly.

Majority of the patients (50%) belonged to 20-24 years.

And on an average 6% of the patients belong to <20 and ≥30 years.

FIG. 1

AGE

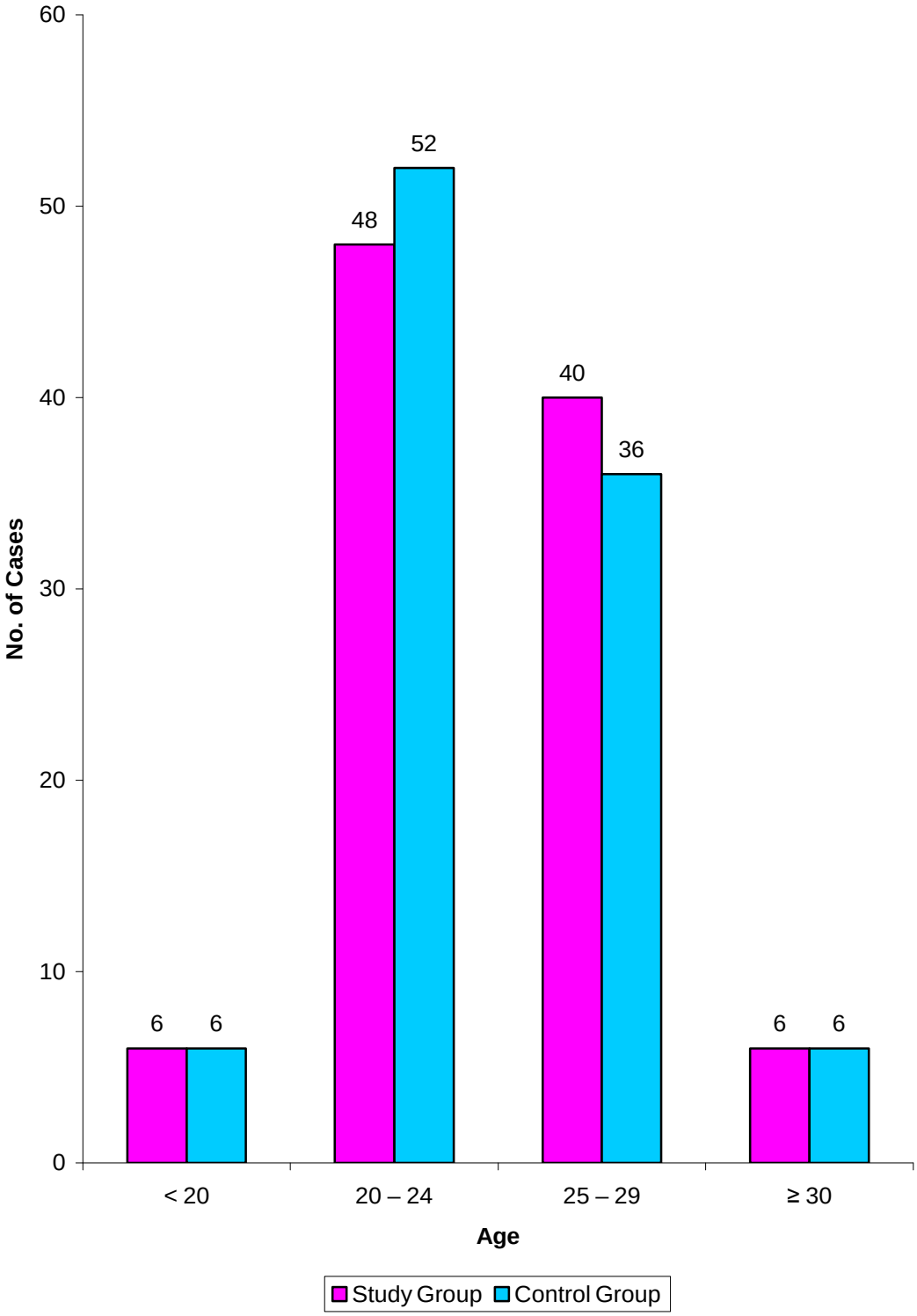

60
50
40
30
20
10
0
No. of Cases
52
48
40
36
6
6
6
6
< 20
20 – 24
25 – 29
≥ 30
Age
Study Group
Control Group

TABLE – 2

SOCIOECONOMIC STATUS

Socioeconomic Status	Number of Cases			
	Study Group		Control Group	
	Number	%	Number	%
V	76	76	72	72
IV	24	24	28	28
S. D.	0.503		0.441	
P	0.410 (NS)			

In our study no patient belonged to the class I, II or III socioeconomic status.

Majority of the patients were under the class V socioeconomic status.

And there was no significant difference between the groups.

FIG. 2

SOCIOECONOMIC STATUS

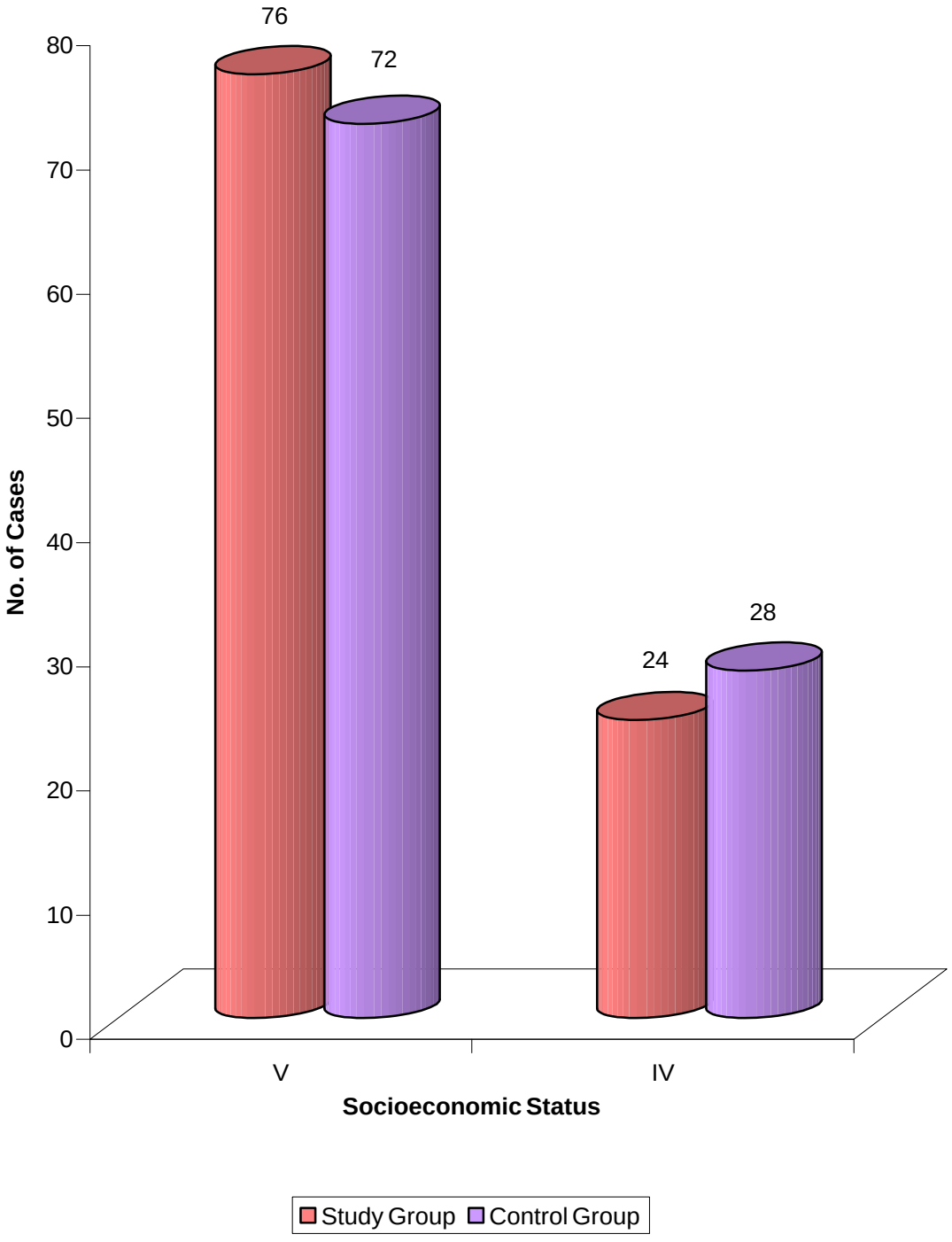


TABLE – 3

OBSTETRIC FORMULA

Obstetric formula	**Number of Cases**			
	Study Group		**Control Group**	
	Number	**%**	**Number**	**%**
Primi	20	20	30	30
2nd gravida	80	80	70	70
SD	0.435			
P	0.718 (NS)			

20 patients in study group and 30 patients in control group were primi gravida.

80 patients in study group and 70 patients in control group were 2nd gravida.

Parity index was comparable in both the groups.

FIG. 3

OBSTETRIC FORMULA

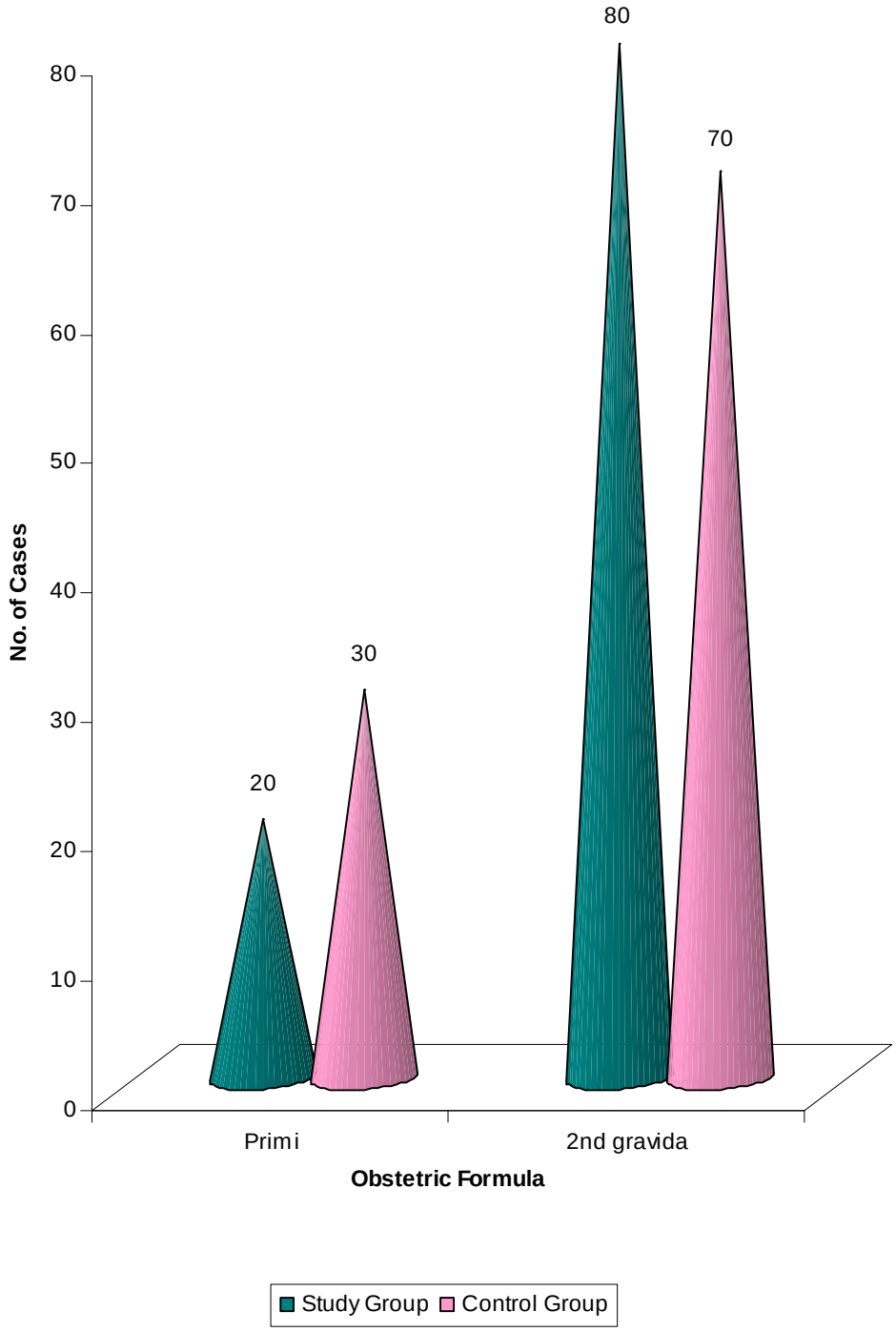


TABLE – 4

BOOKING STATUS

Booking Status	Number of Cases			
	Study Group		Control Group	
	Number	%	Number	%
Booked	80	80	84	84
Unbooked	20	20	16	16
SD	0.412		0.419	
P	0.603 (NS)			

Antenatal booking doesn't differ in both the groups significantly.

20% of the patients in study group and 16% of the patients were unbooked.

FIG. 4

BOOKING STATUS

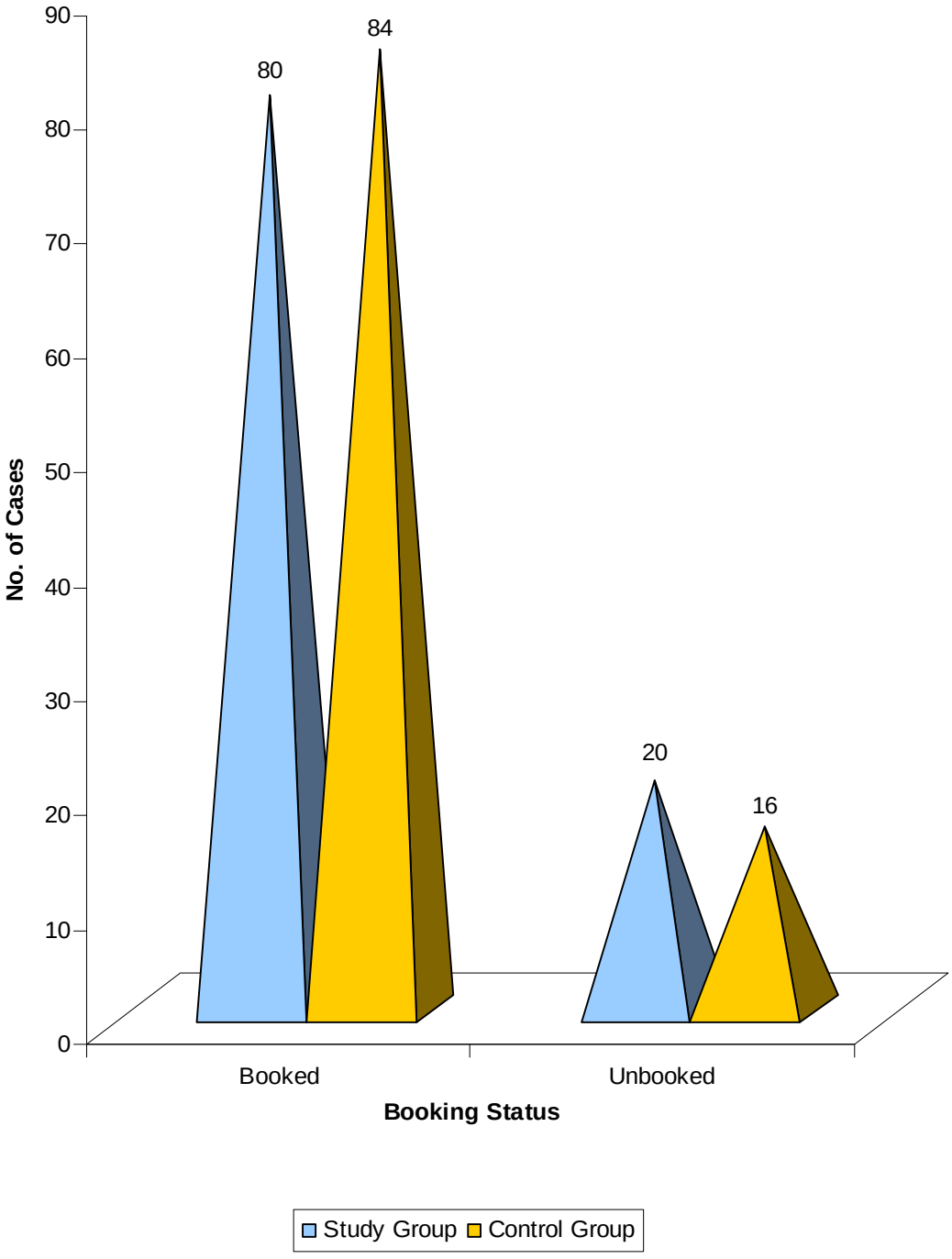


TABLE – 5

SUBJECTIVE CHARACTERS

Subjective characters	Study group		Control group		P
	Mean	S.D.	Mean	S.D.	
Weight (kgs)	55.18	1.71	55.16	1.69	0.219*
Height (cms)	154.12	1.78	153.80	1.71	0.436*
BMI	23.23	0.63	23.32	0.63	0.299*

* (P > 0.05) (NS)

The average weight was 55.18kg in the study group and 55.16kg in the control group.

The average height was 154.12cm in the study group and 153.80cm in the control group.

The average BMI was 23.23kg/m^2 in the study group and 23.32kg/m^2 in the control group.

Subjective characters were comparable between the two groups.

FFIG. 5

SUBJECTIVE CHARACTERS

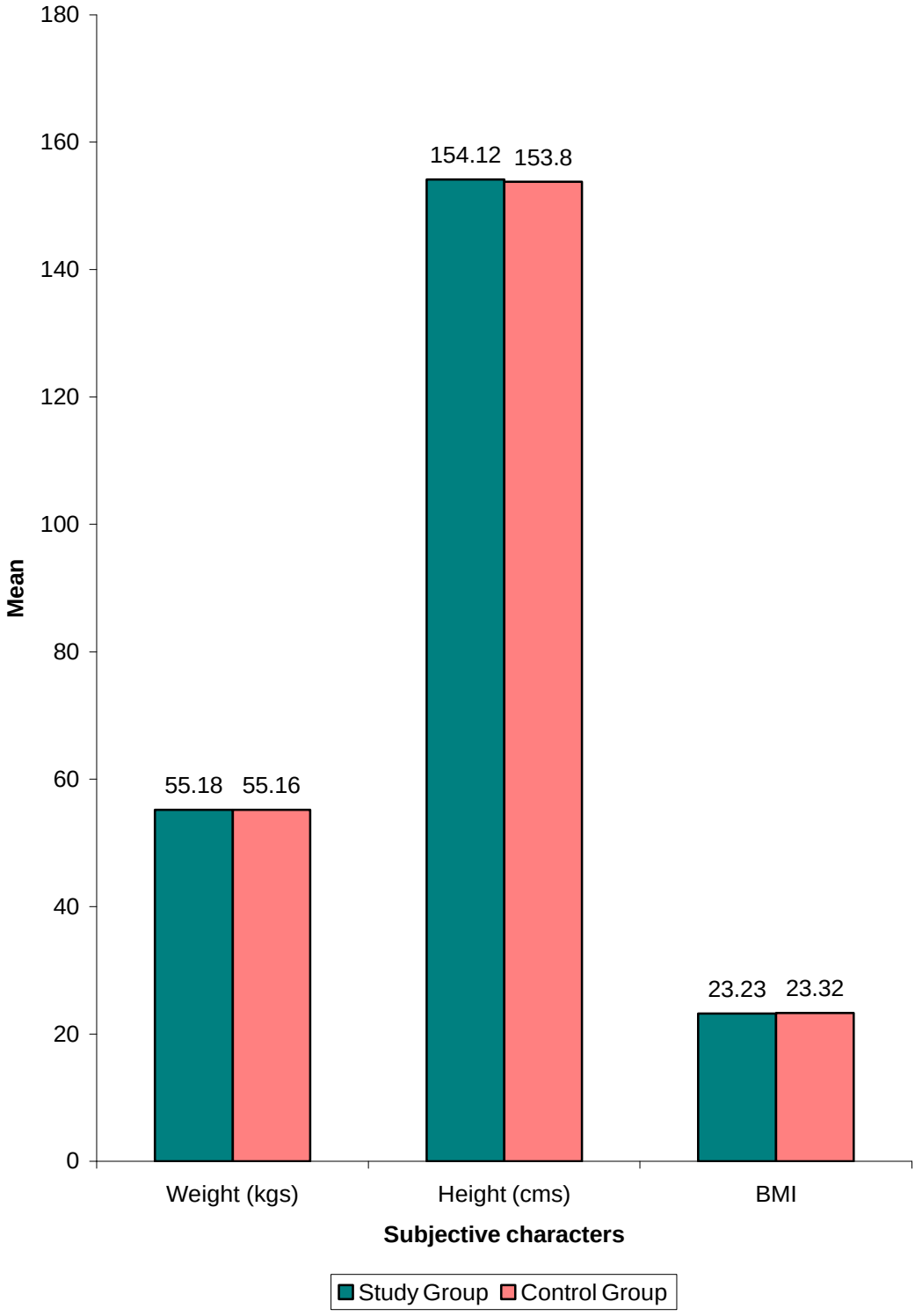


TABLE – 6

CHANGES IN VITAL PARAMETERS

Parameters	Number of cases				P
	Study group		Control group		
	Mean	S.D.	Mean	S.D.	
PULSE RATE / MIN					
Pre delivery	82.38	2.79	82.86	2.60	
Post delivery	83.86	2.64	88.24	2.61	0.0001 (S)
Change	+1.48		+5.38		
SYSTOLIC BP MM HG					
Pre delivery	117.52	5.65	108.68	5.61	
Post delivery	116.40	5.34	104.92	5.29	0.0001 (S)
Change	-1.12		-3.76		
DIASTOLIC BP MM HG					
Pre delivery	76.80	8.87	76.92	8.47	
Post delivery	76.34	8.78	73.64	8.88	0.0001 (S)
Change	-0.46		-3.28		
RESPIRATORY RATE / MIN					
Pre delivery	17.93	0.30	17.80	0.31	
Post delivery	18.14	0.98	18.06	1.07	0.147(NS)
Change	-0.21		-0.26		
SPO_2 %					
Pre delivery	99.90	12.09	99.90	10.13	
Post delivery	99.66	11.94	98.79	9.64	0.0001 (S)
Change	-0.24		-1.11		
URINE O/P ML / HR					
Pre delivery	108.10	2.02	109.70	2.12	
Post delivery	106.90	1.97	106.50	1.86	0.167(NS)
Change	-1.20		-3.20		

Mean increase in pulse rate was 1.48/min in study group and 5.38/min in control group.

Mean fall in systolic BP was 1.12mmHg in study group and 3.76mmHg in control group.

Mean fall in diastolic BP was 0.46mmHg in study group and 3.28mmHg in control group.

Mean increase in respiratory rate was 0.21/min in study group and 0.26/min in control group.

Mean fall in spO_2 was 0.24% in study group and 1.11% in control group.

Mean fall in urine o/p was 1.20ml/min in study group and 3.20ml/min in control group.

PR increases and BP decreases significantly in control group compared with that of study group.

And the post delivery spO_2 was better in the study group.

FIG. 6

CHANGES IN VITAL PARAMETERS

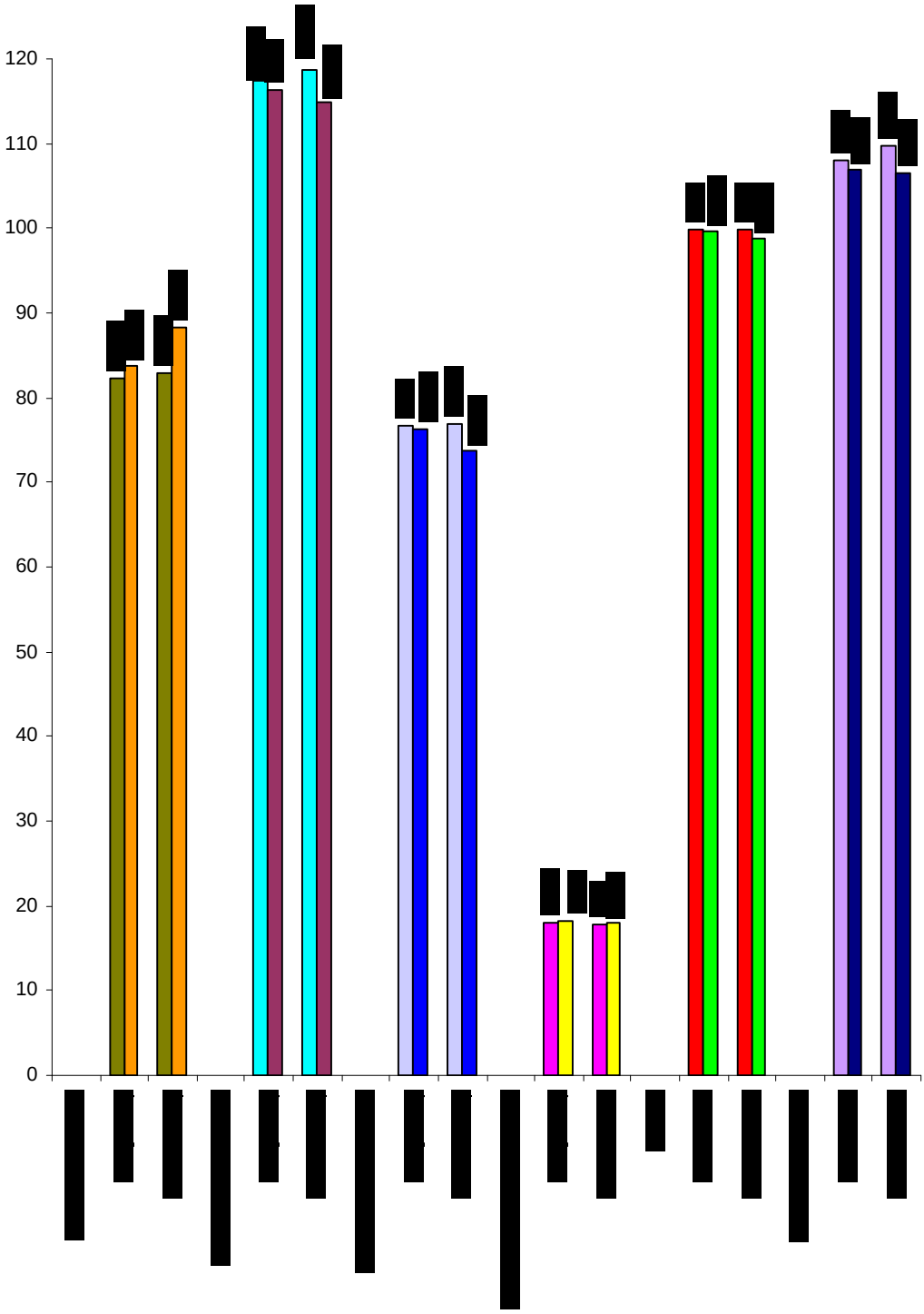


TABLE – 7

CHANGES IN BLOOD INDICES

Blood indices	Study group		Control group		P
	Mean	S. D	Mean	S. D	
HB GM %					
Pre delivery	8.86	1.78	8.88	1.93	
Post delivery	8.84	1.77	8.73	1.91	0.0001(S)
Change	-0.02		-0.15		
PCV %					
Pre delivery	39.04	7.04	38.72	4.56	
Post delivery	38.70	7.01	37.62	4.53	0.0001(S)
Change	-0.34		-1.10		

Mean fall in haemoglobin was 0.02gm% in study group and 0.15gm% in control group.

Mean fall in hematocrit was 0.34% in study group and 1.10% in control group.

The post delivery haemoglobin and hematocrit was significantly reduced in the control group compared to the study group.

Fig. 7

CHANGES IN BLOOD INDICES

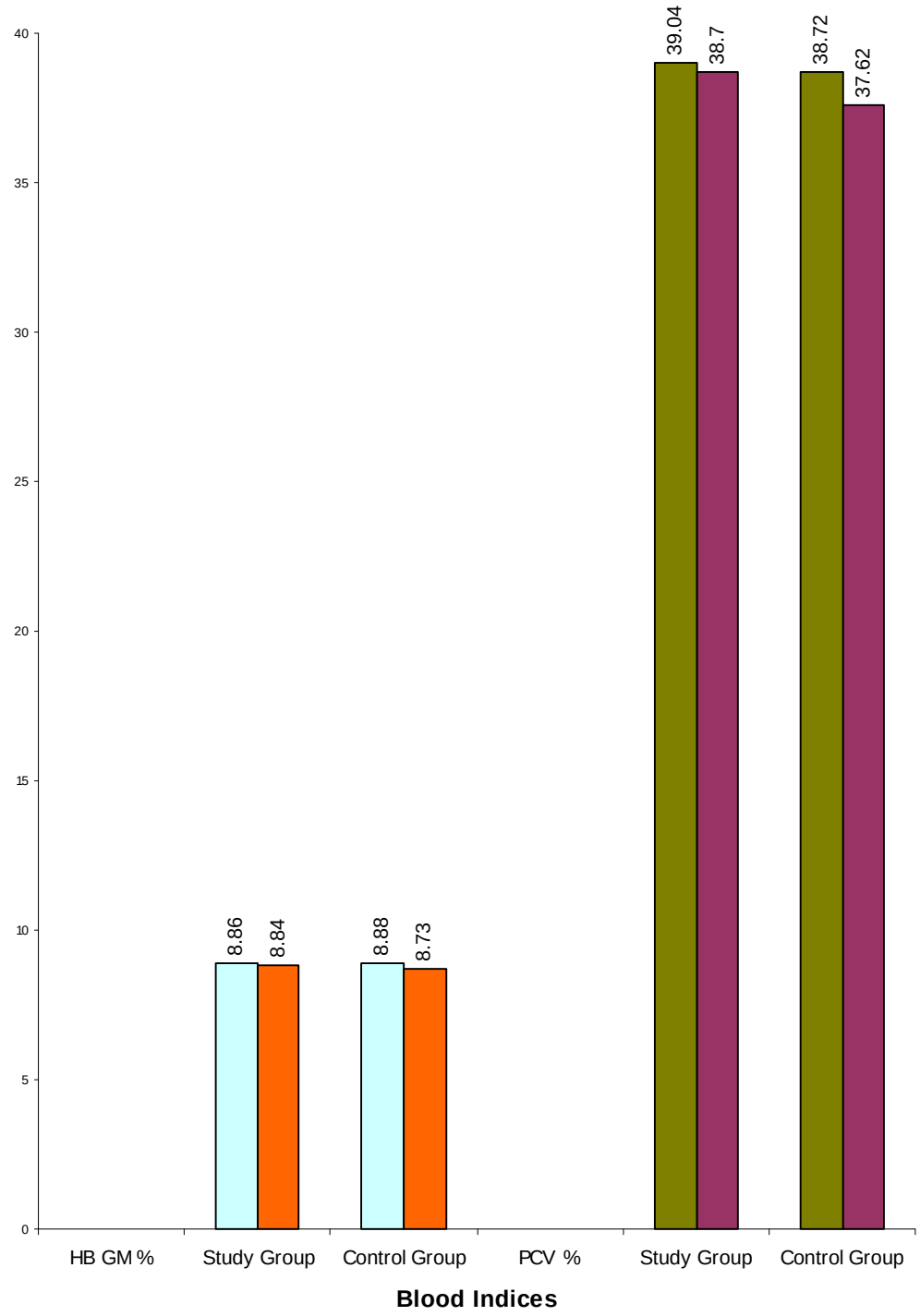


TABLE – 8

ONSET OF LABOUR

Onset of labour	**Number of cases**			
	Study group		**Control group**	
	Number	**%**	**Number**	**%**
Spontaneous	52	52	56	56
Induced	48	48	44	44
SD	1.432		1.889	
P	0.413 (NS)			

Majority of the patients (54%) had spontaneous onset of labour.

And there was no significant difference between the groups.

FIG. 8

ONSET OF LABOUR

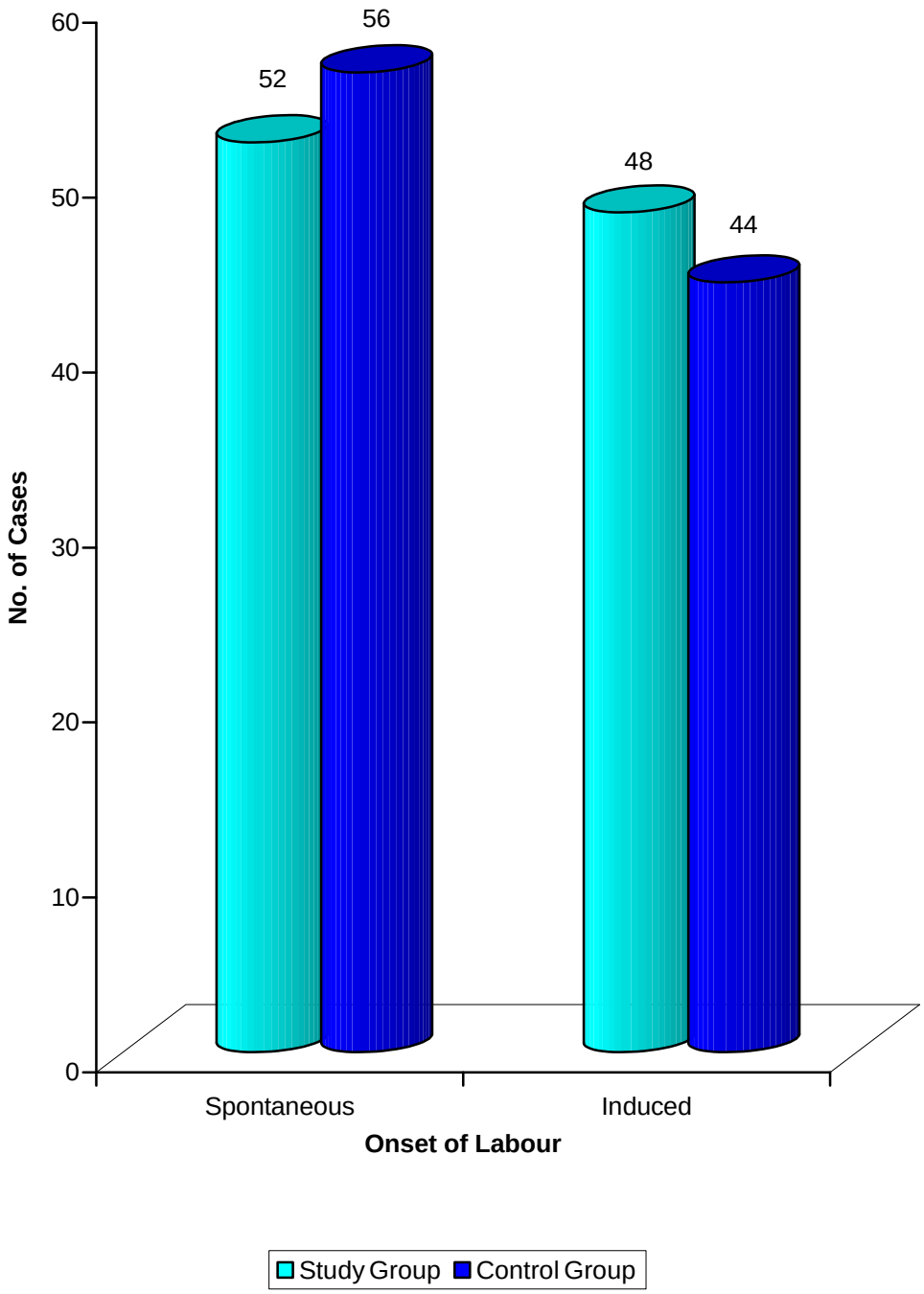


TABLE – 9

MODE OF DELIVERY

Mode of delivery	Number of cases			
	Study group		Control group	
	Number	%	Number	%
Labour natural	72	72	60	60
Labour natural with episiotomy	22	22	36	36
Labour natural with lacerated perineum	06	06	04	04
SD	2.705		2.998	
P	0.631 (NS)			

Majority of the patients (66%) had labour natural.

And there was no significant difference between the groups.

FIG. 9

MODE OF DELIVERY

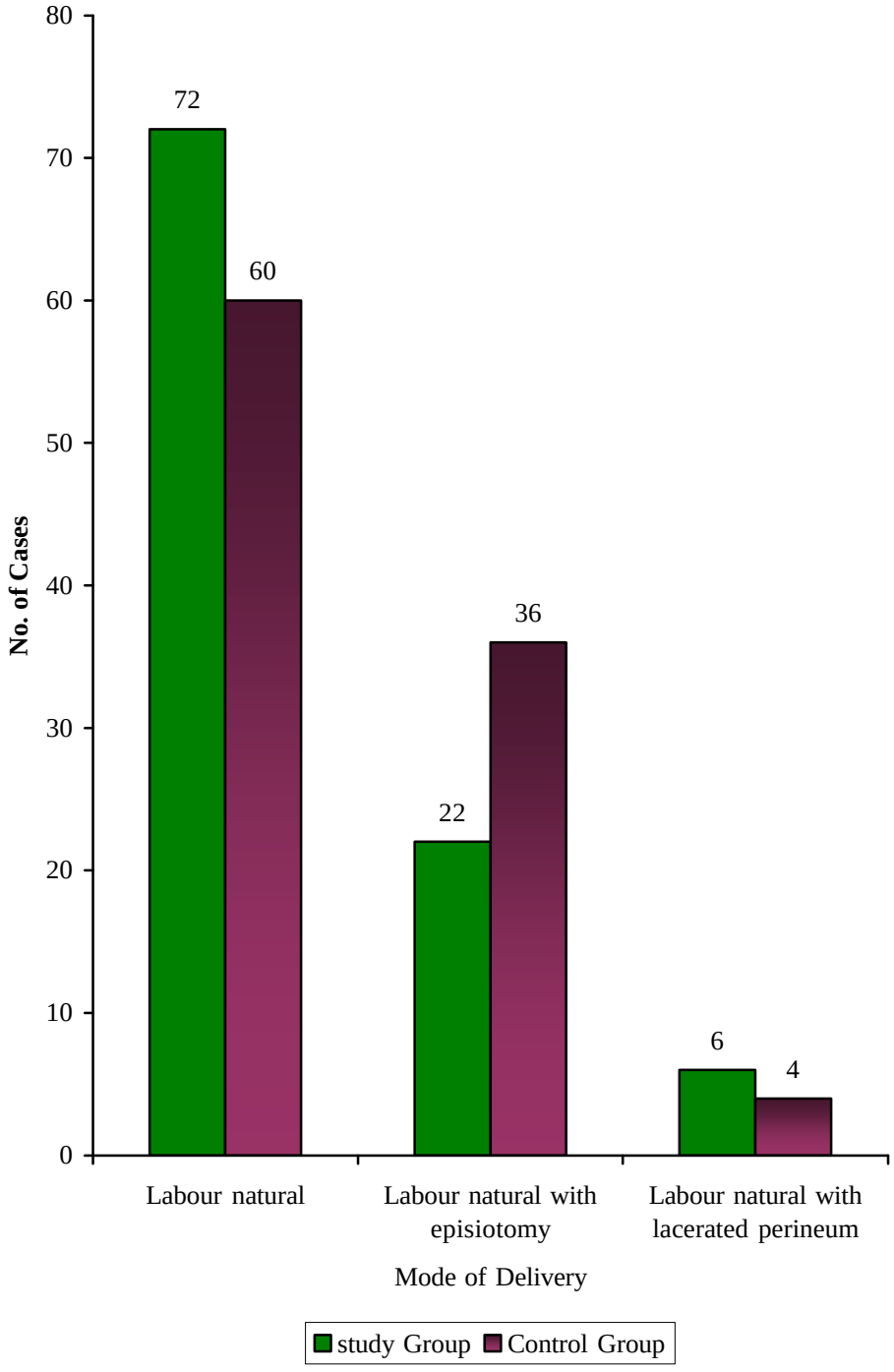


TABLE – 10

CHANGES IN DURATION OF THIRD STAGE

Duration of 3rd stage in minutes	**Study group**	**Control group**
Mean	4.6	4.48
S.D.	1.428	1.854
P	0.141 (NS)	

The mean duration of 3rd stage was 4.6mins in the study group and 4.48mins in the control group.

There was no influence of the drug in the duration of 3rd stage.

FIG. 10

CHANGES IN DURATION OF THIRD STAGE

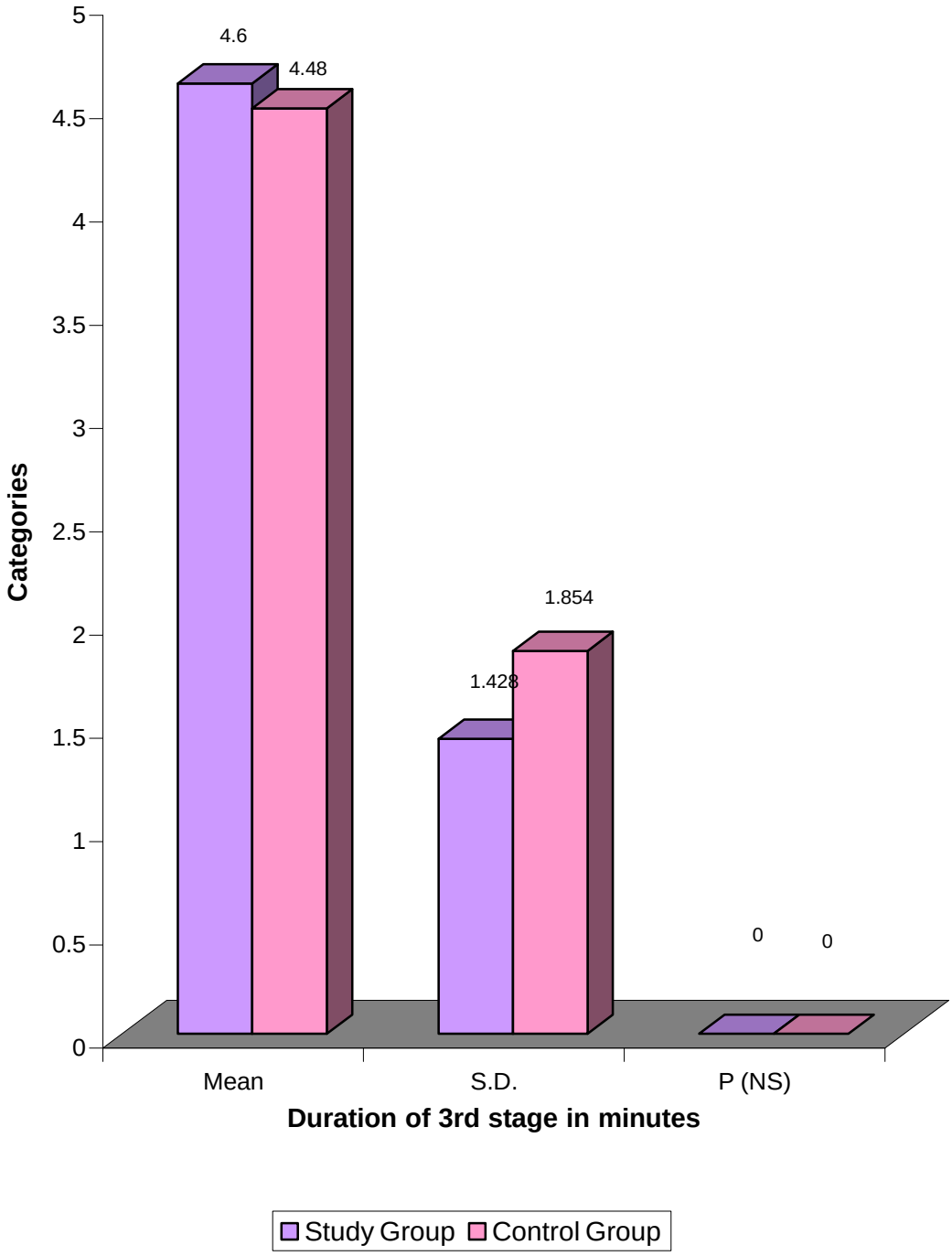


TABLE – 11

BLOOD LOSS

Blood loss in ml	Study group		Control group		P
	Mean	S.D.	Mean	S.D.	
Time of delivery to 30 mins	81.01	50.387	191.65	49.884	0.0001(S)
30 mins to 2 hrs	27.27	6.17	51.72	9.78	0.0001(S)
Time of delivery to 2 hrs	108.27	58.570	247.37	58.070	0.0001(S)

The mean blood loss at the end of 2 hrs was 108.27 ml in study group and 247.37 ml in the control group.

The blood was significantly low in the study group compared to the control group during all periods.

FIG. 11

BLOOD LOSS

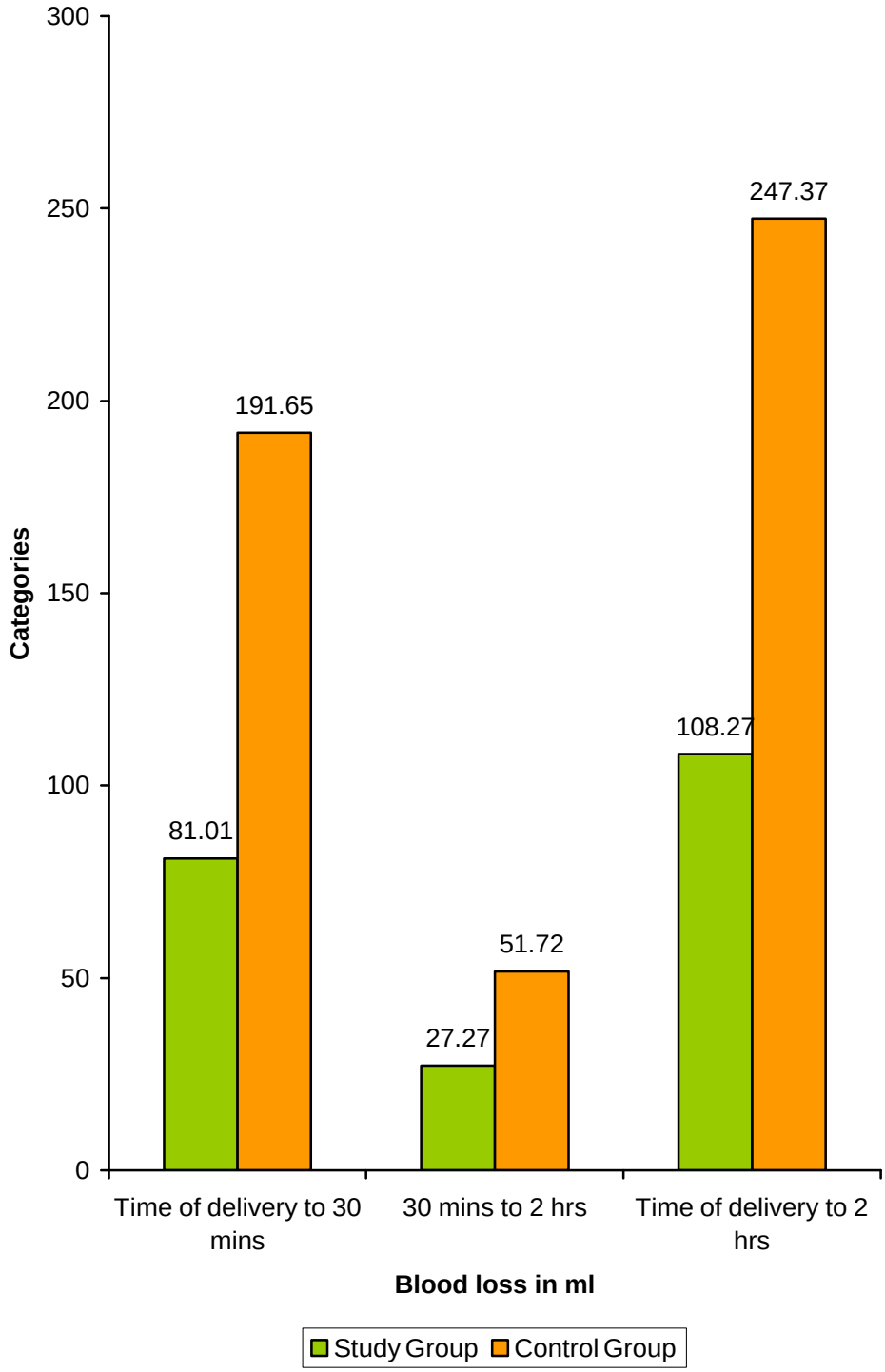


TABLE – 12

ADDITIONAL UTEROTONICS

Additional uterotonics	Study group		Control group	
	Number	%	Number	%
Yes	2	2	22	22
No	98	98	78	78
P	0.002			

22% of the patients in the control group needed additional uterotonics compared to only 2% in the study group.

There was a significant difference in the requirement of uterotonics between the groups.

2 patients in the study group needed additional uterotonics (carboprost and methergin) and both needed blood transfusion.

22 patients in the control group needed additional uterotonics, of which 10 had PPH and other 12 had mild atonicity.

All the 22 patients were given 250 μg carboprost – PGF2α im.

8 patients responded to carboprost.

14 patients needed injection methergin 0.2 mg IV, of which 4 responded and 10 needed per rectal misoprostol 800 μg and blood transfusion.

FIG. 12

ADDITIONAL UTEROTONICS

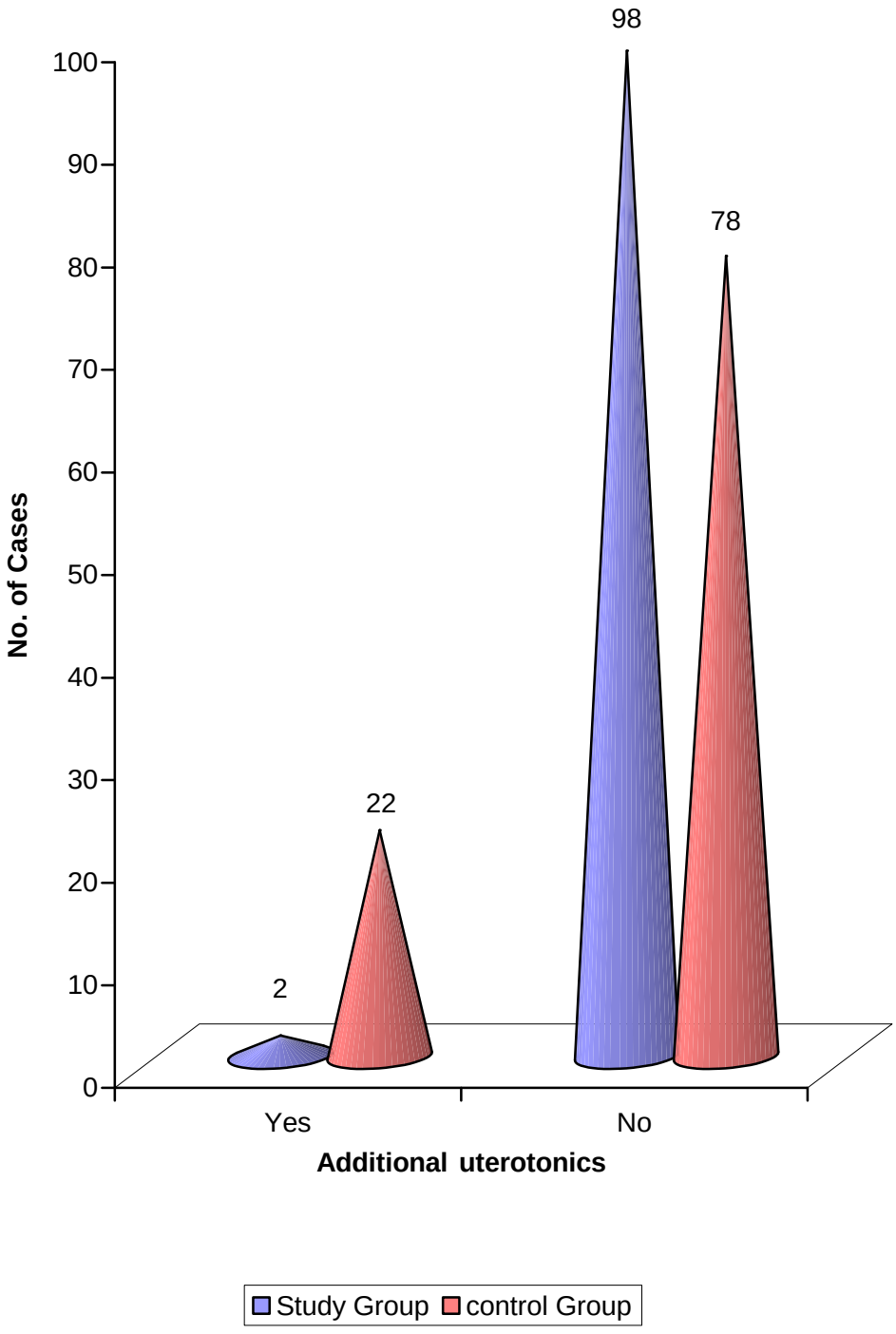


TABLE – 13

MATERNAL BLOOD TRANSFUSION

Blood transfusion	**Study group**		**Control group**	
	Number	**%**	**Number**	**%**
Yes	02	02	10	10
No	98	98	90	90
Chi-Square Value	0.092		0.207	
P	0.0102 (S)			

10% of the patients in the control group needed blood transfusion compared to 2% in the study group.

There was a significant difference in the need for blood transfusion between the groups.

FIG. 13

MATERNAL BLOOD TRANSFUSION

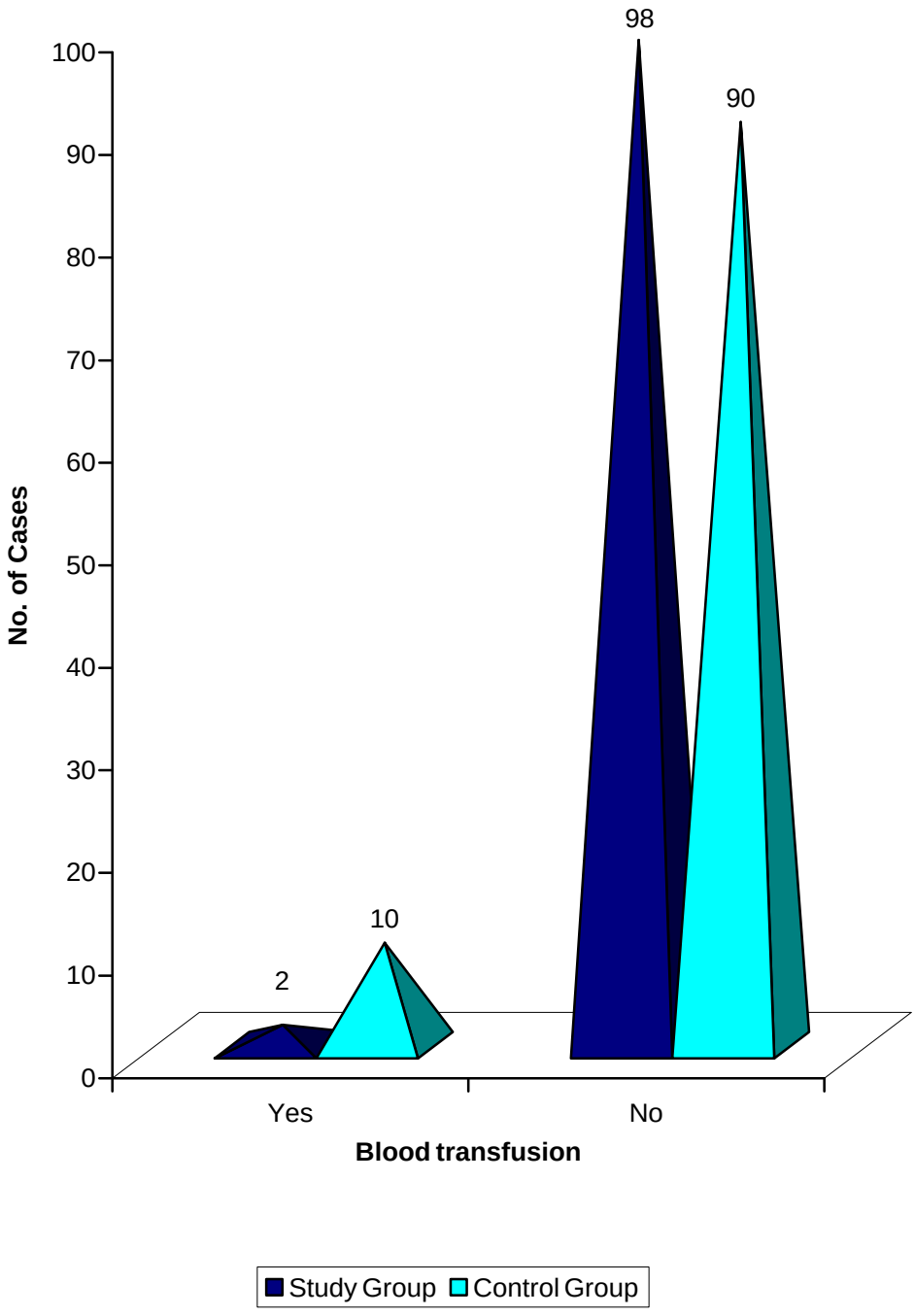


TABLE – 14

MATERNAL COMPLICATIONS

Complications	Study group		Control group	
	Number	**%**	**Number**	**%**
Vomiting	6	6	6	6
Fever	4	4	6	6
Nil	90	90	88	88
Chi-Square Value	0.211		0.213	
P	0.41 (NS)			

There was no significant difference in maternal complications between the groups.

FIG. 14

MATERNAL COMPLICATIONS

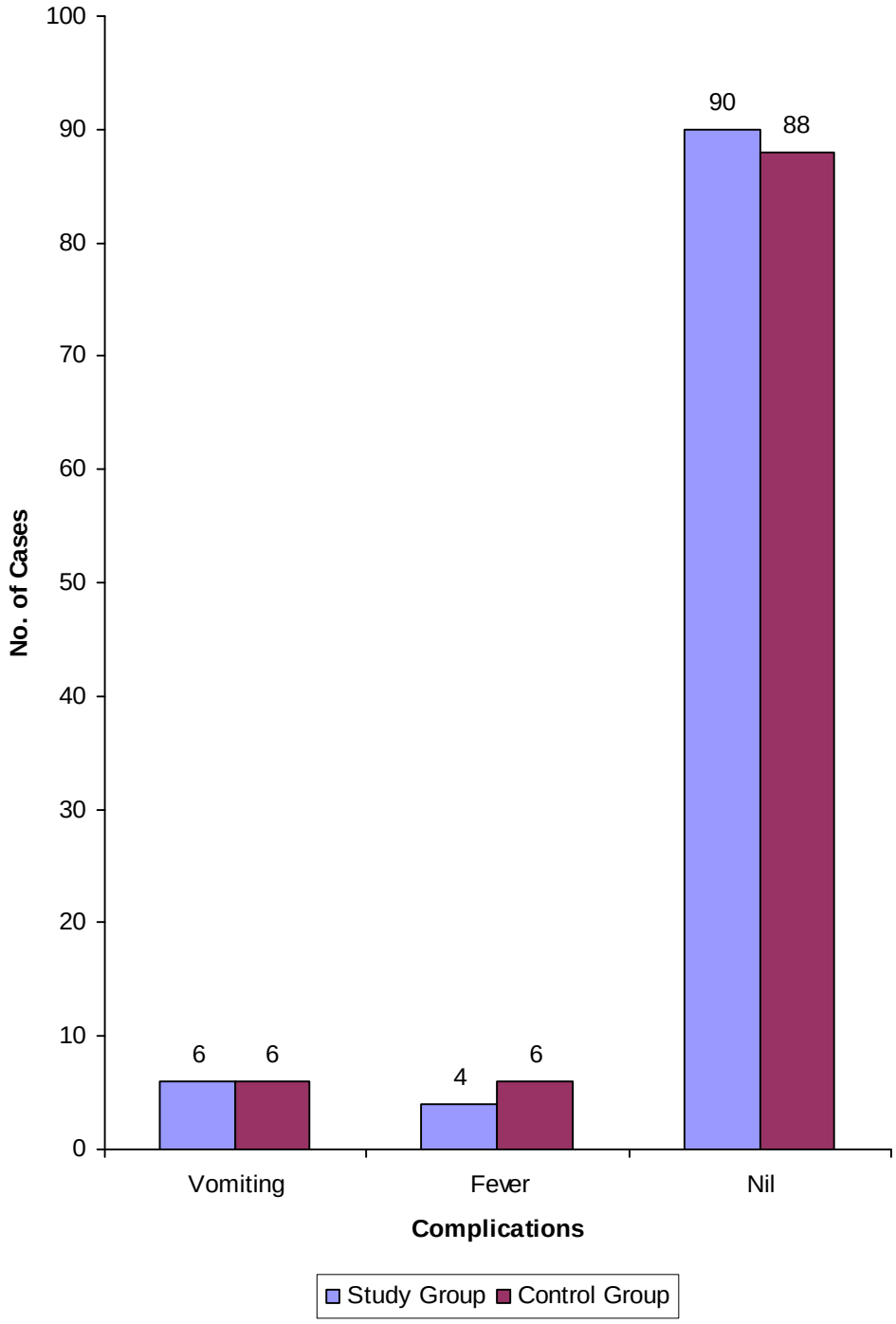


TABLE – 15

APGAR SCORES

Apgar scores	**Study group**		**Control group**	
	Number	**%**	**Number**	**%**
≥ 8 / 10	96	96	94	94
< 8 / 10	04	04	06	06
Chi-Square	0.211		0.212	
P	0.500 (NS)			

The apgar scores was not found to be influenced by the use of the drug.

There was no statistical difference between the groups.

FIG. 15

APGAR SCORES

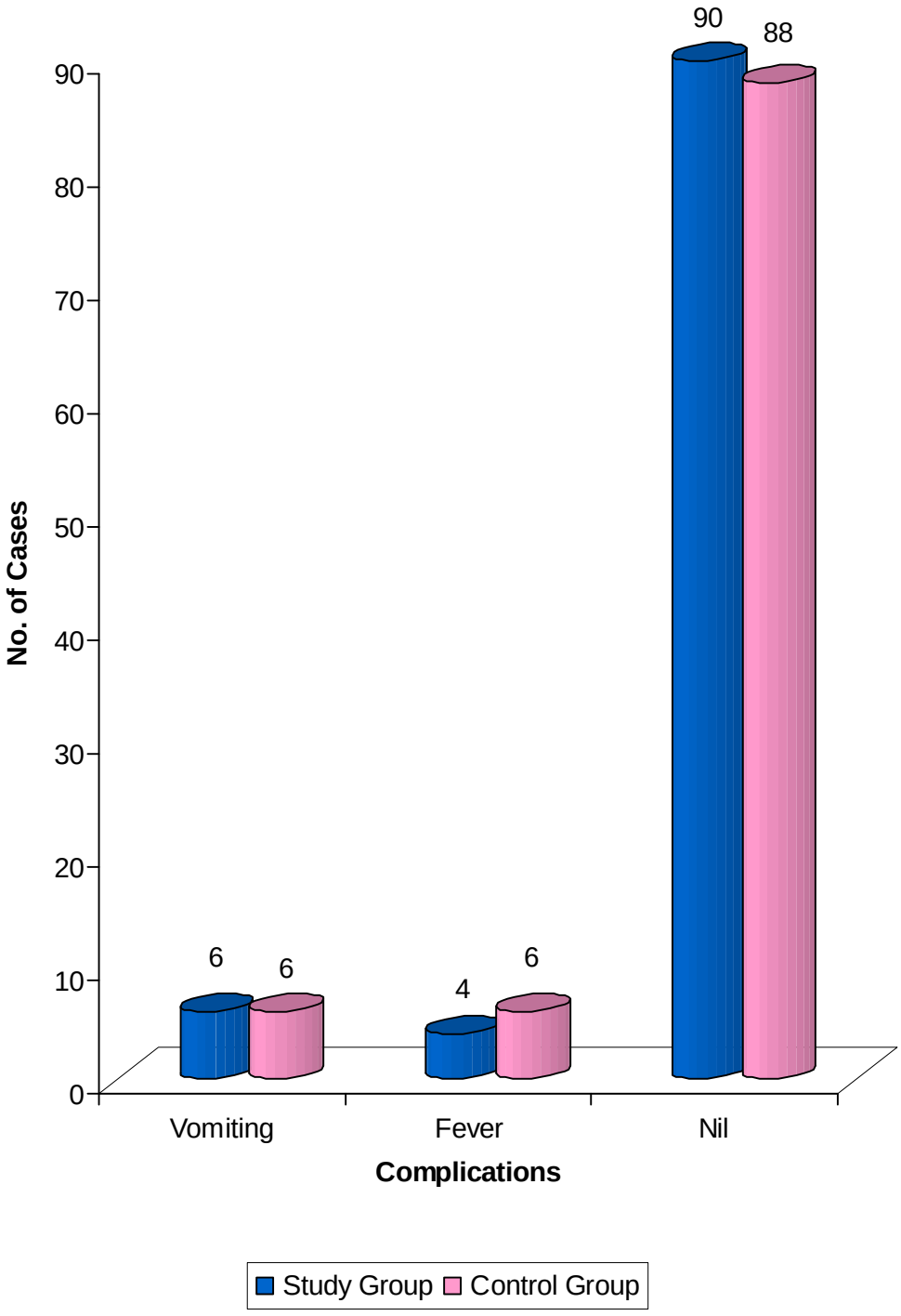


TABLE – 16

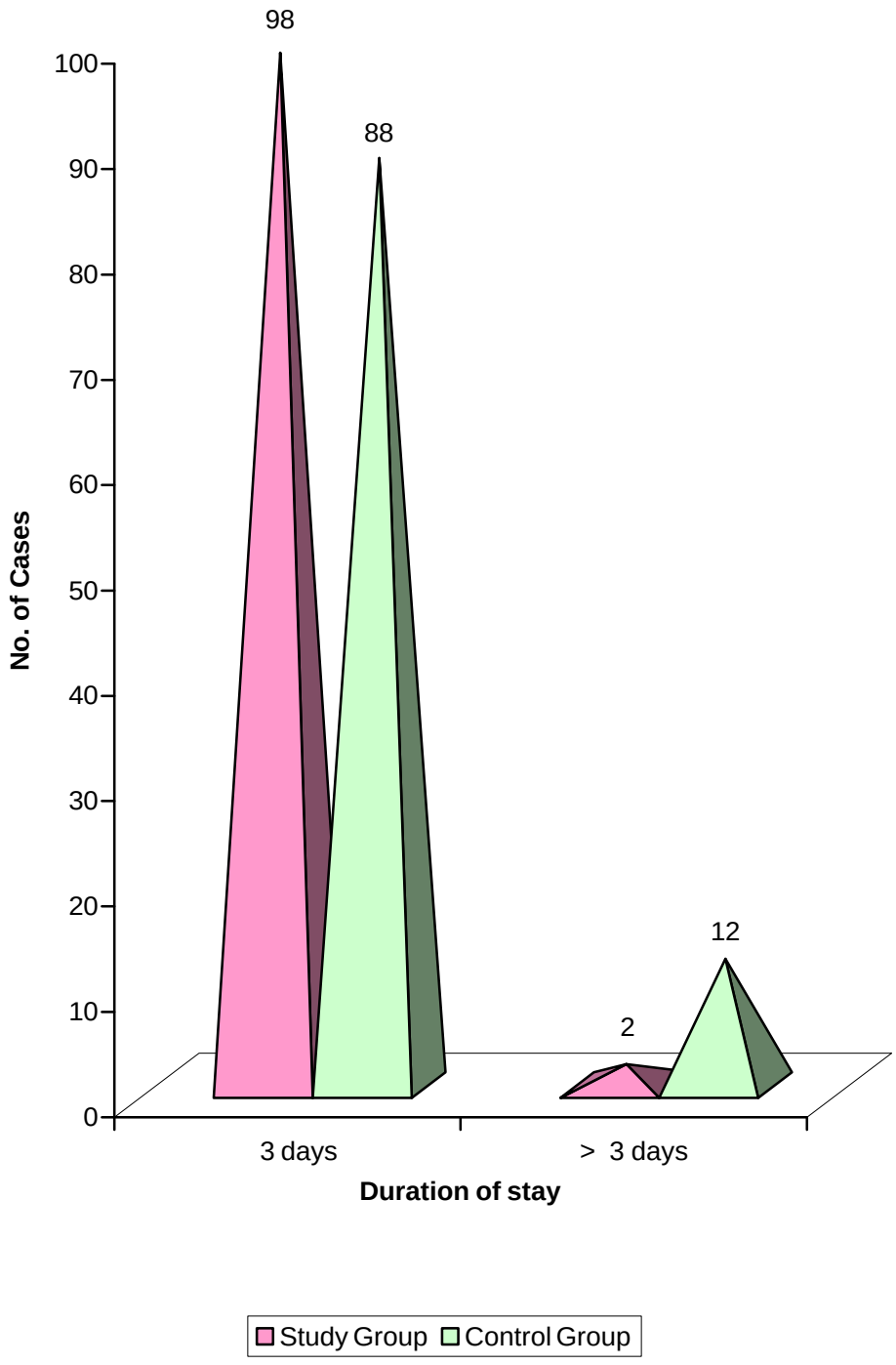
DURATION OF STAY

Duration of stay	**Study group**		**Control group**	
	Number	**%**	**Number**	**%**
≤ 3 days	98	98	88	88
> 3 days	02	02	12	12
Chi-square	1.895		2.022	
P	0.041 (S)			

12% of the patients in the control group had to stay for more than 3 days compared to 2% in the study group.

FIG. 16

DURATION OF STAY



DISCUSSION

DISCUSSION

As obstetric blood loss contributes to one fourth of global maternal death, death resulting from PPH should be avoided. As the fibrinolytic system gets activated after placental delivery antifibrinolytic agents can be used to reduce obstetric blood loss.

As prevention is always better than cure regarding PPH- an antifibrinolytic agent tranexamic acid was used prophylactically in our study to observe its efficacy in reducing blood loss during and after vaginal birth.

1. Maternal age

In our study, the age group of patients included varied from 18 to 35 years. Maximum percentage of patients belong to the age group of 20-24 years. 48% of study group and 52% control group were between 20-24 years. In a study conducted by Yang H, Shi C-Department of Obst & Gynaecology, first teaching hospital of Beijing University, Beijing, China in 2001 october - the mean age was 23.5 years.

2. Socio economic status

In our study 76% of study group and 72% of control group belonged to class V socioeconomic status. 24% of the study group and 28% of the control group belonged to class IV socioeconomic status**.** In a study conducted by the department of obstetrics and gynaecology – Ayub medical college, Pakistan, by Shamshad Bibi et al in 2009, 74% in the study group and 76% in the control group belonged to class V socioeconomic status.

3. Obstetric formula

In our study, second gravida were more in both groups than primigravida. All were Singleton pregnancies. In the study group 20% were Primigravidas and 80% were 2^{nd} gravidas. In the control group 30% were Primigravidas and 70% were 2^{nd} gravidas. In a similar study conducted by Yildrium M.D at Erzincan military hospital, Turkey in april 2011 - second gravidas were 72% and primigravidas were 28%.

4. Booking status

In our study, 80% of study group and 84% of Control group were booked. 20% of study group and 16% of control group were unbooked. In a similar study conducted by Panagiotis and Rezan from Department of Obstetrics and Gynaecology, London in march 2011, 86% of study group and 88% of control group were booked. Proper antenatal care is important to identify the high risk factors in the antenatal period itself and to correct them thereby reducing the incidence of PPH.

5. Subjective characters

In our study mean height was 154.12 cm in study group and 153.80 cm in control group. Mean weight was 55.18 kg in study group and 55.16 kg in control group. Mean BMI was 23.23kg/m^2 in study group and 23.32kg/m^2 in control group. In a similar study conducted by Shanghai International Pence maternity and child health hospital, Shanghai, China – mean height was 153 cm and mean weight was 62 kg.

6. Change in Vital parameters

In our study, mean post delivery increase in PR was 1.48 in study group and 5.38 in control group. Mean fall in SBP was 1.12 in study group and 3.76 in control group. Mean fall in DBP was 0.46 in study group and 3.28 in control group. Mean increase in RR was 0.21 in group A and 0.26 in group B. mean fall in spO2 was 0.24% in the study group and 1.11% in the control group. Mean fall in urine output was 1.20ml in the study group and 3.20ml in the control group and was not statistically significant. There was a significant fall in SBP and rise in PR without any significant change in RR. In a similar study conducted by Natalia Novikova et al in 2010, there was a statistically significant change in vital parameters.

7. Changes in blood indices

In our study statistically significant fall in Hb% occurred after delivery in control group than with study group. Mean fall of Hb% was 0.02gm% in study group and 0.15gm% in control group. Mean fall in hematocrit was 0.34% in the study group and 1.10% in the control group. In a study conducted in the Department of obstetrics and gynaecology, University of Manitoba, 2010, statistically significant drop in haemoglobin was observed in the control group.

8. Onset of labour

In our study 48% in study group had induced labour and 44% in control group had induced labour. Both the groups were comparable.

9. Mode of delivery

In our study 72% in the study group and 60% in the control group had a labour natural, 22% in the study group and 36% in the control group had labour natural with episiotomy, 6% in the study group and 4% in the control group had lacerated perineum. Both the groups were comparable in al three modes of delivery.

10. Changes in duration of 3rd stage of labour

The mean duration of third stage was 4.6mins in the study group and 4.48 mins in the control group. There was no statistical difference between the groups. Duration of third stage is not altered on adding the drug.

11. Blood loss

In our study, there was a statistically significant reduction of blood loss in both periods, that is from time of delivery to 30 mins and also from 30 mins to 2 hrs postpartum. Mean blood loss from time of delivery to 30 mins was 81.01 ml in study group and was 191.65 ml in control group. Mean blood loss from 30 mins to 2 hour post partum was 27.27 ml in study group and 51.72 ml in control group. Mean total blood loss was 108.27 ml in study group and 247.37 ml in control group. In a study conducted at the Centre Hospitalier Regional Universitaire, France in 2010, the mean total blood loss in the study group was 120ml compared to 232.45ml in the control group.

12. Additional uterotonics

In our study, 22% of the patients in the control group needed additional uterotonics compared to only 2% in the study group. The drug significantly decreases the need for additional uterotonics. In a study conducted by Leila Shekhavat et al 2009, Department of obstetrics and gynaecology, Shahid Sedughi Hospital / Shahid Sedughi University of medical sciences and health services, Yazd, Iran – only 4% in the study group needed additional uterotonics.

13. Maternal blood transfusion

In our study, only 2% in the study group compared to 10% in the control group needed blood transfusion. This result was also observed in a similar study conducted by the Division of Obstetrics and gynaecology, University of Oslo, Norway in 2009.

14. Maternal complications

In our study, 6 patients in study group and 6 patients in control group had vomiting which may be related to the drug. But this incidence of vomiting in study group was not statistically significant. 4 patients in study group and 6 patients in control group had fever. 3 of the study group patients with fever had LRI and was treated with antibiotics and discharged on 5^{th} PND. Among 6 patients, who had fever in control group 4 had LRI and 2 had breast engorgement as their babies was admitted in NICU. None of the patients in both groups had thromboembolic complications postnatally.

15. Apgar scores

In our study, the apgar scores were comparable in both groups. 3 babies in study group needed NICU admission for HIE stage I. 4 babies in group B needed NICU admission for HIE Stage I and two babies had sepsis. The inference was that tranexamic acid use was not associated with any impact on neonatal outcome in our study. In a similar study conducted by Department of Obs & Gyn King's College hospital, London, there was no significant difference in the Apgar scores between study and control groups.

16. Duration of stay

2 patients in the study group had to stay for more than 3 days as they were anemic and needed blood transfusion and parenteral iron. 10 patients in the control group were anemic and were transfused blood and given parenteral iron. And 2 more patients in the control group were not discharged as they had fever with breast engorgement.

SUMMARY

SUMMARY

- This study was conducted in the Department of Obstetrics and Gynaecology, Annal Gandhi Memorial Government Hospital, Trichy to clinically observe the blood loss reduced by tranexamic acid during normal labour.
- 200 patients were selected for the study, 100 as study group and 100 as Control group.
- 50% of the cases belonged to the age group 20 – 24 years.
- 74% of the cases belonged to class V socioeconomic status.
- 25% of the cases were primigravida and 75% of the cases were 2^{nd} gravida.
- 82% of the cases were booked cases.
- There was no statistically significant difference in the subjective characters in between the two groups.
- There was statistically significant fall in blood pressure and rise in PR without any significant change in RR in the control group compare to the study group.
- Hb level and hematocrit was significantly reduced in the control group compared to the study group.
- Tranexamic acid significantly reduced the blood loss from the time of delivery to 2 hour post partum.

- The need for additional uterotonics and maternal blood transfusion is significantly reduced in the study group compared to the control group.
- The incidence of vomiting, shivering, fever were statistically insignificant.
- None of the patients in both the groups had thromboembolic complications postnatally.
- The apgar scores and neonatal outcome was similar in both the groups.
- The duration of stay was found to be reduced in the study group when compared to the control group.

CONCLUSION

CONCLUSION

Tranexamic acid injection, an antifibrinolytic agent when given prophylactically at the delivery of the anterior shoulder, by intravenous route appears to reduce the blood loss during normal labour effectively. Some studies demonstrated that tranexamic acid minimally increases the risk of thromboembolism but without statistical significance which was not observed in our study. So, further studies are also needed to support its efficacy.

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BIBLIOGRAPHY

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ANNEXURES

INFORMATION SHEET FOR THE PATIENT AND HER REPRESENTATIVE(S)

We welcome you and thank you for your keen interest in participation in this research project. Before you participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomforts, the precautions and the informations about how the project will be carried out. It is important that you read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are free to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

1. Project title

Role of tranexamic acid in reducing blood loss in normal labour.

2. Department and institute

Department of obstetrics and gynaecology, K.A.P. VISWANATHAN GOVERNMENT MEDICAL COLLEGE, TRICHY

3. Name of the investigator

Dr. B. Sowmya

4. What is the purpose of this project / study?

To compare the efficiency of tranexamic acid and oxytocin with only oxytocin in reducing the amount of bleeding after delivery.

5. What is the selection procedure of participants?

Inclusion Criteria: Primi and 2nd gravid, More than 38 weeks of gestation, spontaneous / induced labour

Exclusion Criteria: Haemoglobin < 8gm%**,** Twin pregnancy**,** Polyhydramnios, EFW > 4 kg**,** Previous H/O PPH**,** Fibroid complicating pregnancy**,** Preeclampsia, Placenta previa, Abruptio placenta, Prolonged and obstructed labour**,** Heart disease complicating pregnancy**,** Renal / liver disease patients**,** Patients on anticoagulants, Previous H/O thromboembolism, Gravidity ≥ 3.

6. What is the procedure of the study?

Both the study group and the control group will be placed on a calibrated obstetric drape during the delivery. The Study group will receive Oxytocin 10 units im within 1 minute of delivery and Inj. Tranexamic acid 10 mg / kg slow direct iv over 5 minutes period at delivery of anterior shoulder. and the control group will receive Oxytocin 10 units im within 1minute of delivery and Placebo injection of normal saline 5 ml slow direct iv over 5 minutes period at delivery of anterior shoulder. Predelivery vital parameters will be noted. Pre-weighed pads will be given to the participants. And it has to be returned to the investigator immediately 2 hrs after delivery. These pads will be weighed immediately to assess the amount of blood loss. And the total amount of blood loss will by adding the blood in the drape and in the pads. Post- delivery vital parameters will be noted. Side effects of the drug if any will be noted.

7. What are the responsibilities of the participants?

The patients will be given the drug immediately after delivery. The participants are expected to use only the pre-weighed diapers given by the investigator and hand over the soiled diapers immediately 2 hrs after delivery.

8. What are the expected risks for the participants?

Tranexamic acid is NOT a new drug and it is widely used to reduce bleeding in conditions such as major heart surgery. There is no conclusive evidence of serious side effects with short term use. But the study treatment may cause clots where they are not needed and, because the drug is not routinely used after childbirth, we do not know all the likely side effects. According to the studies which are previously done, expected risks are very minimal, like shivering, vomiting and giddiness.

9. What are the expected benefits of the study to the participants?

The amount of blood loss will be reduced. Hence the need for blood transfusion will be reduced. The participant will not suffer from anemia during the post partum period. The duration of stay in the hospital is also reduced.

10. Will the participant be compensated for participation in this trial?

No

11. Whether any participation in this study be kept confidential?

Yes

12. Can I withdraw from the study at any time during the study period?

Yes

13. If there is any new findings / informations, would I be informed?

Yes

14. What happens in case of a study related injury?

Study related injuries are found to be very minimal

15. Is there any alternative to the treatment mentioned?

Yes they are available. But it is very expensive (recombinant factor VII_a).

16. Are there costs associated with this research study? Will I receive any payments?

This study is done free of cost to the participant, however you will not receive compensation of any kind for your participation in this research.

For any study related queries, you are free to contact.

Name of the contact person with official address: Dr. B.Sowmya, junior resident, department of obstetrics and gynaecology, K.A.P. VISWANATHAN GOVERNMENT MEDICAL COLLEGE, TRICHY.

Place: Trichy Signature of the investigator :

Date : Witness :

CONSENT FORM FOR THE PATIENT

1. I confirm that I have read and understood the information sheet for the study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that sections of my medical notes and those of my baby/ies may be looked at by responsible individuals involved in the study. I give permission for these individuals to have access to these records.
4. I give permission for my personal doctor to be given information about my participation in this trail.
5. I agree to take part in this study.

Name of the patient : Date :

Signature / Thumbprint :

Name of the person taking consent : Date :

Signature :

INVESTIGATOR'S AND/OR ASSOCIATE'S STATEMENT

I have fully explained to _____ [participant / parent / guardian] the nature and purpose of the above-described procedures and the risks involved in its performance. I have answered and will answer all questions to the best of my ability. I will inform the participant of any changes in the procedures or the risks and benefits if any should occur during or after the course of the study.

Date (MM/DD/YEAR) Signature of Investigator or Associate

PROFORMA

Name : Age : IP NO :

Socio Economic Status : I II III IV V

Date of admission :

Obstetric formula : G P L A

Booking status : Booked / Unbooked

Past history :

Obstertric history :

General examination

Height : Weight : BMI :

PR / min : SpO_2 :

BP / mmhg : Urine o/p in ml / hr :

RR / min :

CVS :

RS :

Abdominal examination :

Vaginal examination :

Basic investigations

Urine : albumin - sugar - deposits -

Hb gm% : Urea :

PCV % : Sugar :

LFT : Creatinine :

Blood group :

Onset of labour : Spontaneous Induced

Mode of delivery : LN LN Ĉ EPI LN Ĉ LP

Duration of third stage in minutes :

Blood loss (ml) : Delivery to 30 mins –

: 30 mins to 2 hrs –

: Total blood loss –

Additional uterotonics : YES NO

2 Hrs postpartum

PR / min : SpO_2 :

BP / min : Urine output in ml / hr :

RR / min :

48 hrs postpartum : Hb gm% - PCV % -

Maternal transfusion : YES NO

Maternal complications :

5 min apgar : ≥ 8/10 < 8/10

Date of delivery :

Duration of hospital stay :

MASTER CHART

NAME CODE	AGE	IP NO	SOCIOECONOMI STATUS	PARITY	BOOKING STATUS	PRE DELIVERY							URINE O/P IN ML/HR	HB GM%	PCV%	ONSET OF LABOUR	MODE OF DELIVERY	DURATION OF 3 RD STAGE	TD TO 30 MIN	30 MIN TO 2 HRS	TD TO 2 HRS	POST DELIVERY								MATERNAL BLOOD TRANSFUSION	MATERNAL COMPLICATIONS	APGAR < 8/10	DURATION OF STAY > 3 DAYS
						HT IN CMS	WT IN KGS	BMI	PR/MIN	BP mm hg	RR/MIN	SPO2%										ADDITIONAL UTEROTONICS	PR/MIN	BP MMHG	RR/MIN	SPO2%	URINE O/P IN ML/HR	HB GM%	PCV%				
S1	19	24390	V	PRIMI	UB	152	53	22.93	80	112/70	17	99	100	8.4	36	S	LN Ĉ E	5	72.5	23	95.5	no	82	110/70	20	99	100	8.4	35	no	nil	no	no
S2	20	27589	IV	G2P1L1	B	152	55	23.80	80	120/70	18	100	120	8.8	38	S	LN	5.5	75	24.5	99.5	no	82	120/70	18	100	110	8.8	38	no	nil	no	no
S3	32	28595	V	G2A1	B	154	54	22.76	82	126/76	18	100	100	8.8	38	S	LN Ĉ E	4.36	75	25.5	100.5	no	82	120/70	18	100	100	8.8	38	no	nil	no	no
S4	22	20956	IV	G2P1L1	B	155	53	22.06	84	110/70	18	100	125	8.4	36	S	LN	5.5	75	24.5	99.5	no	86	108/70	18	100	125	8.2	34	no	nil	no	no
S5	25	24435	V	G2P1L1	B	152	54	23.37	82	122/80	18	100	100	9	38	S	LN	6	75	23	98	no	82	120/80	18	100	100	9	38	no	nil	no	no
S6	24	24467	IV	PRIMI	UB	153	55	23.49	82	120/70	17	99	100	8.8	38	I	LN Ĉ E	4.36	75	25	100	no	84	120/70	17	100	100	8.8	38	no	nil	no	no
S7	29	26789	V	G2A1	B	152	53	22.93	74	120/80	18	100	130	8.6	38	S	LN Ĉ LP	5.3	75	24.5	99.5	no	75	120/80	18	100	130	8.6	38	no	nil	no	no
S8	21	34567	V	G2P1L1	B	153	54	23.06	84	110/70	16	100	120	8	36	S	LN	5.23	75	26	101	no	86	110/70	16	100	120	8	34	no	nil	no	no
S9	26	35678	V	PRIMI	B	156	56	23.01	80	110/80	18	100	130	8.8	40	S	LN Ĉ E	4.2	75	26.5	101.5	no	82	110/80	19	100	130	8.8	40	no	nil	yes	no
S10	23	32414	V	G2P1L1	UB	154	53	22.34	82	116/70	19	100	120	9.2	40	I	LN	5.36	75	24.5	99.5	no	82	110/70	19	100	120	9	40	no	vomiting	no	no
S11	28	35643	V	G2P1L1	B	152	56	24.23	84	116/80	17	100	100	9.2	40	S	LN	6	75	23	98	no	84	116/80	17	100	100	9.2	40	no	nil	no	no
S12	24	37843	V	G2P1L1	B	155	55	22.89	86	120/70	18	100	130	8.8	38	S	LN	4.36	75	24	99	no	88	120/70	18	100	130	8.8	38	no	nil	no	no
S13	24	38921	V	PRIMI	UB	158	59	23.63	78	110/70	18	99	100	9.4	42	S	LN Ĉ E	4.35	76	25	101	no	80	110/70	18	100	100	9.4	42	no	nil	no	no
S14	22	39908	V	G2P1L1	UB	152	54	23.37	84	120/80	19	99	125	8.6	36	S	LN	5.25	78	23	101	no	84	120/80	19	99	125	8.6	34	no	nil	no	no
S15	27	34564	V	G2A1	B	154	53	22.34	80	122/80	18	100	100	10	42	I	LN Ĉ E	5.3	74.5	24.5	99	no	82	122/80	17	100	100	10	42	no	nil	no	no
S16	23	45634	V	PRIMI	B	156	57	23.42	82	120/70	19	100	110	9.2	40	S	LN Ĉ LP	4.18	73.5	23	96.5	no	84	120/70	19	100	110	9.2	40	no	nil	no	no
S17	35	47687	V	G2P1L1	B	152	53	22.93	84	112/70	18	100	100	9.1	38	I	LN	4	73	25.5	98.5	no	86	112/70	18	100	100	9	38	no	nil	no	no
S18	21	47854	V	PRIMI	B	156	55	22.6	80	112/70	17	100	125	8.5	37	I	LN Ĉ E	4.21	76	23	99	no	81	110/70	17	100	125	8.5	37	no	nil	no	no
S19	29	46968	V	PRIMI	B	155	54	22.47	80	110/70	18	100	100	9.1	39	S	LN	4.1	75.5	26	101.5	no	81	110/70	17	100	100	9.1	39	no	nil	no	no
S20	20	57897	V	PRIMI	B	159	60	23.73	82	110/70	19	100	130	8.8	39	S	LN Ĉ E	5.35	76	25	101	no	84	110/70	19	100	130	8.8	39	no	nil	no	no
S21	23	18676	V	G2P1L1	B	153	56	23.92	84	112/70	17	100	100	8.8	38	S	LN	5.26	77	25	102	no	84	110/70	17	100	100	8.8	38	no	vomiting	no	no
S22	25	10948	V	G2P1L1	B	152	53	22.93	82	108/70	16	100	120	8.4	36	I	LN	4.2	78	24.5	102.5	no	82	108/70	16	100	120	8.4	36	no	nil	no	no

S23	27	39058	V	G2A1	UB	155	54	22.47	76	110/70	18	100	100	9	39	S	LN Ĉ E	4	73.5	27	100.5	no	78	110/70	18	100	100	9	39	no	nil	no	no
S24	23	39769	V	G2P1L1	B	155	55	22.89	80	128/76	16	100	100	9	40	S	LN	4	74	23	97	no	78	128/78	16	100	90	9	40	no	nil	no	no
S25	24	34567	V	G2P1L1	B	156	57	23.42	80	110/80	18	100	120	9	42	S	LN	4.35	74.5	26.5	101	no	81	110/80	18	100	120	9	42	no	nil	no	no
S26	18	45677	V	G2P1L1	B	153	56	23.92	80	120/80	19	100	100	8.8	39	I	LN	4.37	76.5	25	101.5	no	84	120/80	19	100	100	8.8	39	no	nil	no	no
S27	26	67373	V	G2P1L1	B	155	53	22.06	82	110/70	18	100	100	8.8	40	S	LN	4.1	78	24.5	102.5	no	83	110/70	18	100	100	8.6	38	no	nil	no	no
S28	28	45777	V	PRIMI	UB	153	57	24.34	84	116/70	19	100	130	8.8	42	I	LN Ĉ E	5.3	80	27	107	no	86	116/70	19	100	130	8.8	42	no	nil	no	no
S29	24	12377	V	G2P1L1	B	156	54	22.18	86	114/86	17	100	100	8.8	39	I	LN	5.37	74.5	23	97.5	no	86	114/86	19	100	100	8.8	39	no	fever	no	no
S30	23	59776	V	G2P1L1	B	153	55	23.49	88	110/80	18	100	100	8.8	38	I	LN	3	73	26	99	no	88	110/80	18	100	110	8.8	38	no	nil	no	no
S31	29	58776	V	G2P1L1	B	154	56	23.61	84	120/70	18	100	120	8.6	37	I	LN	4.48	72	27	99	no	85	120/70	18	100	120	8.6	37	no	nil	no	no
S32	25	56788	IV	G2P1L1	B	152	57	24.67	82	110/70	18	99	100	8.6	40	I	LN	4.3	70	25	95	no	84	110/70	18	99	100	8.6	40	no	nil	no	no
S33	25	77676	V	G2P1L1	B	155	57	23.72	80	112/70	18	100	100	9	41	I	LN	4.2	74	23	97	no	82	114/70	18	100	100	8.8	38	no	nil	no	no
S34	22	55678	V	G2P1L1	UB	153	53	22.64	84	110/80	19	100	125	8.2	40	S	LN Ĉ LP	4.2	75	26.5	101.5	no	88	110/80	19	100	125	8.2	40	no	nil	no	no
S35	20	10453	V	G2P1L1	UB	159	58	22.94	80	126/70	18	100	100	8.2	35	S	LN	4.25	76.5	25.5	102	no	82	126/70	18	100	100	8.2	35	no	nil	no	no
S36	27	10457	IV	G2P1L1	B	154	54	22.76	82	110/70	18	100	100	9.2	39	S	LN	4.39	73.5	24.5	98	no	82	110/70	18	100	100	9	39	no	vomiting	no	no
S37	30	10987	IV	G2P1L1	B	156	57	23.42	84	110/80	17	100	130	9.2	42	S	LN	5.3	74.5	26	100.5	no	84	110/80	17	100	130	9.2	42	no	nil	no	no
S38	21	10432	IV	G2A1	B	153	56	23.92	82	116/82	19	100	100	9.4	42	I	LN	4.43	74	28	102	no	82	110/88	19	100	100	9.4	41	no	nil	no	no
S39	26	17432	V	G2P1L1	B	155	55	22.89	84	120/80	17	100	100	9	40	I	LN	4	75	25	100	no	82	110/70	17	100	100	9	40	no	nil	no	no
S40	22	20987	IV	PRIMI	B	152	57	24.67	84	110/70	16	100	100	8.6	39	S	LN Ĉ E	4	75	23	98	no	85	110/70	16	100	100	8.6	39	no	fever	no	no
S41	27	26486	V	G2P1L1	B	153	53	22.64	82	122/80	19	100	120	10	39	S	LN	4.1	74.5	30	104.5	yes	84	122/80	18	100	120	10	39	no	nil	yes	no
S42	24	24748	IV	G2P1L1	B	153	54	23.06	86	120/70	18	100	100	8.8	38	I	LN	4.35	76	24.5	100.5	no	90	124/76	18	100	100	8.8	38	no	nil	no	no
S43	25	27462	V	G2P1L1	B	155	57	23.72	86	110/70	17	100	100	8.8	40	I	LN	4.3	77	26.5	103.5	no	90	110/70	17	100	100	8.8	40	no	nil	no	no
S44	24	28608	IV	G2P1L1	B	153	55	23.49	82	114/82	16	100	125	8.6	40	I	LN	5	76.5	25.5	102	no	86	114/82	16	100	125	8.6	38	no	nil	no	no
S45	28	48589	IV	G2P1L0	B	154	56	23.61	86	112/70	18	100	100	8.4	38	I	LN	4	78	23	101	no	88	112/70	18	100	100	8.4	38	no	nil	no	no
S46	23	32356	V	G2A1	UB	155	55	22.89	84	116/86	18	100	100	8.2	36	S	LN Ĉ E	4.15	367	143	510	no	86	110/70	18	100	100	8.2	36	yes	nil	no	yes
S47	29	47221	V	G2P1L1	B	156	57	23.42	80	122/86	19	100	100	9	39		LN	4.25	76.5	26	102.5	no	84	122/86	19	100	100	9	39	no	nil	no	no
S48	27	16677	V	G2P1L0	B	153	54	23.06	82	120/80	17	100	100	9.2	39	I	LN	5.12	75	23	98	no	86	120/80	17	100	100	9	39	no	nil	no	no
S49	22	16674	IV	G2PIL1	B	154	56	23.61	82	114/82	17	100	100	9.4	42	I	LN	4.5	76.5	24.5	101	no	88	110/80	17	100	110	9.4	40	no	nil	no	no
S50	19	13683	V	G2P1L1	B	154	56	23.61	84	130/80	19	100	130	9	44	S	LN	5	75	23	98	no	88	130/80	19	100	130	9	44	no	nil	no	no
S51	28	35643	V	G2P1L1	B	152	56	24.23	84	116/80	17	100	100	9.2	40	S	LN	6	75	23	98	no	84	116/80	17	100	100	9.2	40	no	nil	no	no
S52	24	37843	V	G2P1L1	B	155	55	22.89	86	120/70	18	100	130	8.8	38	S	LN	4.36	75	24	99	no	88	120/70	18	100	130	8.8	38	no	nil	no	no

S53	24	38921	V	PRIMI	UB	158	59	23.63	78	110/70	18	99	100	9.4	42	S	LN Ĉ E	4.35	76	25	101	no	80	110/70	18	100	100	9.4	42	no	nil	no	no
S54	22	39908	V	G2P1L1	UB	152	54	23.37	84	120/80	19	99	125	8.6	36	S	LN	5.25	78	23	101	no	84	120/80	19	99	125	8.6	34	no	nil	no	no
S55	27	34564	V	G2A1	B	154	53	22.34	80	122/80	18	100	100	10	42	I	LN Ĉ E	5.3	74.5	24.5	99	no	82	122/80	17	100	100	10	42	no	nil	no	no
S56	23	45634	V	PRIMI	B	156	57	23.42	82	120/70	19	100	110	9.2	40	S	LN Ĉ LP	4.18	73.5	23	96.5	no	84	120/70	19	100	110	9.2	40	no	nil	no	no
S57	35	47687	V	G2P1L1	B	152	53	22.93	84	112/70	18	100	100	9.1	38	I	LN	4	73	25.5	98.5	no	86	112/70	18	100	100	9	38	no	nil	no	no
S58	21	47854	V	PRIMI	B	156	55	22.6	80	112/70	17	100	125	8.5	37	I	LN Ĉ E	4.21	76	23	99	no	81	110/70	17	100	125	8.5	37	no	nil	no	no
S59	29	46968	V	PRIMI	B	155	54	22.47	80	110/70	18	100	100	9.1	39	S	LN	4.1	75.5	26	101.5	no	81	110/70	17	100	100	9.1	39	no	nil	no	no
S60	20	57897	V	PRIMI	B	159	60	23.73	82	110/70	19	100	130	8.8	39	S	LN Ĉ E	5.35	76	25	101	no	84	110/70	19	100	130	8.8	39	no	nil	no	no
S61	23	18676	V	G2P1L1	B	153	56	23.92	84	112/70	17	100	100	8.8	38	S	LN	5.26	77	25	102	no	84	110/70	17	100	100	8.8	38	no	vomiting	no	no
S62	25	10948	V	G2P1L1	B	152	53	22.93	82	108/70	16	100	120	8.4	36	I	LN	4.2	78	24.5	102.5	no	82	108/70	16	100	120	8.4	36	no	nil	no	no
S63	27	39058	V	G2A1	UB	155	54	22.47	76	110/70	18	100	100	9	39	S	LN Ĉ E	4	73.5	27	100.5	no	78	110/70	18	100	100	9	39	no	nil	no	no
S64	23	39769	V	G2P1L1	B	155	55	22.89	80	128/76	16	100	100	9	40	S	LN	4	74	23	97	no	78	128/78	16	100	90	9	40	no	nil	no	no
S65	24	34567	V	G2P1L1	B	156	57	23.42	80	110/80	18	100	120	9	42	S	LN	4.35	74.5	26.5	101	no	81	110/80	18	100	120	9	42	no	nil	no	no
S66	18	45677	V	G2P1L1	B	153	56	23.92	80	120/80	19	100	100	8.8	39	I	LN	4.37	76.5	25	101.5	no	84	120/80	19	100	100	8.8	39	no	nil	no	no
S67	26	67373	V	G2P1L1	B	155	53	22.06	82	110/70	18	100	100	8.8	40	S	LN	4.1	78	24.5	102.5	no	83	110/70	18	100	100	8.6	38	no	nil	no	no
S68	28	45777	V	PRIMI	UB	153	57	24.34	84	116/70	19	100	130	8.8	42	I	LN Ĉ E	5.3	80	27	107	no	86	116/70	19	100	130	8.8	42	no	nil	no	no
S69	24	12377	V	G2P1L1	B	156	54	22.18	86	114/86	17	100	100	8.8	39	I	LN	5.37	74.5	23	97.5	no	86	114/86	19	100	100	8.8	39	no	fever	no	no
S70	23	59776	V	G2P1L1	B	153	55	23.49	88	110/80	18	100	100	8.8	38	I	LN	3	73	26	99	no	88	110/80	18	100	110	8.8	38	no	nil	no	no
S71	19	24390	V	PRIMI	UB	152	53	22.93	80	112/70	17	99	100	8.4	36	S	LN Ĉ E	5	72.5	23	95.5	no	82	110/70	20	99	100	8.4	35	no	nil	no	no
S72	20	27589	IV	G2P1L1	B	152	55	23.80	80	120/70	18	100	120	8.8	38	S	LN	5.5	75	24.5	99.5	no	82	120/70	18	100	110	8.8	38	no	nil	no	no
S73	32	28595	V	G2A1	B	154	54	22.76	82	126/76	18	100	100	8.8	38	S	LN Ĉ E	4.36	75	25.5	100.5	no	82	120/70	18	100	100	8.8	38	no	nil	no	no
S74	22	20956	IV	G2P1L1	B	155	53	22.06	84	110/70	18	100	125	8.4	36	S	LN	5.5	75	24.5	99.5	no	86	108/70	18	100	125	8.2	34	no	nil	no	no
S75	25	24435	V	G2P1L1	B	152	54	23.37	82	122/80	18	100	100	9	38	S	LN	6	75	23	98	no	82	120/80	18	100	100	9	38	no	nil	no	no
S76	24	24467	IV	PRIMI	UB	153	55	23.49	82	120/70	17	99	100	8.8	38	I	LN Ĉ E	4.36	75	25	100	no	84	120/70	17	100	100	8.8	38	no	nil	no	no
S77	29	26789	V	G2A1	B	152	53	22.93	74	120/80	18	100	130	8.6	38	S	LN Ĉ LP	5.3	75	24.5	99.5	no	75	120/80	18	100	130	8.6	38	no	nil	no	no
S78	21	34567	V	G2P1L1	B	153	54	23.06	84	110/70	16	100	120	8	36	S	LN	5.23	75	26	101	no	86	110/70	16	100	120	8	34	no	nil	no	no
S79	26	35678	V	PRIMI	B	156	56	23.01	80	110/80	18	100	130	8.8	40	S	LN Ĉ E	4.2	75	26.5	101.5	no	82	110/80	19	100	130	8.8	40	no	nil	yes	no
S80	23	32414	V	G2P1L1	UB	154	53	22.34	82	116/70	19	100	120	9.2	40	I	LN	5.36	75	24.5	99.5	no	82	110/70	19	100	120	9	40	no	vomiting	no	no
S81	27	26486	V	G2P1L1	B	153	53	22.64	82	122/80	19	100	120	10	39	S	LN	4.1	74.5	30	104.5	yes	84	122/80	18	100	120	10	39	no	nil	yes	no
S82	24	24748	IV	G2P1L1	B	153	54	23.06	86	120/70	18	100	100	8.8	38	I	LN	4.35	76	24.5	100.5	no	90	124/76	18	100	100	8.8	38	no	nil	no	no

S83	25	27462	V	G2P1L1	B	155	57	23.72	86	110/70	17	100	100	8.8	40	I	LN	4.3	77	26.5	103.5	no	90	110/70	17	100	100	8.8	40	no	nil	no	no
S84	24	28608	IV	G2P1L1	B	153	55	23.49	82	114/82	16	100	125	8.6	40	I	LN	5	76.5	25.5	102	no	86	114/82	16	100	125	8.6	38	no	nil	no	no
S85	28	48589	IV	G2P1L0	B	154	56	23.61	86	112/70	18	100	100	8.4	38	I	LN	4	78	23	101	no	88	112/70	18	100	100	8.4	38	no	nil	no	no
S86	23	32356	V	G2A1	UB	155	55	22.89	84	116/86	18	100	100	8.2	36	S	LN Ĉ E	4.15	367	143	510	no	86	110/70	18	100	100	8.2	36	yes	nil	no	yes
S87	29	47221	V	G2P1L1	B	156	57	23.42	80	122/86	19	100	100	9	39		LN	4.25	76.5	26	102.5	no	84	122/86	19	100	100	9	39	no	nil	no	no
S88	27	16677	V	G2P1L0	B	153	54	23.06	82	120/80	17	100	100	9.2	39	I	LN	5.12	75	23	98	no	86	120/80	17	100	100	9	39	no	nil	no	no
S89	22	16674	IV	G2PIL1	B	154	56	23.61	82	114/82	17	100	100	9.4	42	I	LN	4.5	76.5	24.5	101	no	88	110/80	17	100	110	9.4	40	no	nil	no	no
S90	19	13683	V	G2P1L1	B	154	56	23.61	84	130/80	19	100	130	9	44	S	LN	5	75	23	98	no	88	130/80	19	100	130	9	44	no	nil	no	no
S91	29	58776	V	G2P1L1	B	154	56	23.61	84	120/70	18	100	120	8.6	37	I	LN	4.48	72	27	99	no	85	120/70	18	100	120	8.6	37	no	nil	no	no
S92	25	56788	IV	G2P1L1	B	152	57	24.67	82	110/70	18	99	100	8.6	40	I	LN	4.3	70	25	95	no	84	110/70	18	99	100	8.6	40	no	nil	no	no
S93	25	77676	V	G2P1L1	B	155	57	23.72	80	112/70	18	100	100	9	41	I	LN	4.2	74	23	97	no	82	114/70	18	100	100	8.8	38	no	nil	no	no
S94	22	55678	V	G2P1L1	UB	153	53	22.64	84	110/80	19	100	125	8.2	40	S	LN Ĉ LP	4.2	75	26.5	101.5	no	88	110/80	19	100	125	8.2	40	no	nil	no	no
S95	20	10453	V	G2P1L1	UB	159	58	22.94	80	126/70	18	100	100	8.2	35	S	LN	4.25	76.5	25.5	102	no	82	126/70	18	100	100	8.2	35	no	nil	no	no
S96	27	10457	IV	G2P1L1	B	154	54	22.76	82	110/70	18	100	100	9.2	39	S	LN	4.39	73.5	24.5	98	no	82	110/70	18	100	100	9	39	no	vomiting	no	no
S97	30	10987	IV	G2P1L1	B	156	57	23.42	84	110/80	17	100	130	9.2	42	S	LN	5.3	74.5	26	100.5	no	84	110/80	17	100	130	9.2	42	no	nil	no	no
S98	21	10432	IV	G2A1	B	153	56	23.92	82	116/82	19	100	100	9.4	42	I	LN	4.43	74	28	102	no	82	110/88	19	100	100	9.4	41	no	nil	no	no
S99	26	17432	V	G2P1L1	B	155	55	22.89	84	120/80	17	100	100	9	40	I	LN	4	75	25	100	no	82	110/70	17	100	100	9	40	no	nil	no	no
S100	22	20987	IV	PRIMI	B	152	57	24.67	84	110/70	16	100	100	8.6	39	S	LN Ĉ E	4	75	23	98	no	85	110/70	16	100	100	8.6	39	no	fever	no	no
C1	20	10091	IV	PRIMI	B	152	54	23.37	80	110/70	18	100	100	8.8	42	S	LN Ĉ E	5.3	173	36	209	no	86	110/70	18	100	100	8.6	42	no	nil	no	no
C2	22	10100	V	G2PIL1	UB	152	53	22.93	80	122/80	17	100	100	8.8	40	S	LN	5.35	174	42	216	no	88	110/70	19	100	100	8.8	40	no	nil	no	no
C3	24	34354	V	G2PIL1	B	154	55	23.19	86	116/72	19	99	100	8.6	38	I	LN	4.35	178	37	215	no	90	110/70	19	99	100	8.6	36	no	vomiting	no	no
C4	25	36778	V	G2A1	B	153	54	23.06	84	120/80	18	100	100	8.2	36	S	LN Ĉ E	4.55	379	143	522	yes	90	110/70	18	100	100	8.2	36	yes	nil	no	yes
C5	34	35957	IV	G2PIL1	UB	152	55	23.8	80	120/80	18	100	125	9.1	39	I	LN	4.3	174.5	36.5	211	no	86	110/70	18	100	125	9	39	no	nil	no	no
C6	21	32748	V	PRIMI	B	156	56	23.01	82	130/86	17	100	100	9.1	38	I	LN Ĉ E	4.5	173	45	218	no	86	130/80	17	100	100	9.1	38	no	nil	no	no
C7	29	10114	IV	G2PIL1	B	154	53	22.34	80	120/80	19	100	100	9.2	37	I	LN	4.25	177	36	213	no	84	110/70	19	99	100	9.2	37	no	nil	no	no
C8	21	42857	V	G2PIL1	B	153	55	23.49	82	118/82	18	100	125	9	36	S	LN Ĉ LP	4.35	176.5	42	218.5	no	86	110/80	18	100	130	8.8	36	no	nil	no	no
C9	23	43857	V	PRIMI	B	158	60	24.03	84	120/80	17	100	100	9	36	S	LN Ĉ E	4.3	173.5	43	216.5	no	88	110/70	19	100	100	9	36	no	nil	no	no
C10	28	44647	IV	G2PIL1	B	153	54	23.06	82	122/78	19	100	100	9	38	S	LN	4.4	178	43	221	no	80	120/70	19	100	100	8.6	36	no	nil	no	no
C11	24	10029	V	G2PIL1	B	156	56	23.01	86	120/80	19	100	100	8.8	37	I	LN	3.55	173	36.5	209.5	no	90	110/70	19	99	100	8.8	37	no	nil	no	no
C12	22	10020	V	PRIMI	B	153	57	24.34	82	126/82	17	100	100	8.8	38	I	LN Ĉ E	5.2	176.5	37	213.5	no	86	124/78	17	100	100	8.8	38	no	vomiting	no	no

C13	23	38575	IV	G2PIL1	B	152	53	22.93	80	120/70	16	100	100	8.4	36	S	LN	4	175	36	210.5	no	88	110/70	16	100	100	8.4	36	no	nil	no	no
C14	27	28579	V	G2PIL1	B	155	57	23.72	92	126/80	18	100	125	8.6	40	S	LN	5.3	178	44	222	no	92	116/70	18	99	125	8.2	34	no	nil	no	no
C15	19	42957	V	PRIMI	B	154	54	22.76	84	120/70	18	100	100	8.2	37	I	LN	4.2	375	145	520	no	88	118/70	18	100	110	8.2	37	yes	fever	no	yes
C16	20	11098	IV	G2PIL1	B	152	55	23.8	84	120/82	19	100	100	9.4	42	S	LN	4.25	376	154	530	yes	88	110/70	19	100	100	9.4	42	yes	nil	no	yes
C17	26	58938	V	G2A1	B	155	53	22.06	86	110/86	18	100	100	10	44	I	LN Ĉ E	4.28	173	36.5	209.5	no	90	110/80	18	100	100	10	44	no	nil	no	no
C18	25	11129	V	PRIMI	B	154	57	24.03	88	110/80	17	100	130	8.4	40	I	LN Ĉ E	4.39	384	156	540	yes	90	110/70	17	99	130	8.2	36	yes	nil	no	yes
C19	24	28475	IV	G2PIL1	B	153	56	24.23	82	120/80	17	100	100	8.6	39	I	LN	3.5	178	36	214	no	88	120/80	17	100	100	8.6	39	no	nil	no	no
C20	26	12332	V	PRIMI	B	152	54	23.37	78	126/84	19	100	100	8.8	38	I	LN Ĉ E	5.3	173	43	216	no	86	120/80	19	100	100	8	35	no	nil	yes	no
C21	25	39757	V	G2PIL1	B	154	53	22.34	80	120/80	19	100	100	9.4	39	I	LN	5.34	177	45	222	no	85	120/70	19	100	100	9.4	39	no	nil	no	no
C22	32	38009	V	PRIMI	UB	155	57	23.72	80	110/80	19	100	110	8.8	38	I	LN Ĉ E	4.35	177	39	215.5	no	86	110/70	19	99	110	8.8	38	no	fever	no	no
C23	27	12987	IV	PRIMI	B	152	55	23.8	82	110/70	19	100	100	9.4	37	S	LN Ĉ E	4.5	175	42	217	no	88	110/70	18	100	100	9	37	no	nil	no	no
C24	23	13984	IV	PRIMI	B	155	56	23.3	82	114/78	18	99	100	9	40	S	LN Ĉ E	3.5	174	36	209.5	no	88	110/70	18	99	90	9	38	no	nil	no	no
C25	27	59003	IV	G2A1	B	153	54	23.06	78	110/70	18	100	100	8.2	36	S	LN Ĉ E	4.39	176	45	220.5	yes	85	110/70	18	100	100	8.2	32	no	nil	no	no
C26	24	59039	IV	G2P1L0	B	152	57	24.67	84	120/80	18	100	125	8.4	34	I	LN Ĉ E	4.58	174	37	210.5	no	90	110/70	18	99	125	8.4	34	no	vomiting	no	no
C27	20	13900	V	G2PIL1	B	154	57	24.03	76	116/78	18	100	100	8.8	40	I	LN	5	175	36	210.5	no	86	110/70	18	100	100	8.2	37	no	nil	no	no
C28	28	58939	V	G2PIL1	UB	158	59	23.63	80	120/80	18	100	100	9.4	42	I	LN	4.5	177	50	226.5	yes	84	110/80	18	100	100	9.1	40	no	nil	no	no
C29	23	13990	V	G2P1L0	B	153	54	23.06	84	120/78	19	100	100	9.2	41	S	LN Ĉ E	4.35	174	43	216.5	no	88	120/70	19	99	100	9.2	38	no	nil	no	no
C30	18	53928	V	G2PIL1	B	152	53	22.93	82	120/80	17	100	135	10	40	S	LN	4.25	175	42.5	217.5	no	86	110/70	17	100	135	8.6	37	no	nil	yes	no
C31	29	14009	IV	G2PIL1	B	155	55	22.89	80	110/80	19	100	100	9.2	39	I	LN	4.15	177	45	222	no	84	110/70	20	100	100	9.2	39	no	nil	no	no
C32	21	47119	V	PRIMI	B	156	54	22.18	82	110/80	18	100	100	9.4	42	I	LN Ĉ E	5	174	37	210.5	no	86	110/70	18	99	100	9.1	42	no	nil	no	no
C33	25	42095	IV	G2PIL1	B	153	56	23.92	80	110/80	19	100	125	9.4	40	S	LN	4	178	36	214	no	80	110/70	19	100	125	9.1	40	no	nil	no	no
C34	20	14490	V	G2PIL1	B	152	55	23.8	80	122/86	18	100	100	8.6	39	S	LN Ĉ LP	3.56	175	44	219	no	84	120/80	18	100	100	8.6	36	no	nil	no	no
C35	24	49284	V	PRIMI	B	154	54	22.76	82	120/80	18	100	100	8.8	37	I	LN	4.38	177	43	220	yes	88	120/80	18	100	100	8.6	36	no	nil	no	no
C36	25	14493	IV	G2PIL1	B	153	56	23.92	84	120/70	18	100	115	8.4	36	I	LN	4.5	178	43	221	yes	88	110/70	18	100	110	8.4	36	no	nil	no	no
C37	27	34958	V	G2PIL1	B	155	56	23.3	86	120/80	18	99	100	8.6	36	S	LN	4.25	175	45	219.5	yes	88	120/80	18	99	100	8.6	36	no	nil	yes	no
C38	21	32948	V	G2PIL1	B	153	53	22.64	82	110/80	17	100	100	8.8	38	S	LN	4.28	173	36	209	no	86	110/80	17	100	100	8.8	36	no	nil	no	no
C39	30	14596	V	PRIMI	B	152	54	23.37	80	120/70	16	100	100	8.2	37	I	LN Ĉ E	4.25	177	44	220.5	yes	88	120/70	16	100	100	8.2	36	no	nil	no	no
C40	21	33048	V	G2PIL1	UB	154	57	24.03	82	120/80	19	100	120	8.4	39	I	LN	4.1	175	40	215	no	86	120/80	19	99	120	8.4	39	no	nil	no	no
C41	26	45595	V	G2PIL1	B	155	55	22.89	86	110/80	18	100	100	8.6	38	S	LN	4.14	177	43	220	yes	90	110/70	19	100	100	8.2	35	yes	nil	no	yes
C42	23	14593	V	G2PIL1	B	153	56	23.92	86	110/86	19	100	100	8.8	40	S	LN	5.24	178	45	223	no	90	110/86	19	99	115	8.2	35	no	nil	no	no

C43	24	33848	V	PRIMI	B	159	58	22.94	86	110/70	18	100	100	8.4	37	S	LN Ĉ E	5.25	175	43	218	no	90	110/70	18	100	100	8.4	36	no	nil	no	no
C44	23	14900	V	G2PIL1	UB	154	57	24.03	84	120/80	17	100	130	8.8	40	S	LN	5.5	173	40	213	no	86	120/80	17	100	130	8.8	40	no	fever	no	no
C45	25	22858	V	G2PIL1	B	152	53	22.93	82	110/70	19	100	100	9.1	42	S	LN	4.56	177	44	221	yes	88	110/70	19	100	100	9.1	40	no	nil	no	no
C46	19	15009	V	G2PIL1	B	156	56	23.01	86	110/80	18	100	100	9.2	40	S	LN	4.35	177	39	215.5	no	90	108/70	18	99	100	8.6	39	no	nil	no	no
C47	20	50093	V	G2PIL1	B	155	53	22.06	86	122/76	19	99	100	9.4	40	S	LN	4.23	178	40	218	no	90	122/76	19	99	110	9.4	40	no	nil	no	no
C48	22	15005	V	G2PIL1	B	153	55	23.49	84	110/80	17	99	125	9	41	S	LN	4.27	175	44	219	no	88	110/80	17	99	125	9	40	no	nil	no	no
C49	26	19848	V	G2PIL1	UB	153	53	22.64	80	120/82	19	100	100	8.8	39	S	LN	4.5	173	37	210	no	84	120/82	18	100	100	8.6	39	no	nil	no	no
C50	24	16001	V	PRIMI	UB	152	56	24.23	78	110/80	18	100	135	8.6	38	S	LN Ĉ E	5.2	175	45	219.5	no	82	110/70	18	99	130	8.6	37	no	nil	no	no
C51	27	59003	IV	G2A1	B	153	54	23.06	78	110/70	18	100	100	8.2	36	S	LN Ĉ E	4.39	176	45	220.5	yes	85	110/70	18	100	100	8.2	32	no	nil	no	no
C52	24	59039	IV	G2P1L0	B	152	57	24.67	84	120/80	18	100	125	8.4	34	I	LN Ĉ E	4.58	174	37	210.5	no	90	110/70	18	99	125	8.4	34	no	vomiting	no	no
C53	20	13900	V	G2PIL1	B	154	57	24.03	76	116/78	18	100	100	8.8	40	I	LN	5	175	36	210.5	no	86	110/70	18	100	100	8.2	37	no	nil	no	no
C54	28	58939	V	G2PIL1	UB	158	59	23.63	80	120/80	18	100	100	9.4	42	I	LN	4.5	177	50	226.5	yes	84	110/80	18	100	100	9.1	40	no	nil	no	no
C55	23	13990	V	G2P1L0	B	153	54	23.06	84	120/78	19	100	100	9.2	41	S	LN Ĉ E	4.35	174	43	216.5	no	88	120/70	19	99	100	9.2	38	no	nil	no	no
C56	18	53928	V	G2PIL1	B	152	53	22.93	82	120/80	17	100	135	10	40	S	LN	4.25	175	42.5	217.5	no	86	110/70	17	100	135	8.6	37	no	nil	yes	no
C57	29	14009	IV	G2PIL1	B	155	55	22.89	80	110/80	19	100	100	9.2	39	I	LN	4.15	177	45	222	no	84	110/70	20	100	100	9.2	39	no	nil	no	no
C58	21	47119	V	PRIMI	B	156	54	22.18	82	110/80	18	100	100	9.4	42	I	LN Ĉ E	5	174	37	210.5	no	86	110/70	18	99	100	9.1	42	no	nil	no	no
C59	25	42095	IV	G2PIL1	B	153	56	23.92	80	110/80	19	100	125	9.4	40	S	LN	4	178	36	214	no	80	110/70	19	100	125	9.1	40	no	nil	no	no
C60	20	14490	V	G2PIL1	B	152	55	23.8	80	122/86	18	100	100	8.6	39	S	LN Ĉ LP	3.56	175	44	219	no	84	120/80	18	100	100	8.6	36	no	nil	no	no
C61	24	49284	V	PRIMI	B	154	54	22.76	82	120/80	18	100	100	8.8	37	I	LN	4.38	177	43	220	yes	88	120/80	18	100	100	8.6	36	no	nil	no	no
C62	25	14493	IV	G2PIL1	B	153	56	23.92	84	120/70	18	100	115	8.4	36	I	LN	4.5	178	43	221	yes	88	110/70	18	100	110	8.4	36	no	nil	no	no
C63	27	34958	V	G2PIL1	B	155	56	23.3	86	120/80	18	99	100	8.6	36	S	LN	4.25	175	45	219.5	yes	88	120/80	18	99	100	8.6	36	no	nil	yes	no
C64	21	32948	V	G2PIL1	B	153	53	22.64	82	110/80	17	100	100	8.8	38	S	LN	4.28	173	36	209	no	86	110/80	17	100	100	8.8	36	no	nil	no	no
C65	30	14596	V	PRIMI	B	152	54	23.37	80	120/70	16	100	100	8.2	37	I	LN Ĉ E	4.25	177	44	220.5	yes	88	120/70	16	100	100	8.2	36	no	nil	no	no
C66	21	33048	V	G2PIL1	UB	154	57	24.03	82	120/80	19	100	120	8.4	39	I	LN	4.1	175	40	215	no	86	120/80	19	99	120	8.4	39	no	nil	no	no
C67	26	45595	V	G2PIL1	B	155	55	22.89	86	110/80	18	100	100	8.6	38	S	LN	4.14	177	43	220	yes	90	110/70	19	100	100	8.2	35	yes	nil	no	yes
C68	23	14593	V	G2PIL1	B	153	56	23.92	86	110/86	19	100	100	8.8	40	S	LN	5.24	178	45	223	no	90	110/86	19	99	115	8.2	35	no	nil	no	no
C69	24	33848	V	PRIMI	B	159	58	22.94	86	110/70	18	100	100	8.4	37	S	LN Ĉ E	5.25	175	43	218	no	90	110/70	18	100	100	8.4	36	no	nil	no	no
C70	23	14900	V	G2PIL1	UB	154	57	24.03	84	120/80	17	100	130	8.8	40	S	LN	5.5	173	40	213	no	86	120/80	17	100	130	8.8	40	no	fever	no	no
C71	25	22858	V	G2PIL1	B	152	53	22.93	82	110/70	19	100	100	9.1	42	S	LN	4.56	177	44	221	yes	88	110/70	19	100	100	9.1	40	no	nil	no	no
C72	19	15009	V	G2PIL1	B	156	56	23.01	86	110/80	18	100	100	9.2	40	S	LN	4.35	177	39	215.5	no	90	108/70	18	99	100	8.6	39	no	nil	no	no

C73	20	50093	V	G2PIL1	B	155	53	22.06	86	122/76	19	99	100	9.4	40	S	LN	4.23	178	40	218	no	90	122/76	19	99	110	9.4	40	no	nil	no	no
C74	22	15005	V	G2PIL1	B	153	55	23.49	84	110/80	17	99	125	9	41	S	LN	4.27	175	44	219	no	88	110/80	17	99	125	9	40	no	nil	no	no
C75	26	19848	V	G2PIL1	UB	153	53	22.64	80	120/82	19	100	100	8.8	39	S	LN	4.5	173	37	210	no	84	120/82	18	100	100	8.6	39	no	nil	no	no
C76	24	16001	V	PRIMI	UB	152	56	24.23	78	110/80	18	100	135	8.6	38	S	LN Ĉ E	5.2	175	45	219.5	no	82	110/70	18	99	130	8.6	37	no	nil	no	no
C77	20	10091	IV	PRIMI	B	152	54	23.37	80	110/70	18	100	100	8.8	42	S	LN Ĉ E	5.3	173	36	209	no	86	110/70	18	100	100	8.6	42	no	nil	no	no
C78	22	10100	V	G2PIL1	UB	152	53	22.93	80	122/80	17	100	100	8.8	40	S	LN	5.35	174	42	216	no	88	110/70	19	100	100	8.8	40	no	nil	no	no
C79	24	34354	V	G2PIL1	B	154	55	23.19	86	116/72	19	99	100	8.6	38	I	LN	4.35	178	37	215	no	90	110/70	19	99	100	8.6	36	no	vomiting	no	no
C80	25	36778	V	G2A1	B	153	54	23.06	84	120/80	18	100	100	8.2	36	S	LN Ĉ E	4.55	379	143	522	yes	90	110/70	18	100	100	8.2	36	yes	nil	no	yes
C81	34	35957	IV	G2PIL1	UB	152	55	23.8	80	120/80	18	100	125	9.1	39	I	LN	4.3	175	36.5	211	no	86	110/70	18	100	125	9	39	no	nil	no	no
C82	21	32748	V	PRIMI	B	156	56	23.01	82	130/86	17	100	100	9.1	38	I	LN Ĉ E	4.5	173	45	218	no	86	130/80	17	100	100	9.1	38	no	nil	no	no
C83	29	10114	IV	G2PIL1	B	154	53	22.34	80	120/80	19	100	100	9.2	37	I	LN	4.25	177	36	213	no	84	110/70	19	99	100	9.2	37	no	nil	no	no
C84	21	42857	V	G2PIL1	B	153	55	23.49	82	118/82	18	100	125	9	36	S	LN Ĉ LP	4.35	177	42	218.5	no	86	110/80	18	100	130	8.8	36	no	nil	no	no
C85	23	43857	V	PRIMI	B	158	60	24.03	84	120/80	17	100	100	9	36	S	LN Ĉ E	4.3	174	43	216.5	no	88	110/70	19	100	100	9	36	no	nil	no	no
C86	28	44647	IV	G2PIL1	B	153	54	23.06	82	122/78	19	100	100	9	38	S	LN	4.4	178	43	221	no	80	120/70	19	100	100	8.6	36	no	nil	no	no
C87	24	10029	V	G2PIL1	B	156	56	23.01	86	120/80	19	100	100	8.8	37	I	LN	3.55	173	36.5	209.5	no	90	110/70	19	99	100	8.8	37	no	nil	no	no
C88	22	10020	V	PRIMI	B	153	57	24.34	82	126/82	17	100	100	8.8	38	I	LN Ĉ E	5.2	177	37	213.5	no	86	124/78	17	100	100	8.8	38	no	vomiting	no	no
C89	23	38575	IV	G2PIL1	B	152	53	22.93	80	120/70	16	100	100	8.4	36	S	LN	4	175	36	210.5	no	88	110/70	16	100	100	8.4	36	no	nil	no	no
C90	27	28579	V	G2PIL1	B	155	57	23.72	92	126/80	18	100	125	8.6	40	S	LN	5.3	178	44	222	no	92	116/70	18	99	125	8.2	34	no	nil	no	no
C91	19	42957	V	PRIMI	B	154	54	22.76	84	120/70	18	100	100	8.2	37	I	LN	4.2	375	145	520	no	88	118/70	18	100	110	8.2	37	yes	fever	no	yes
C92	20	11098	IV	G2PIL1	B	152	55	23.8	84	120/82	19	100	100	9.4	42	S	LN	4.25	376	154	530	yes	88	110/70	19	100	100	9.4	42	yes	nil	no	yes
C93	26	58938	V	G2A1	B	155	53	22.06	86	110/86	18	100	100	10	44	I	LN Ĉ E	4.28	173	36.5	209.5	no	90	110/80	18	100	100	10	44	no	nil	no	no
C94	25	11129	V	PRIMI	B	154	57	24.03	88	110/80	17	100	130	8.4	40	I	LN Ĉ E	4.39	384	156	540	yes	90	110/70	17	99	130	8.2	36	yes	nil	no	yes
C95	24	28475	IV	G2PIL1	B	153	56	24.23	82	120/80	17	100	100	8.6	39	I	LN	3.5	178	36	214	no	88	120/80	17	100	100	8.6	39	no	nil	no	no
C96	26	12332	V	PRIMI	B	152	54	23.37	78	126/84	19	100	100	8.8	38	I	LN Ĉ E	5.3	173	43	216	no	86	120/80	19	100	100	8	35	no	nil	yes	no
C97	25	39757	V	G2PIL1	B	154	53	22.34	80	120/80	19	100	100	9.4	39	I	LN	5.34	177	45	222	no	85	120/70	19	100	100	9.4	39	no	nil	no	no
C98	32	38009	V	PRIMI	UB	155	57	23.72	80	110/80	19	100	110	8.8	38	I	LN Ĉ E	4.35	177	39	215.5	no	86	110/70	19	99	110	8.8	38	no	fever	no	no
C99	27	12987	IV	PRIMI	B	152	55	23.8	82	110/70	19	100	100	9.4	37	S	LN Ĉ E	4.5	175	42	217	no	88	110/70	18	100	100	9	37	no	nil	no	no
C100	23	13984	IV	PRIMI	B	155	56	23.3	82	114/78	18	99	100	9	40	S	LN Ĉ E	3.5	174	36	209.5	no	88	110/70	18	99	90	9	38	no	nil	no	no