A COMPARATIVE STUDY ON IMMEDIATE VERSUS DELAYED INDUCTION IN TERM PREMATURE RUPTURE OF MEMBRANES

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CERTIFICATE

This is to certify that the dissertation entitled "**A COMPARATIVE STUDY ON IMMEDIATE VERSUS DELAYED INDUCTION IN TERM PREMATURE RUPTURE OF MEMBRANES"** is a bonafide work done by **Dr. J. BETTY AGNES** in the Institute of Obstetrics and Gynaecology (Madras Medical College) Egmore, Chennai in partial fulfillment of the university rules and regulations for award of MS degree in Obstetrics and Gynaecology under my guidance and supervision during the academic year 2011-2013.

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I solemnly declare that this dissertation entitled **"A COMPARATIVE STUDY ON IMMEDIATE VERSUS DELAYED INDUCTION IN TERM PREMATURE RUPTURE OF MEMBRANES"** was done by me at Institute of Obstetrics & Gynaecology, Madras Medical College during 2011 – 2013 under the guidance and supervision of Prof. Dr. G. UMA SHANTHI, M.D., D.G.O.. This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.S. Degree in Obstretics & Gynaecology (Branch-II)

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Dear Dr. J. Betty Agnes

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "A comparative study on immediate versus delayed induction in term premature rupture of membrane" No.08082012.

The following members of Ethics Committee were present in the meeting held on 10/08/2012 conducted at Madras Medical College, Chennai -3.

1. Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2. Prof. Pregna B. Dolia MD Vice Principal, Madras Medical College, Chennai -3 Director , Institute of Biochemistry, MMC, Ch-3	-- Member Secretary
3. Prof. B. Vasanthi MD Prof of Pharmacology ,MMC, Ch-3	-- Member
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5. Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
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7. Tmt. Arnold Soulina MA MSW	-- Social Scientist

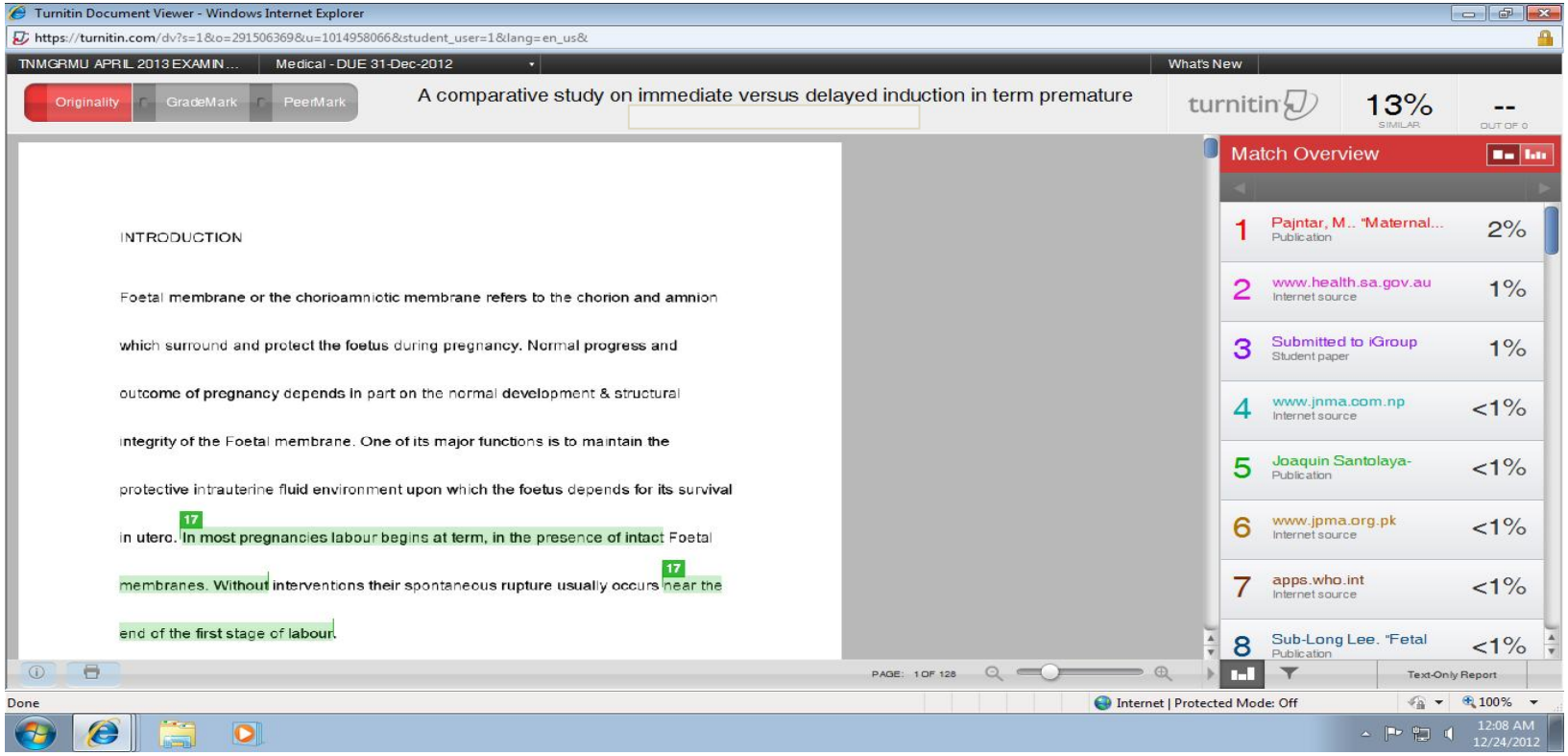
We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

PLAGIARISM REPORT



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INTRODUCTION

INTRODUCTION

Foetal membrane or the chorioamniotic membrane refers to the chorion and amnion which surround and protect the foetus during pregnancy. Normal progress and outcome of pregnancy depends in part on the normal development & structural integrity of the Foetal membrane. One of its major functions is to maintain the protective intrauterine fluid environment upon which the foetus depends for its survival in utero. In most pregnancies labour begins at term, in the presence of intact Foetal membranes. Without interventions their spontaneous rupture usually occurs near the end of the first stage of labour.

Premature rupture of membranes (PROM) is defined as the spontaneous rupture of amniotic membrane with a release of amniotic fluid before the onset of labour. If the membranes rupture after 37 weeks of gestation it is called term Premature Rupture of Membranes. If the rupture of membranes (ROM) occur before 37 weeks of gestation is termed as the preterm premature rupture of membrane (PPROM).

Premature rupture of membrane has an incidence of about 10% of all pregnancies[11] and is a significant event as it can cause maternal complications, increased operative procedures, neonatal morbidity and mortality.

The management of premature rupture of membranes (PROM) at term is still controversial. Some authors like Cammu H et al believe that the expectant management of premature rupture of membranes at term does not increase perinatal and maternal morbidity, and that an aggressive attitude to premature rupture of membranes with immediate induction of labour leads to an increased cesarean section rate. [1, 2]

On the other hand, there are some authors like Neuhaus W et al who report on a significant increase in the rates of neonatal and maternal infection and Foetal distress if delivery occurs over 24 hours after premature rupture of membranes. [3, 4] Immediate induction of labour has shown to reduce the duration of hospitalization and occurrence of neonatal and maternal infection. [5]

Studies (like Wagner et al) have shown that patients with premature rupture of membranes who were induced within 6 hours of rupture of membranes, 90% delivered within 24 hours of rupture of membrane as compared to group managed expectantly in which 60% delivered within 24 hours. [6] Also, with increasing time since the rupture of membranes to delivery, a higher incidence of histological chorioamnionitis was observed in some studies.[7]

There are still other authors like Rydhstrom et al who found no difference in the rate of obstetric interventions during labour between the conservative management for up to 3 days in women with Premature Rupture of Membranes at term and immediate induction of labour. [8]

The purpose of this study was to compare the maternal and neonatal outcomes between immediate and delayed induction (after 12 hours) with PGE2 gel in women with term premature rupture of membranes (PROM). It was conducted in women admitted in the labour room in the Institute Of Obstetrics and Gynaecology, Egmore.

AIM OF THE STUDY

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To compare the maternal and neonatal outcome between immediate and delayed induction with PGE2 gel in women with term premature rupture of membranes.

REVIEW OF LITERATURE

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DEFINITION OF PREMATURE RUPTURE OF MEMBRANES (PROM)

PROM has been defined in 2 ways by different authors. The definitions include:

1. Rupture of the membranes at any time before the onset of labour irrespective of the duration of gestation. [9,10,11]

2. Rupture of membranes occurring at least one hour before onset of labour.[12,13,14]

According to Tanya M et al, Am Fam Physician 2006 Feb 15; 73(4):659-664, if the rupture of membranes (ROM) occurs after 28 weeks but before 37 weeks, it is termed as preterm premature rupture of membranes (PPROM).

High rupture of membranes: It is due to rupture of membranes at a site distant from the internal os. Sometimes with high rupture of membranes, spontaneous cessation of leaking can occur.

INCIDENCE OF PROM

The incidence of PROM is variable. The incidence of PROM is 2.7 – 17 %. [15] It is responsible for 1/3rd of all preterm births. PROM is one of the most common complications of pregnancy, occurring in about 10% of all pregnancies. [16] According to Gunn et al in 1970- it varies from 2-18 %, Burgeoise et al (1988) – 7.35%, Aktar et al – 3.3% and Duff P in 1991 gave an incidence of between 8-10 %. Pre-mature rupture of the membranes at term is common occurring in 6-19% of all term birth. [17] According to Gabbe GS et al, 1986- With a conservative approach- The length of time between the rupture of membranes and delivery is inversely related to the gestational age. IF PROM occurs before 26 weeks of gestation, 30 -40 % of cases will gain at least one additional week before delivery, and 20 % will gain over 4 weeks. Between 28- 34 weeks of gestation, delivery within the first week after PROM occurs in 70- 80 % of the patients. At term, nearly 80 % of women go into labour within the first 24 hours after rupture of membranes. [18]

In order to understand the etiology of how premature rupture of membranes occur and understand the different modalities of management,

it is wise to review the development, anatomy and physiology of the foetal membranes.

ANATOMY OF FOETAL MEMBRANES

The human amnion either develops from the delamination of the cytotrophoblast at about the 7^{th} or 8^{th} day of development of the normal ovum, or it develops essentially as an extension of the Foetal ectoderm of the embryonic disc. Trophoblastic cells lined with parietal extra embryonic mesoderm constitute the chorion. Initially amniotic cavity appears as a minute vesicle and later develops into a small sac that covers the dorsal surface of the growing embryo. The roof of this cavity is formed by amniogenic cells derived from the trophoblast, while its floor is formed by the ectoderm. As the amnion enlarges it gradually engulfs the growing embryo which prolapses into its cavity. Distension of the amniotic sac eventually brings it into contact with the interior of the chorion, resulting in obliteration of the extra-embryonic coelom. Further expansion of the amniotic cavity occurs at the expense of the uterine cavity. Gradually, the decidua capsularis fuses with the decidua parietalis and the uterine cavity is also obliterated. Still further expansion of the amniotic cavity is achieved by enlargement of the uterus.

At the time of parturition the fused amnion and chorion (along with the greatly thinned out decidua capsularis) constitute what are called membranes.

AMNION

The amnion is the inner of the two Foetal membranes and as such, is in contact with the contents of the amniotic sac, namely the amniotic fluid and the foetus. The chorionic membrane is adjacent to the outer surface of the amniotic membrane, and separates the amnion from the decidua. This part of the amnion is called placental amnion, while the remainder is referred to as the reflected amnion. A third area that directly overlies the internal cervical OS is known as dependent amnion.

Amniotic membrane is not simply an epithelial lining for the uterine cavity but a well differentiated tissue. There are five layers which from within outwards as follows; [19]

1. Epithelium: Composed of a single layer of cuboidal cells.

2. Basement Membrane: It is a narrow band of reticular tissue lying along the base of the epithelial cells to which it is securely adherent. It is normally well defined over both the placental and reflected parts of the amnion.

3. Compact layer: A relatively dense, acellular layer and is composed of randomly scattered reticular fibrils, lying immediately deep to the basement membrane to which it is densely adherent.

4. Fibroblast layer: It is composed of a fibroblast network set in a mesh of reticulum. The only cells normally present are fibroblast and Hofbauer cells. It forms a considerable part of the thickness of the amnion.

5. Spongy layer: Composed of many collagenous bundles and it is capable of great distension and is responsible for permitting the amnion some degree of movement upon the underlying fixed chorion.

The normal amnion is 0.02 – 0.5 mm in thickness. It varies greatly in thickness as a result of alteration in the mucin and fluid content. Blood vessels or nerves could not be found in the amnion at any stage of development. Lymphatic channels could not be identified in the spaces in the fibroblastic and spongy layers. [19]

CHORION

The chorion, being the outer of the two human Foetal membranes, is in contact with the amnion on its inner aspect and the maternal decidua on its outer aspect.

The portion of the chorion overlying the placenta is called placental chorion, remainder is called the reflected chorion and the portion overlying the internal os of the cervix is known as the dependent chorion. The chorion is made up of 4 different layers on histological examination. They are from within outwards as follows;

a. Cellular layer: This is a narrow layer consisting almost entirely of an interlacing fibroblast network similar to that present in the fibroblast layer of the amion.

b. Reticular layer: This layer forms the major part of the reticular tissue of chorion. It is made up of a network of reticulum in which fibroblasts and Hofbauer cells are embedded.

c. Basement membrane: this layer is a narrow band of reticular tissue forming the basement membrane of the trophoblast which lies upon its deeper surface. The name pseudobasement membrane is used to avoid confusion with the basement membrane of the amnion.

d. Trophoblast : This is a layer of trophoblast cells about 4-6 cells in thickness, but is extremely variable, ranging from 0.04 to 0.40 mm. Syncitio trophoblastic tissue is not normally visible in the reflected chorion at term, although it is present earlier in pregnancy. In some areas the chorion is healthy and functionally active. In other areas there is evidence of cellular degeneration and pyknosis of cell nuclei.

There is no evidence to show that the chorion at term has a capillary blood supply for its own nutrition. In early pregnancy the chorion leave possesses actively functioning chorionic villi. There is a complex system of vessels throughout the reticular layer of the entire chorion. As pregnancy advances the villi of the chorion frondosum develop into the placenta and simultaneously the villi of the chorionic leave atrophy. The blood vessels supplying these atrophic villi also degenerate, but whereas villi persist within the trophoblast layer of the chorion as atrophic or ghost villi, the vessels altogether disappear.

PHYSIOLOGY OF FOETAL MEMBRANES

Foetal membranes contain an organization of enzymes requiring both synthesis and degradation of prostaglandins using specific methods. [17]

Chorioamnion serve as the site of storage and ultimately release of the prostaglandin precursor, arachidonic acid. The human membranes contain the enzyme phospholipase A2 which catalyses the hydrolysis of the glycerophospholipids leading to release of free arachidonic acid. So, Foetal membranes have the capacity to provide the obligate precursor for the synthesis of PGE2 and PGF2α while the contiguous uterine deciduas are known to contain prostaglandin synthetase system and occupy a central role in the initiation of human parturition. The placental villous tissue, membranes, umbilical cord, Foetal skin, myometrium and deciduas also have the ability to metabolise exogenous prostaglandins. [17] The enzyme regulating the degradation of prostaglandins are distributed throughout the pregnant uterus. The highest activity of the metabolizing enzymes is found in the chorion and placenta. These structures also display an ability to synthesize prostaglandins in vitro. The chorion could be the major source of endogenous intrauterine prostaglandins, since both the amnion and the deciduas possess low potential for metabolizing prostaglandins; these substances could originate in the chorion and diffuse through the amnion into the amniotic fluid and through the deciduas into the myometrium without undergoing sizeable inactivation. [17] Prostaglandins facilitate myometrial contractions by inhibiting calcium sequestration in the sarcoplasmic reticulum. Progesterone is essential for the establishment and

maintenance of pregnancy in all the mammalian species. The withdrawal of progesterone is a pre-requisite for the onset of labour in humans.

The possibility exists that progesterone exerts a stabilizing effect in human Foetal membranes which regulates the expression of the activity of phospholipase A2. The biochemical events leading to the onset of uterine contractions could be triggered by local progesterone and has many of the physical and chemical characteristics of transcortin which appears to be associated with the human Foetal membranes largely after 37 weeks gestation. This binding of progesterone allows for the lysozymal enzyme activation. It has also been suggested that the ratio of estradiol and progesterone rather than their absolute concentration, may be more significant. More significant changes in the ratio locally in the Foetal membranes and the deciduas may bring about the changes in the sensitivity and excitability of myometrium at term to start the labour.

The chorioamnion also possess extensive enzymatic capabilities for steroid hormone metabolism including 5-alpha reductase, 3-β hydroxyl steroid dehydrogenase, D5-4 isomerase, 20 α steroid – oxido reductase, 17 beta – dehydrogenase and other enzyme activities.

PHYSICAL PROPERTIES OF FOETAL MEMBRANES

Evidence indicates that pre-term membranes are stronger than term membranes and indeed PROM occurs in 10% of pregnancies at term while in only 0.7 – 2% of pregnancies before 37 completed weeks. The relative rarity of pre-term PROM has prompted investigators to examine the physical properties of the Foetal membranes in order to determine whether rupture is caused by an inherent weakness of the membrane material or by local defects in the membrane structure. [20]

The chorioamniotic membranes exhibit physical properties characteristic of viscoelastic material. After a stress (e.g. contraction, foetal movement) the membranes exhibit deformation characteristics of both elastic and viscous materials simultaneously. With recovery, only the elastic component which has memory will return to its original state. Thus, less than the total deformation is recovered. The viscous component of the membranes might be influenced by the chemical constitution of the amniotic fluid with resultant changes in fluid osmolarity. The elastic component could be influenced by changes in the collagen network.

In the majority of pregnancies the Foetal membranes rupture spontaneously at term during the active phase of labour. Since a pressure of 56-58 mm of water is enough to rupture normal membranes over a circle of 10 cm diameter, this could explain membrane rupture at the end

of first stage of labour. Since it requires much greater force to affect membrane rupture over a smaller, diameter, in order to explain pre-term premature rupture of membranes in the presence of an undilated cervix, it must be assumed that the membranes are pathologically altered in some manner at the site of rupture, regardless of their condition elsewhere in the uterine cavity. [20]

Early studies demonstrated that although the amnion is generally one third as thick as the chorion, it is five times as strong in its ability to withstand stress. However, the combined membranes are stronger since the chorion contributes a significant portion of tensile strength. Chorion is three quarters as defective as amnion in developing the tensile force. These initial studies consistently failed to demonstrate difference between prematurely and non prematurely ruptured membranes in either rupture tension or initial resting membrane thickness. In fact, the bursting pressure of membranes from patients with pre-term PROM was significantly higher than that of term membranes (Polishuk et al 1964). Since the membranes generally were not evaluated at the actual site of rupture these results suggested that the local defect might be responsible for pre-mature PROM.

During the course of labour the contraction during which spontaneous rupture of membranes occurred was not the strongest one to

which the membranes were subject in 86% of the cases raised the possibility that membranes subject to repeated stresses were altered, becoming more brittle and heterogeneous. There was definite histological changes in the membranes following repetitive stretching in the form of loss of amniotic surface epithelium, splitting and breaking down of the compact layer, and separation of the amnion from the spongy layer. [20]

The chorioamniotic membranes are subjected to multiple stresses during pregnancy. There is normal chronic stress resulting from physiologic expansion accompanying growth of the foetus and accumulation of amniotic fluid. The membranes have been stretched to twice their resting surface area by the enlarging uterus. Braxton Hicks contractions are physiologically present throughout the pregnancy. [20]

The thickness of the membranes was reduced near the rupture site. They speculated that this thinning might represent a local phenomenon secondary to chronic stress during gestation, which slowly produces membrane changes. [20]

Where pressure is applied to the membranes the resultant stretched extension consists of 2 components, an elastic component that is recoverable and a non-recoverable component called the creep extension. After any deformation, the membrane will become thinner than it was

originally, as a function of the non-recoverable creep extension. Preterm membranes can sustain greater stress application than term membranes because of less strain hardening and a greater ability to creep allowing membranes to thin out more before rupturing. [20]

The mechanical stress is induced by friction and adhesive forces that inhibit movement of chorion against the amnion or deciduas and prevent dissipation of locally applied forces arising from Foetal movements. Amniotic fluid proteins such an albumin and globulin are good adhesive and might predispose to this situation. On the contrary, surface active phospholipids (surfactants), present in the amniotic fluid can adhere to the membranes making them hydrophobic, and decreasing their surface energy, thus improving their release and boundary lubricating properties. The data indicate that the surface energy of the chorion and amnion in cases of premature rupture of membranes is significantly higher than the membranes that do not rupture prematurely. These membranes do not possess the properties necessary to avoid the buildup of local mechanical stress and protect them from tear. [20]

AMNIOTIC FLUID

The foetus is surrounded by amniotic fluid. The terms ‘liquor amnii’ and amniotic fluid, both imply a relation between the membrane and the

fluid, beyond mere anatomical containment, and many have believed the membranes to be the origin of the amniotic fluid and the regulator of its water and solute content.

Thus composition of the amniotic fluid is different in the two halves of pregnancy. In the first half, the concentration of the major solutes are more closely related to those in the Foetal than in the maternal serum, and the amniotic fluid may be regarded as part of the Foetal extracellular fluid space.

Sodium and water have been shown to pass through the Foetal skin until the time the skin becomes impermeable, probably at about 20 week when the close relation between the Foetal weight and the amniotic fluid volume breaks down.

In the second half of pregnancy, the biochemical composition of the amniotic fluid changes progressively as pregnancy advances. It may be that increasing stratification and cornification of the Foetal skin impedes and finally prevents diffusion. Thereafter, the changing characteristics may reflect the maturation of the Foetal renal function, explaining the rise in urea and creatinine concentrations and the fall in osmolarity and sodium concentration. The sources of origin of amniotic fluid are as follows;

1. Transudation from maternal blood across the membranes.

2. Foetal contributions

    a. Transudation across skin, lungs, and umbilical cord.

    b. Secretions from tracheo-bronchial tree, genito urinary tract and oropharynx.

3. Secretions from amniotic epithelium

The volume of amniotic fluid increases rapidly with the growth of the products of conception averaging about 50 ml at 12 weeks of pregnancy. At 20 weeks the volume is about 400 ml, at 35 weeks; it reaches a peak of nearly one liter. During the last few weeks of pregnancy its volume decreases and at 43 weeks the range varies from 100 to 600 ml.

COMPOSITION OF AMNIOTIC FLUID

The amniotic fluid is a heterogeneous suspension. It consists of 98-99% water, 1-2% solids, about one half of the solids are organic, and of this 50% is protein. Other organic constituents are glucose, urea, NPN uric acid and creatinine.

ELECTROLYTES

During the first half of the pregnancy, sodium and chloride concentrations are more similar to Foetal than maternal serum. Later, the fluid becomes progressively hypotonic with decreasing sodium and chloride value. Potassium ,calcium, magnesium, phosphorus, zinc, iron and sulphur are also present with no significant changes as pregnancy advances. The mean level of bound zinc in amniotic fluid is 3.1μmol/L; Low amniotic fluid zinc level is associated with increased risk of infection.

HORMONES

Various hormones present in the amniotic fluid include, pregnanediol, oestriol, 17 – keto steroids and human prolactin.

ENZYMES

Alkaline phosphatase increases until 7^{th} month of pregnancy and then remains constant. The concentration of acid phosphatise is similar to that of the maternal serum. Other enzymes like lysozymes are also present in amniotic fluid. Prostaglandins have also been identified in the amniotic fluid.

It has been shown that about 4% of water is exchanged per hour in the amniotic fluid. At term, the exchange from maternal to amniotic fluid is very small or negligible while the transfer rates from the foetus to the mother are high, being maximum from the foetus to the amniotic fluid. A considerable amount of amniotic fluid is lost by swallowing at the rate of 700 ml/24 hrs by the foetus.

ETIOLOGY OF PROM

In most pregnancies, labour begins in the presence of intact Foetal membranes. Without intervention, the membranes usually remain intact until approximately 8 cms of cervical dilation. The pressure necessary to cause membrane rupture experimentally not only is greater than the baseline resting tone of the intrauterine cavity, but also generally exceeds that generated by normal labour. The clinical entity of PROM that can occur in the absence of labour with an undilated cervix even at bed rest and also remote from term is an enigma that remains only imperfectly explained. Hence, a number of hypotheses have been proposed in an attempt to explain its etiology. At present, majority of instances of PROM probably are secondary to multiple factors. [21]

1. Etiology of PROM has been related to many variables including;

    a. Maternal age

    b. Parity

    c. Trauma

2. Presenting part acts like a ball valve, preventing the intrauterine pressure acting directly on the bag of membranes. Badly fitting presenting part as in malpresentations and cephalopelvic disproportion result in the intrauterine pressure being directly transmitted to the bag of membranes, causing it to rupture prematurely.

3. A number of pregnancy related conditions have been implicated in the etiology of PROM in individual instances. Multiple gestation and polyhydramnios have been noted, presumably acting by stretching the membranes excessively. [22]

4. Anatomic variations of the membranes such as marginal cord insertion might constitute a local defect, reducing tolerance to stress

at that site. A 47% incidence of PROM in association with this condition.

5. It was the inherent weakness of the membranes that is responsible for PROM. [20, 24] Congenital and acquired fenestrations of membranes have also been implicated as causative factors.

6. It has also been speculated that viral infection may involve the membranes with secondary rupture. [19]

7. Degeneration of amniotic epithelial cells is considered as a cause for premature rupture of membranes at term. [19] Electron microscopy has revealed extensive degenerative changes in amniotic epithelial cells. It has been reported that plasminogen is fixed to the damaged amniotic epithelial cells and this may have a role in PROM especially in pre-term cases. Subsequent activation of the plasminogen to the powerful protease plasmin may be responsible for cellular damage leading to PROM.

8. The occurrence of a congenital defect in the amniotic membranes appearing as a small semilunar communication between the amniotic cavity and the space between amnion and chorion, situated near the insertion of the cord, which allows amniotic fluid to pass

from the amniotic cavity to this space, where it leaks directly above the internal OS.

9. Variable thickness and tensile strength of the membranes have been reported as etiological factors.

10. The strength of Foetal membranes was inversely proportional to the Foetal weight i.e. Tensile strength was reduced with increased Foetal weight. It is possible to postulate that the higher Foetal weight may be responsible for the higher intrauterine pressure. This in turn is most likely to result in rupture of membranes with or without other underlying causes. [13]

11. The dilated cervix in patients with cervical incompetence exposes the Foetal membranes directly to the vaginal micro flora and secretions, predisposing to both chorioamnionitis and PROM. Rupture of membranes in patients with an incompetent cervix is also frequently the inadvertent consequence of attempts to manage this condition by placement of a cervical encerclage. [25] Prostaglandins implicated as playing a role in post encirclage PROM.

12. Ripening of cervix (the connective tissue of which, like the amnion, contains large amounts of collagen) and weakening of the amniotic

membrane may be modulated by similar mechanisms that decrease the collagen content of these structures. The collagen content of the amnion decreased significantly during the last 8 weeks of pregnancy. In addition, the collagen content of amnion obtained from patients with PROM was significantly lower than that of amnion from patient without PROM, even after controlling for gestational age. There seems to be a reduction in collagen content in pre-term amnions that rupture. [26] However, this reduction was not due to a general decrease of all collagen types but rather to specific and remarkable reduction in type III collagen. Type III collagen is interstitial collagen within the extra cellular matrix and is responsible for the elastic tensile strength of the tissue. No difference in collagen types was observed at term whether or not PROM occurred.

13. The granulocyte elastase is capable of preferentially degrading Type III collagen. Any condition resulting in a neutrophilic infiltration of the amnion, such as infection might cause PROM.

14. Enzymes present in chorioamnion or amniotic fluid could depolymerise collagen by destroying the collagen cross link area. [20] Since micro-organisms present in the cervico-vaginal flora also

produce proteases, exposure of the membranes to the genital tract micro flora could cause local membrane weakening and PROM.

15. Alterations in collagen would affect the elastic properties of the membranes while changes in the fluid osmolarity might affect its viscous component. Amniotic fluid prolactin appears to play a role in regulating the volume, osmolarity and electrolyte concentration of amniotic fluid and might therefore influence the viscoelastic properties of the Foetal membranes. [25]

16. It is also possible that proteolytic enzymes from bacteria, and the inflammatory response they elicit in the host, might so weaken the membranes that PROM occur. The effect of Group B streptococcal infection on the amnion is in the form of decrease in desmosome counts and alterations of the basement membrane. [27]

17. The membranes collected from patients with PROM following labour have significantly higher peroxidase activity. [28] Peroxidase in conjunction with hydrogen peroxide produced by bacteria and a halide constitute a potent antimicrobial system that is not only cytotoxic but capable of oxidatively cleaving peptide bonds and thus causing membrane weakness. These investigators also reported that treatment of Foetal membranes with lysolecithin reduces their

bursting pressure. Amniotic fluid contains lecithin, which can be converted to lysolecithin by the action of phospholipase A2. Therefore in the presence of bacterial contamination of the membranes these two mechanisms might act in concert to cause PROM. It has been suggested that occult intra-uterine or ascending choriodecidual bacterial invasion in some instances precedes PROM. The thought that mild or moderate uterine activity may be brought about by subclinical infection is supported by the finding of phospholipase A2 activity in vaginal flora bacteria (Eg. B-fragilis, peptostreptococcus species). This activity is postulated to trigger labour through prostaglandin synthesis from native amniotic membrane phospholipids. The contractions thus produced could cause early membrane rupture, especially if they have been subjected to stress over a prolonged period. The sequence of events is therefore thought to be infection, occult labour, membrane weakening, and then PROM. An alternate pathway for the initiation of uterine activity (and thus PROM) by infection process is as follows:

Bacterial lipopolysaccharides (Endotoxin) in high concentration and inter leukin-1 (Pyrogen) are apparently

both capable of inducing production of PGE2 by amniotic epithelium, thus serving as signals for initiation of labour in presence of maternal or intra-amniotic infection.

18. A study of Foetal immunoglobulin is associated with PROM. The cord IgA and IgM levels were significantly elevated compared with levels in control infants. [29] More important; there was both clinical and immunological evidence (elevated IgA) of two distinct peaks of infection. The first occurred within 12 hours of rupture, while the other not until 12 hours of rupture, suggesting that for patient in the first group infection was present before rupture and might have been the cause of rupture.

19. When compared cervical cultures from women having PROM with cultures from a control group of women, results showed that anaerobes, especially B. fragilis was present in women with PROM.

20. Defects in the membranes may arise secondary to poor nutritional status or ingestion of toxic substances. Ascorbic acid is required for the production and maintenance of collagen in tissues. A relationship was found between low plasma ascorbic acid levels and PROM in patients from lower socio-economic classes.

21. Copper plays an important role in the maturation of collagen and elastin, and it has been shown that copper deficient diet will result in increased fragility of supporting structures. [20]

22. Zinc is a requisite constituent of the amniotic fluid zinc-polypeptide complex bacterial inhibitor in amniotic fluid. Zinc deficiency might result in failure of the bacterial inhibitor to prevent intraamniotic infection and hence, PROM.

23. Sexual intercourse: Theoretically could initiate PROM by means of several mechanisms.

    a. Bacteria in seminal fluid or vaginal secretion may be deposited adjacent to the cervical OS and thus in proximity to the membranes.

    b. Uterine contractions stimulated by orgasm or the action of seminal prostaglandins can lead to premature labour.

    c. Seminal fluid enzymes could have a direct toxic effect on membranes.[25]

    d. The relationship between coitus and chorioamnionitis was established. There was an increased incidence of chorioamnionitis limited to the extra placental membranes. The

rupture of the membranes before the onset of labour was increased two fold in those patients with recent coitus.

24. Sometimes, PROM can be iatrogenic like in the case of amniocentesis.

DIAGNOSIS

Diagnosis of ruptured membrane can be established clinically or by laboratory methods. Most often the diagnosis is obvious by history of leak and direct demonstration of leaking through cervical os on carefully performed per speculum examination.

HISTORY

History of sudden passage of fluid from vagina in a gravid patient is strongly suggestive of ruptured membranes.

VISUALIZATION OF AMNIOTIC FLUID IN THE VAGINA:

A sterile speculum is introduced into the vagina to observe if amniotic fluid is seen escaping out of the cervix. Copious fluid pouring out is pathognomonic of rupture of membranes. Amniotic fluid is colorless and may contain white flecks (vernix). If no fluid is immediately seen, ask the

patient to cough and observe for a gush of fluid per vagina or applying slight fundal pressure over the uterus may provoke leaking.

LABORATORY DIAGNOSIS

In clinical practice many times pregnant women present with the history of watery vaginal discharge and physical examination may not reveal the diagnosis of PROM. This is particularly so when cervical os is closed or flat membrane felt over the presenting part on account of high leak. Other discharges like urine, excessive vaginal discharge and inflammatory exudates may also obscure the clinical diagnosis. In such conditions laboratory diagnosis helps. They are:

1. **NITRAZINE TEST**: The vaginal PH is normally 4.5 – 5.5. Amniotic fluid, usually has a pH of 7 – 7.5. Nitrazine paper quickly will turn deep blue if the vaginal fluid has an alkaline pH. The membranes probably are intact if the colour of the paper remains yellow or changes to olive yellow. Antiseptic solutions, urine, blood and vaginal infections alter the vaginal pH and cause false positive result. This test is simple, rapid, inexpensive and fairly reliable method.

2. **FERN TEST:** Ferning results from the drying out of salts contained in the amniotic fluid. The ferning is due to crystallization of

sodium chloride derived from the amniotic fluid. To perform the test, a sample of fluid is placed on a glass slide and allowed to dry. The preparation is observed under microscope, looking for a crystallization pattern that resembles a fern. The accuracy of the test is affected by blood or meconium; the test may produce false positive results if the sample is obtained from the cervix, because dry cervical mucus forms an arborization pattern that may be confused with PROM. The fern test gives 4.8% false negative and 4.4% false positive results. The diagnosis of PROM is close to 100% reliable if the vaginal fluid gives both positive nitrazine and positive fern test.

3. **EVAPORATION TEST:** For the evaporation test endocervical samples are heated until the water content has evaporated. If a white residue is left, amniotic fluid is present. If the residue is brown the membranes are intact.

4. **ULTRASOUND EXAMINATION:** USG should not be used as the primary means of diagnosis of PROM. False positive findings may occur in patients with oligohydramnios resulting from causes other than PROM, and false negative results may occur in patients with discrete amniotic fluid losses. However it should be assumed that PROM has occurred if ultrasound examination shows little or no fluid in the uterus. In

contrast, the presence of a normal amount of fluid makes the diagnosis of PROM unlikely.

5. **INTRA-AMNIOTIC FLUORESCEIN:** Injection of fluorescein into the amniotic cavity is rarely indicated for the diagnosis of PROM. This procedure may be performed when PROM cannot be confirmed with non invasive technique. In these cases 1 ml of sterile solution of 5% sodium fluorescein is injected into the amniotic cavity. A tampon is placed in the vagina and examined with a long wave, ultraviolet light 1 or 2 hours later. The detection of fluorescent material is equivalent to a positive diagnosis of PROM, one ml of sterile indigo carmine may be used instead of fluorescein and the tampon is inspected for the presence of a blue discoloration.

6. **AMNIOSCOPY:** Amnioscopy is an invasive procedure rarely indicated in the diagnosis or management of PROM. It requires a dilated cervix to introduce a metallic or plastic cone for direct visualization of the membranes and the AF. Amnioscopy may cause PROM in patients with intact membranes and may carry a large bacterial inoculation into the amniotic cavity in patients with PROM.

7. **DIAMINE OXIDASE TEST**: Diamine oxidase is an enzyme produced by decidua, which diffuses into the AF, measurement of diamine

oxidase by paper strips placed in contact with the vagina is an accurate way to diagnose PROM. The test requires relatively elabourate labouratory procedure and is not ready for general use.

8. **FOETAL FIBRONECTIN**: Foetal fibronectin is a large molecular weight glycoprotein present in large amounts in the AF. This substance can be detected in the endocervix or the vagina of patients with PROM by means of an enzyme linked immunosorbent assay. The test seems to be highly accurate and is not affected by blood, but meconium may interfere.

9. **ALPHA FETOPROTEIN TEST (AFP)**: AFP is present in high concentration in AF, but does not exist in vaginal secretions or in the urine. Therefore determination of this substance in the vaginal secretion is an accurate test for the diagnosis of PROM. A study using a rapid calorimetric monoclonal antibody AFP test found a sensitivity of 98% for AFP, 77% for nitrazine and 62% for ferning. Specificity was 100% for AFP test. Maternal blood contamination affects the accuracy of test.

10. **IDENTIFICATION OF LANUGO**: This is a microscopy technique for detecting rupture of Foetal membranes. Lanugo and uric acid crystals in vaginal fluid can be identified. The findings of Foetal hair were specific, yet the process was time consuming, requiring preparation of

multiple slides. Foetal hair was present in scanty quantity and identification of urate crystals was non specific. Because of these difficulties, the technique was abandoned.

11. **STAINING FOR LIPID**: Nile blue sulfate staining was introduced for the identification of desquamated Foetal epithelial cells. Oxazone present in Nile blue sulfate stains, the Foetal cells orange brown.

COMPLICATIONS OF PREMATURE RUPTURE OF MEMBRANES

MATERNAL COMPLICATIONS

1) Chorioamnionitis:

Infection occurs frequently in patients with PROM. The early diagnosis and prompt treatment are essential. The overall evidence of chorioamnionitis ranges from 4.2% - 10.5%.[15]

The diagnosis of chorioamnionitis is clinical. According to Gibbs et al, it requires the presence of fever >100.4 deg F and atleast 2 of the following conditions – Maternal tachycardia (HR > 100 bpm), Foetal tachycardia (>160bpm), uterine tenderness, foul smelling vaginal discharge, maternal leukocytosis (>15,000), C reactive Protein >2.7 mg/dL.[15]

Amniotic fluid culture is valuable for identifying the bacteria causing infection and their antibiotic sensitivity. The amniotic cavity generally is sterile. The term microbial invasion of the amniotic cavity refers to the presence of a positive amniotic fluid culture, regardless of the presence or absence of clinical signs or symptoms of infection.

Pathologic chorioamnionitis refers to the presence of acute inflammatory lesions in placenta and membranes, varying degrees of polymorphonuclear leukocytic infiltration of the chorioamnion is found more frequently than the clinical disease.

The determination of C-reactive protein (CRP) in blood a substance that increases markedly in patients with infection helps in diagnosing chorioamnionitis. The median CRP concentration during pregnancy ranges from 0.7 to 0.9 mg/dl.

A valuable amniotic fluid test is the leukocyte esterase assay. A positive assay has 91% sensitivity and 95% positive predictive value for the diagnosis of chorioamnionitis. The incidence of chorioamnionitis is more if the latent period is more than 24 hours. 1.7% of the patients developed fever within 24 hours after PROM, 7.5% between 24-48 hours and 8.6% beyond 48 hours. [30]

The patients may have endometritis, parameteritis, and pyelonephritis. In rare cases of extensive infection with uterine necrosis, multiple abscess or clostridial infection, a life saving hysterectomy may be necessary. Occasionally uncontrolled infection may lead to septicemia, shock, disseminated intravascular coagulation (DIC), adult respiratory distress syndrome and maternal death.

Unless the patient is grossly neglected maternal mortality should not occur due to PROM. Maternal mortality and morbidity are primarily related to sepsis and complications arising from efforts to affect delivery such as oxytocin induction or caesarean section.

2) Abruptio placenta

Patients with PROM have an incidence of abruption placenta of approximately 6%. Abruptio usually occurs within the setting of prolonged and severe oligohydroamnios. Nelson et al in a retrospective analysis of all patients with prolonged PROM, estimated the risk of abruption during expectant management to be 4%. The reason for the high incidence of abruption in patients with PROM is the progressive decrease in intrauterine surface area causing detachment of the placenta.

3) Cord prolapse

If it is associated with malpresentation.

4) Dry labour

After continuous escape of liquor for a long duration.

5) Caesarean section wound infection

According to Pandit et al regarding caesarean section wound infection Out of 30 cases (Journal of Nepal Medical Association 2003), 10 (33.33%) had premature rupture of membrane, 7 cases had rupture of membrane more than 24 hours, 2 cases had rupture of membrane more than 6 hours. In 1 case it was only 3 hours duration. Out of 7 who had rupture of membrane more than 24 hours, 4 developed major and 3 developed minor wound infections. Thus major wound infection which required resuturing had either moderate meconium or PROM > 24 hour or more number of per vaginal examinations done.

FOETAL AND NEONATAL COMPLICATIONS

1) Neonatal Sepsis

PROM increases the risk of infection in the neonate to around 1.3% following prolonged rupture of membrane and 8.7% of neonatal sepsis

following prolonged and clinical amnionitis. Significant predictive risk factors were histological evidence of inflammation in the placental chorionic plate, gestational age less than 34 weeks, male sex, APGAR score of less than 6 in 5 minutes and clinical amnionitis. Perinatal mortality is due to sepsis and respiratory distress. In a recent study of PROM, the neonatal mortality was reported as 6.7% of which 55% was due to infection. Volume of AF remaining after PROM is of importance as it possesses antibacterial activity. Neonatal infection may manifest as septicaemia, meningitis, pneumonia, pyoderma, umbilical sepsis and conjunctivitis. The first manifestations of impending Foetal infection are non reactive NST and the absence of Foetal breathing movements. The overall incidence of perinatal mortality reported in the literature ranges from 2.6 to 11%.

2) Perinatal Asphyxia

PROM can predispose to Foetal asphyxiation through several mechanisms. They include cord complications, either cord compression or prolapse, malpresentation and Foetal compromise secondary to maternal fever and chorioamnionitis. Clinical markers such as low APGAR scores, meconium staining and abnormal Foetal heart rate patterns have been used.

3) Foetal deformities

An important fact to consider when planning management of PPROM is the high incidence of congenital malformations. In a study by Gunn et al, 1970- 8% of perinatal deaths in women with PPROM were caused by multiple congenital abnormalities. Facial and skeletal deformities may occur as a result of prolonged PROM, as a result of severe, prolonged oligohydroamnios. With the lack of fluid, the foetus loses the protective cushion against compression and has severe limitation in the ability to move the limbs leading to deformities. But most of these cases occur with PROM < 26 weeks and with a latency period of >5 weeks. (Nimrod et al, 1984)

4) Cerebral Palsy

It is a long term sequel of PROM, particularly in cases complicated by acute chorioamnionitis or intrapartum acidosis and hypoxia. Unfortunately these complications occur rather frequently with PPROM. [15]

MANAGEMENT OF PROM AT TERM

Most patients (80-90%) with PROM at term will get into labour within 24 hours of rupture of membranes (ROM). Most clinicians choose an arbitrary latent period (rupture of membranes and onset of labour) then

induce at the end of that time if necessary. Such allowed latent periods usually vary between immediate and 24 hours.

The longer the time between membrane rupture and delivery, the greater the risk of infection, especially if vaginal examinations are performed frequently. [31]

To prevent infection, sterile speculum examination is to be done and repeated vaginal examination is to be avoided.

In term pregnancy, with diagnosed rupture of membranes and no evidence of infection or obstetric hazard, it has been suggested that there is no need to rush. A delay of at atleast 12 hours will allow many women to reach active labour spontaneously and their chance of spontaneous delivery is enhanced.

Antibiotic therapy in premature rupture of membrane is useful in reducing neonatal and maternal infection. Antibiotics also decrease the risk of postpartum endometritis.

The first step is to identify the women who are in need of immediate delivery-women in advanced labour, those with acute chorioamnionitis / subclinical infections, women at a high risk for severe infections (like immunocompromised, on corticosteroid therapy, insulin dependent

diabetics), foetuses with non reassuring well being testing and foetuses with lethal abnormalities. [15]

The patients in active labour are accelerated. For patients with an unfavourable cervix, some authors advocate immediate induction while some prefer expectant management.

The important inferences from various studies on PROM are given below:

1. Clinical chorioamnionitis, positive maternal group B streptococcal status were identified as independent predictors of neonatal infection in PROM (Am American Journal of Obstetrics and Gynaecology 1998 September 179 (635 to 9).

2. Both active and expectant management were in general acceptable forms of care. Similar rates of neonatal infection and caesarean section were found with active or expectant forms of management. (International Term PROM Trial – Hannah et al.1996) (Level I evidence).

3. No difference in neonatal infection or caesarean section between active and expectant management. But, active management is associated with significant reduction in Chorio amnionitis, endometritis, NICU admission. (Cochrane review).

4. A higher rate of spontaneous deliveries was found among nulliparous women with prolonged latency (48 hours) as compared to brief latency (<24 hours) prior to induction. (BJOG: Volume 103, Issue 8, Pages 755-762, August 1996).

5. Even when the cervix is unfavourable, the majority of women labour spontaneously within 12 hours (Dare et al 2006).

6. The risk of PROM at term relate to maternal and neonatal infection, prolapsed cord and Foetal compromise resulting in operative delivery or low 5 minute APGAR score (RCOG 2001)

If left alone, more than 50% of women get in to labour within 12 hours of PROM. Induction after this may result in lesser number of operative deliveries / failed induction. At the same time neonatal and maternal infection may not be much increased. Hence in this study maternal and neonatal outcome in immediate induction is compared with that of delayed induction (after 12 hours).

MATERIALS AND METHODS

MATERIALS AND METHODS

SOURCE OF DATA

This was a COMPARATIVE STUDY involving women admitted to the Institute of Obstetrics and Gynaecology with rupture of membranes prior to onset of labour (gestational age more than 37weeks up to 41 weeks & meeting other strict inclusion criteria as described below) and the neonates born to these women.

STUDY PERIOD

One year (2011-2012)

STUDY LOCATION

Institute of Obstetrics and Gynaecology, Egmore, Chennai-8.

METHOD OF DATA COLLECTION

INCLUSION CRITERIA

Women with

1. Term premature rupture of membranes < 12 hours duration at the time of admission.

2. No evidence of foetal distress.

3. No evidence of sepsis (*maternal tachycardia, pyrexia, uterine tenderness*).

4. No other risk factors in pregnancy e.g. *medical complications, malpresentation, abnormal lie, multiple pregnancy and previous caesarean section.*

5. Modified Bishops score < 6

6. All neonates born to women included in the study.

EXCLUSION CRITERIA

1. Premature rupture of membranes for > 12 hours at the time of admission.

2. Gestational age < 37 weeks, > 41 weeks.

3. Evidence of foetal distress / sepsis.

4. Medical complications, malpresentation, abnormal lie, multiple pregnancy and previous caesarean section.

5. Suspected CPD

6. Women in active labour.

7. Patients who are HIV positive or immune compromised.

PROCEDURE OF CONDUCTING THE STUDY

Singleton deliveries that follow rupture of membranes prior to the onset of spontaneous labour were included in the study (Premature rupture of membrane as described by Prichard IA et al, 1980) as long as the gestational age included in the study was more than 37 weeks upto 41 weeks. It was decided to analyze the term PROM because expectant management is the accepted norm in preterm PROM, but there is no such consensus in term PROM.

Patients who presented with pre labour rupture of membranes were admitted to the labour room. A detailed history was taken including age, menstrual and obstetric history with emphasis on exact time of rupture of membranes, duration and amount of leaking. In general examination, pulse, blood pressure, temperatures were noted followed by systemic examination. In obstetric examination, uterine height, presentation, position, lie of foetus and amount of liquor were noted. Duration and number of contractions were noted if present.

A sterile speculum examination was conducted. Rupture of membranes (ROM) was confirmed by visualization of the amniotic fluid

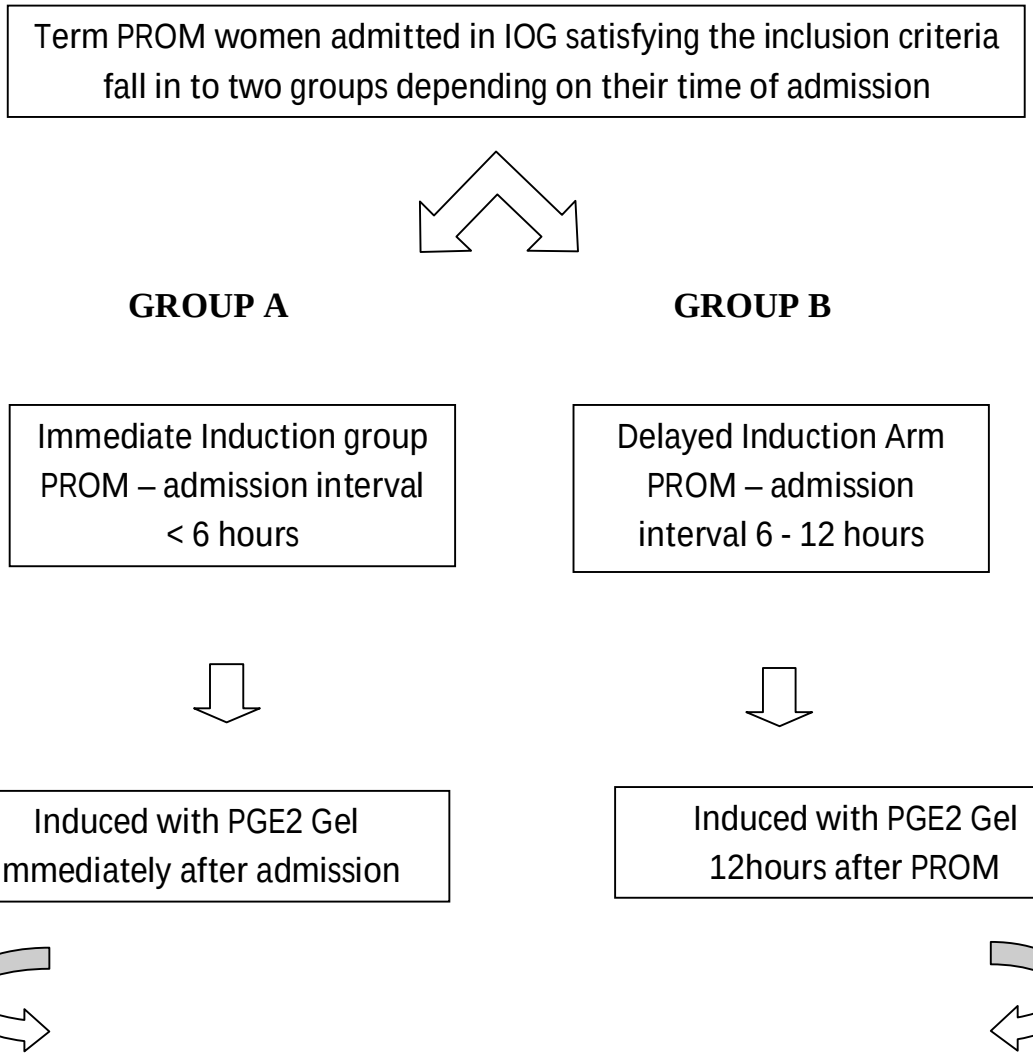
passing from the cervical os or by the presence of a pool of fluid in the posterior fornix. A high vaginal swab (HVS) was taken and sent for culture (In delayed induction arm,this was taken 12 hours after ROM ,while applying PGE2). Then, a per vaginal examination was conducted. The position, consistency, length and dilatation of the cervix along with the position of the presenting part were noted and the Modified Bishop's score was calculated.

MODIFIED BISHOP SCORE/ CALDER SCORE

MODIFIED BISHOP SCORE/ CALDER SCORE	**0**	**1**	**2**	**3**
Length	4 cms	2-4 cms	1-2 cms	<1 cm
Dilatation	<1cm	1-2 cms	2-4 cms	>4 cms
Consistency	Firm	Average	Soft	-
Position	Posterior	Mid	Anterior	-
Station of presenting part in relation to ischial spines	-3cm	-2 cm	-1/0 cm	+1/+2 cm

TOTAL SCORE

- **0 - 5 = UNFAVOURABLE.**
- **6 - 12 = FAVOURABLE.**



1. All women were monitored with cardiotocography.
2. Prophylactic antibiotics i.e. Ampicillin 1gm IV bd, Gentamycin 80mg IV bd.
3. Maternal pulse, BP & temperature monitored 4th hourly.
4. TC, High Vaginal swab taken for all patients.
5. If Bishop's score was unfavourable after 6 hours, 2nd dose of PGE2 Gel was repeated.
6. If favourable labour was augmented with Oxytocin.
7. All babies were examined by the Paediatrician after delivery for clinical evidence of early onset sepsis.Sepsis screen(TC,CRP,platelet count) was done for all babies. If positive, blood culture & sensitivity done.
8. If mothers show evidence of infection, relevant investigations taken(both antenatally and postnatally).

DIAGNOSIS OF CHORIOAMNIONITIS

The following criteria were used to determine chorioamnionitis. (Gibbs et al)

- fever >100.4 deg F
- and at least 2 of the following conditions –
    - Maternal tachycardia (HR > 100 bpm),
    - Foetal tachycardia (>160bpm),
    - uterine tenderness,
    - foul smelling vaginal discharge ,
    - maternal leukocytosis (>15,000/ dL)

Augmentation of labour with oxytocin was started once the patient went into active labour depending on the contractions (Cervix was well effaced and 3 cms dilated). Indications for Lower Segment Caesarian Sections (LSCS) were noted. Labour outcome of the cases were observed.

In the Post partum period, patients were further evaluated with a Urine Culture in those who had symptoms of urinary tract infection (burning micturition and increased frequency of urination). In the presence of a LSCS wound infection, a swab from the wound was sent for culture.

The neonates born to the women in the study were examined by the paediatrician immediately after birth and then once daily. Symptoms and signs of neonatal sepsis were looked for. A sepsis screen was performed (TC, platelet

count,CRP). All the neonates who were screen positive (any one test) were subjected to blood culture and sensitivity and were given antibiotics (Inj. Ciprofloxacin, Inj. Amikacin) for 5days. If culture positive, sensitive antibiotics were given for 15 days.

NOTE

Early onset Neonatal Sepsis (i.e. sepsis within 72 hours of birth) is attributed to exposure to bacteria in the antepartum and peripartum period. Late onset Neonatal Sepsis (more than 72 hours after birth) is usually nosocomial and hence not related to PROM (Manual of Neonatology, John. P. Cloherty).

SEPSIS SCREEN

(Manual of Neonatology, John. P. Cloherty)

- Blood culture and sensitivity
- Indirect markers:
    - Total leukocyte count - <5000/cumm or >15,000/cumm
    - Band forms
    - Toxic granules
    - Micro ESR - >15mm at the end of 1st hour
    - C-reactive protein > 1.2
    - Platelets - <1.5 lakhs/cu mm

The following outcomes were compared between the two groups.

1) PROM - delivery interval
2) No. of PGE2 doses
3) Mode of delivery
4) Newborn depression (l - min and 5 - min APGAR scores)
5) Neonatal sepsis
6) Maternal morbidity
7) Duration of hospital stay

RESULTS
AND
OBSERVATIONS

RESULTS AND OBSERVATIONS

Of the total no of deliveries in 2011-12 - there were 743 cases of term PROM (incidence: 5.2%).After applying the inclusion and exclusion criteria, there were 200 cases eligible for the study. They were divided into early and delayed induction groups depending on the time of admission.

PROM to admission interval < 6 hours - Early induction group

PROM to admission interval 6-12 hours - Delayed induction group

TOTAL NUMBER OF CASES INCLUDED IN THE STUDY: 200

DISTRIBUTION OF CASES INTO TWO GROUPS: (Table 1)

- Group A: PROM - admission interval < 6 hours.
- Group B: PROM - admission interval 6 - 12 hours.

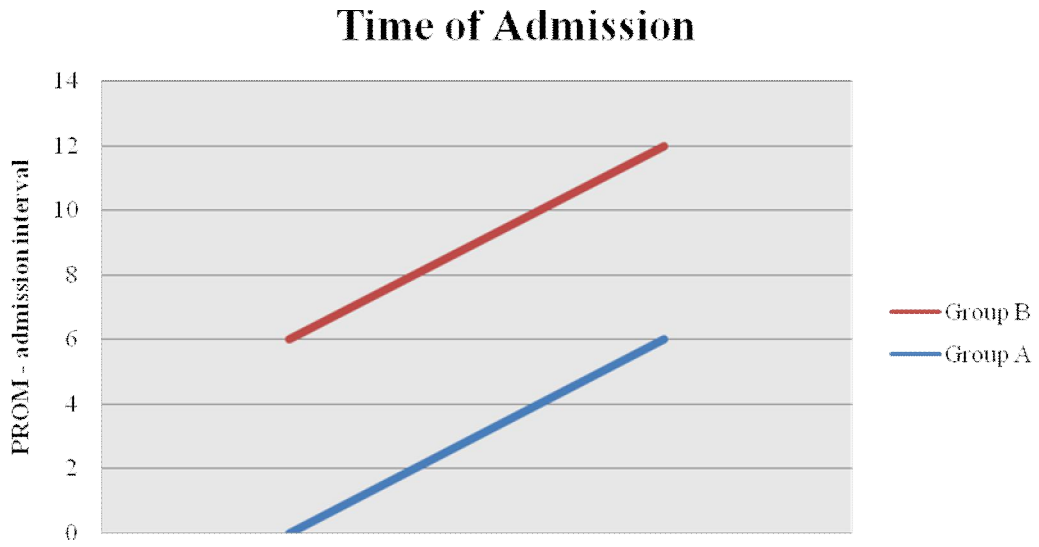
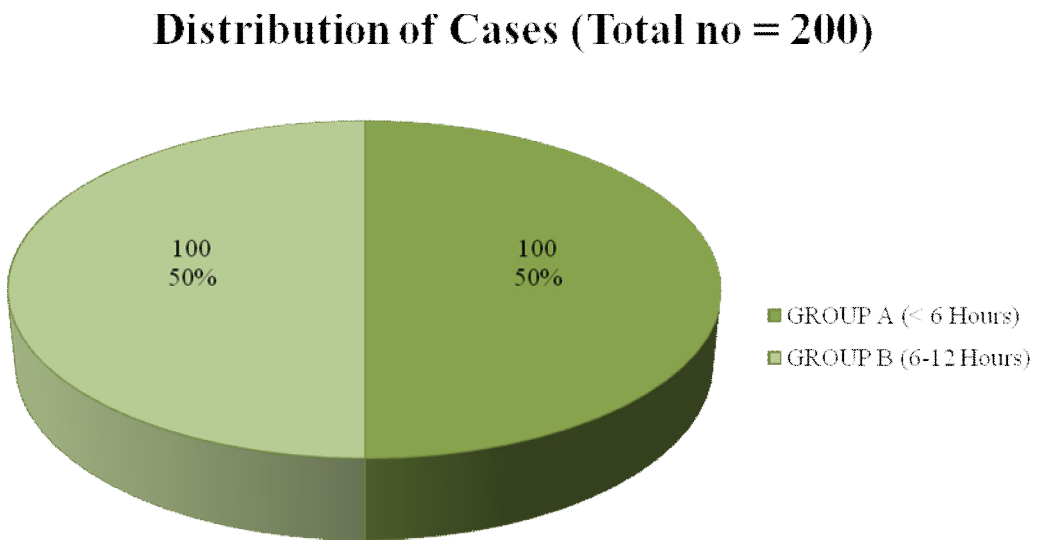


Table 1: DISTRIBUTION OF CASES

GROUP A (< 6 Hours)	GROUP B (6-12 Hours)
100 (50%)	100 (50%)

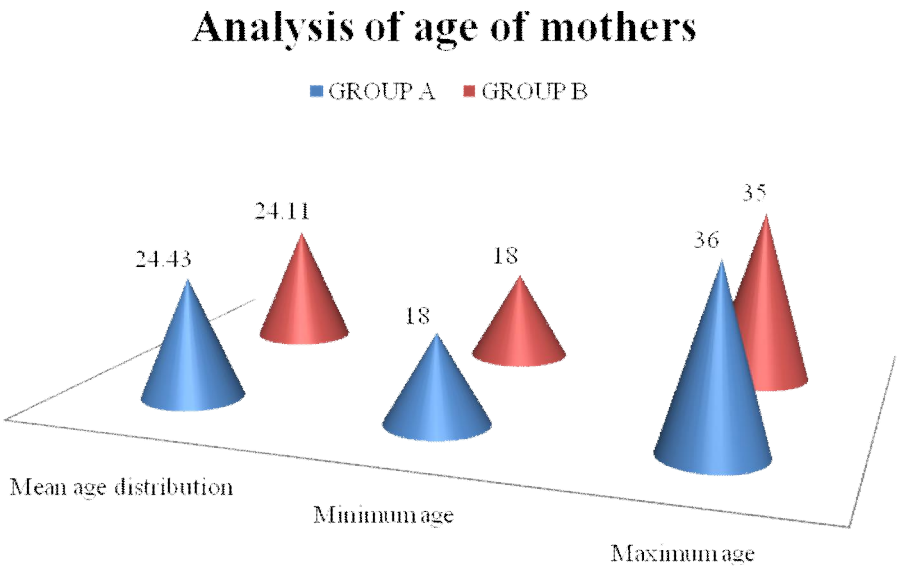


ANALYSIS OF AGE OF MOTHERS (Table 2)

In Group A, the age of mothers ranged from 18 years to 36 years with a mean of 24.43 years (S.D: 3.38). In Group B, maternal age ranged from 18 to 35 years with a mean of 24.11 years (S.D: 3.58). P value (t test): 0.514 – not significant. The two groups were similar in age distribution.

Table 2: ANALYSIS OF AGE OF MOTHERS

ANALYSIS OF AGE OF MOTHERS	GROUP A (n = 100)	GROUP B (n = 100)
Mean age distribution	24.43 years	24.11 years
Minimum age	18 years	18 years
Maximum age	36 years	35 years

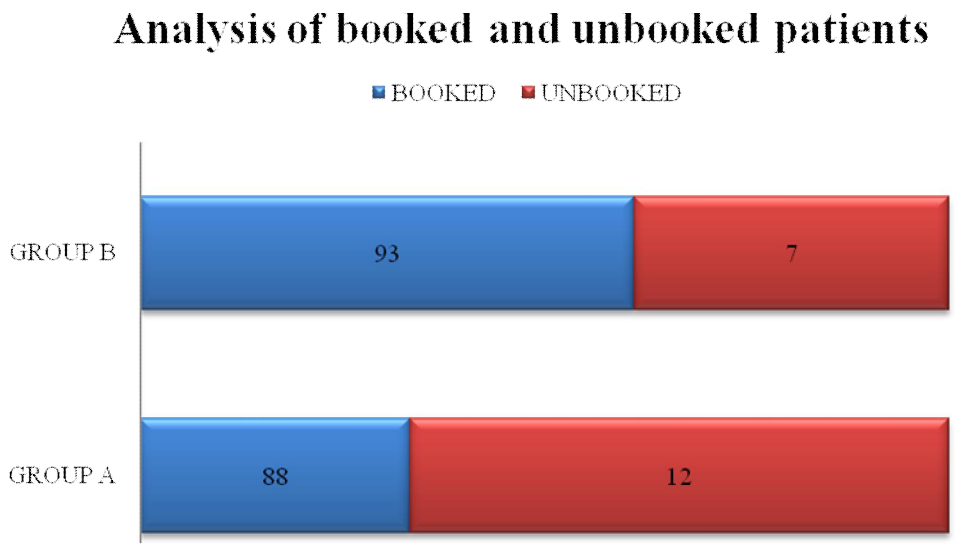


ANALYSIS OF BOOKED AND UNBOOKED PATIENTS (Table 3)

Cases are considered booked if the patients have had 3 antenatal checkups of which at least one in the third trimester. Most patients in both the groups were booked. Of the unbooked patients, 12 were in group A while 7 were in group B.

Table 3: ANALYSIS OF BOOKED AND UNBOOKED PATIENTS

	GROUP A	GROUP B	P VALUE
BOOKED	88	93	0.22
UNBOOKED	12	7	

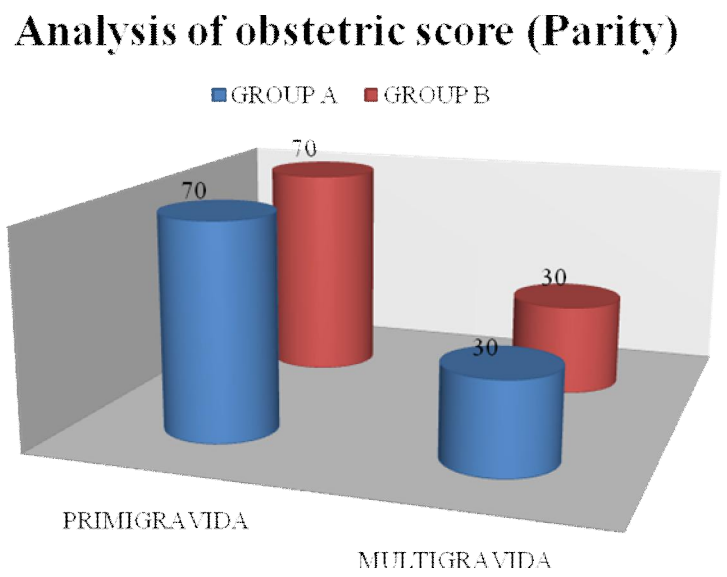


ANALYSIS OF OBSTETRIC SCORE (PARITY) (Table 4)

For comparability, 70 primigravida and 30 multigravida were included in each group.G2A1 were included in the primigravida.

Table 4: **ANALYSIS OF OBSTETRIC SCORE (PARITY)**

PARITY	GROUP A (n = 100)	GROUP B (n = 100)
Primigravida	70	70
Multigravida	30	30

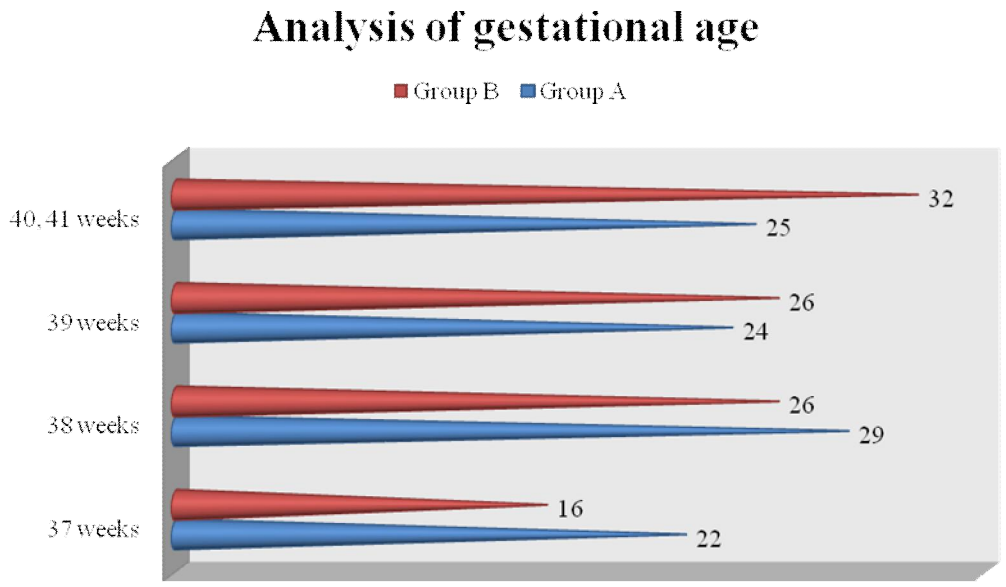


ANALYSIS OF GESTATIONAL AGE (Table 5)

The patients with gestational ages ranging from 37 to 41 weeks were included in the study. The patients in both groups were comparable with regard to gestational age (P: 0.562).The mean GA in both groups was 38 weeks.

Gestational Age (weeks)	Group A (n=100)	Group B (n=100)	P value
37	22	16	0.562
38	29	26	
39	24	26	
40,41	25	32	
Mean GA	38.54	38.3	

Table 5: ANALYSIS OF GESTATIONAL AGE



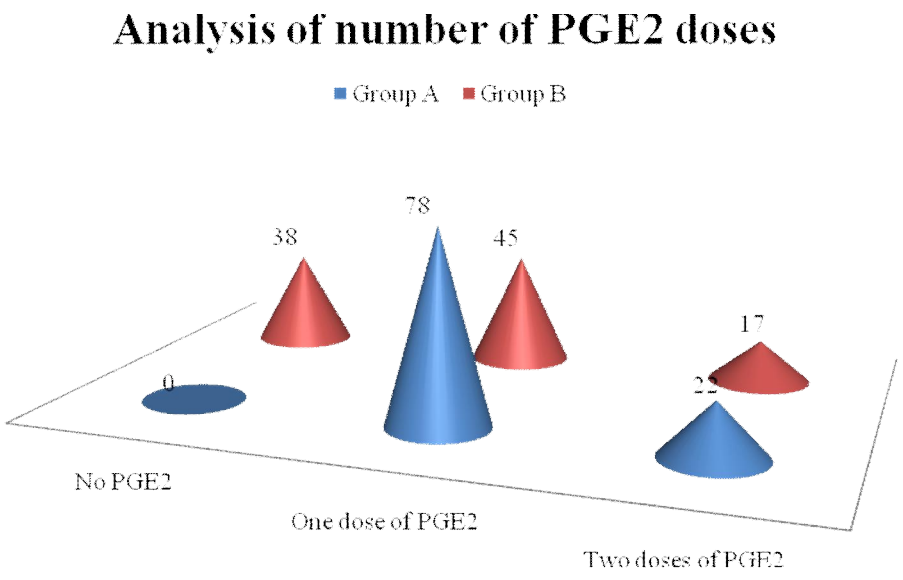
ANALYSIS OF NUMBER OF PGE2 DOSES (Table 6)

38 cases in the delayed induction group entered active labour during the waiting period. They did not require induction. Significantly higher doses of PGE2 (p value 0.00) were required in the immediate induction group as compared to the delayed induction group (122 versus 79). 22 patients in the immediate induction group needed 2 doses of PGE2 while only 17 in the delayed induction group needed 2 doses.

Table 6: ANALYSIS OF NUMBER OF PGE2 DOSES

NO. OF PGE2 DOSES	GROUP A (n = 100)	GROUP B (n = 100)
0	0	38
1	78	45
2	22	17

Pearson Chi-Square P-value = 0.000 (Significant)



PROM-DELIVERY INTERVAL (Table 7 & 7A)

Most of the patients (48%) delivered within 14to 20 hours of PROM. The earliest PROM-delivery interval was 8 hours (one patient in early induction group). One of the patients in the delayed induction group had the longest PROM-delivery interval of 30 hours. More number of patients (78%) in the early induction group delivered within 14 hours of PROM as compared to the delayed induction group. The PROM-delivery interval was significantly more in the delayed induction group as compared to the early induction group(statistically significant: Pearson chi P value: 0.00).

Table 7: PROM-DELIVERY INTERVAL

PROM-DELIVERY INTERVAL	GROUP A(100)	GROUP B (100)
8-14 hours	49	19
14-20 hours	46	50
>20 hours	5	31

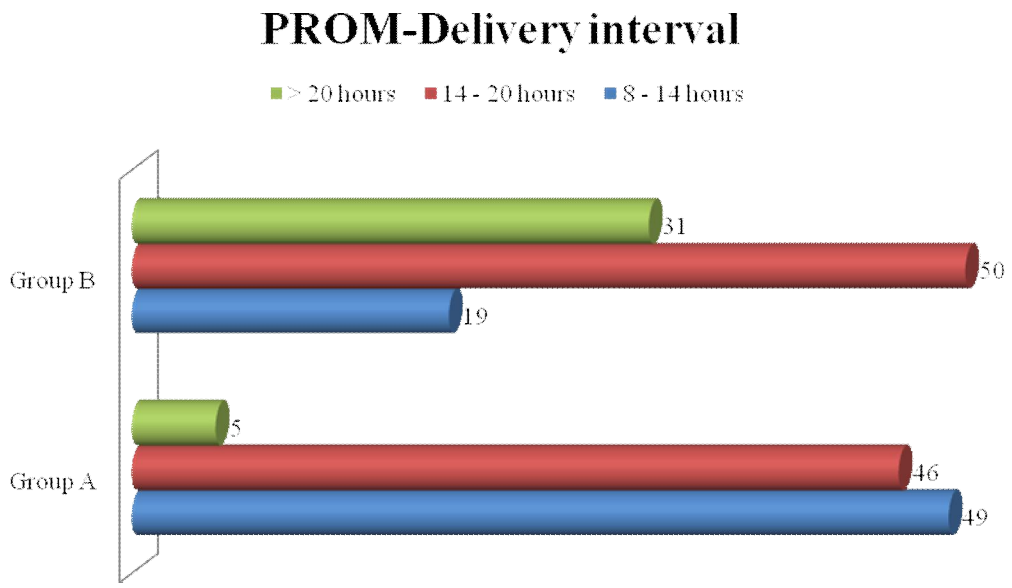
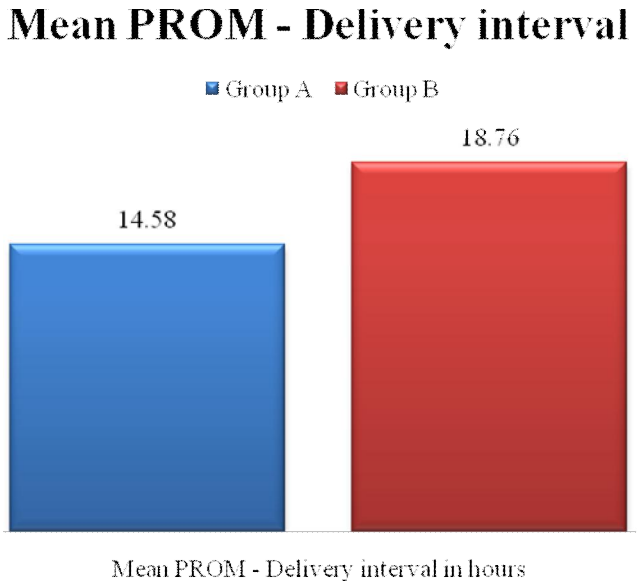


Table 7A: MEAN PROM-DELIVERY INTERVAL

	GROUP A (100)	GROUP B (100)	P VALUE
Mean PROM-delivery interval	14.58 hours	18.79 hours	0.00(Significant)

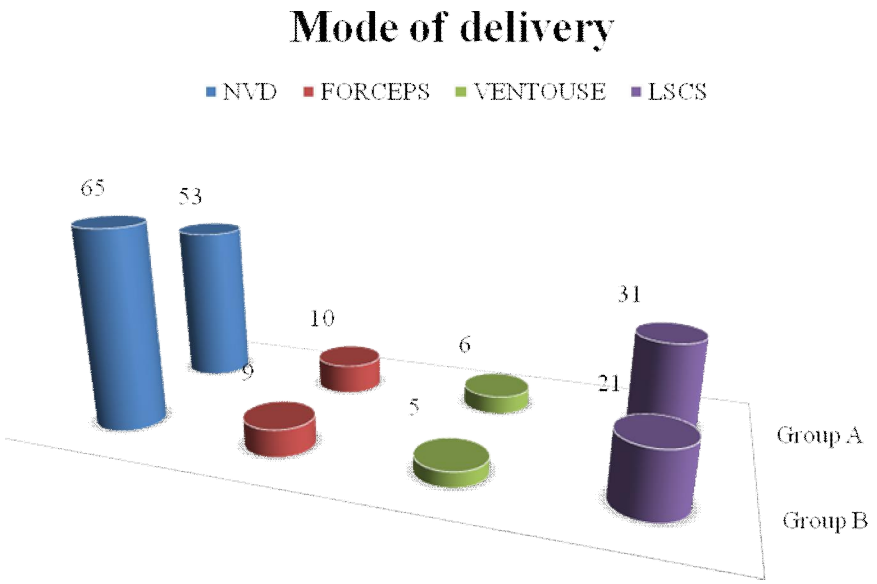


MODE OF DELIVERY (Table 8)

There were more number of Caesarean sections (31) in the early induction group when compared to the delayed induction group (21) which was statistically significant.(P value:0.049).The percentage of operative vaginal deliveries were almost the same in both groups.

Table 8: MODE OF DELIVERY

	GROUP A (100)	GROUP B (100)	P VALUE
NVD	53	65	
FORCEPS	10	9	
VENTOUSE	6	5	
LSCS	31	21	0.049



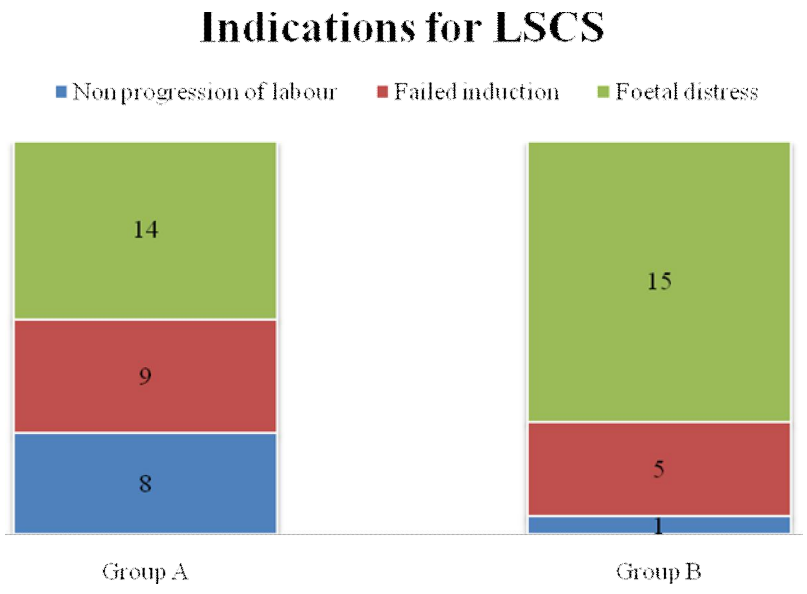
INDICATIONS FOR LSCS (Table 9)

71% of LSCS done in group B were for foetal distress as compared to 45% in group A. There were significantly more failed inductions and labour abnormalities in group A when compared to group B.

Table 9: INDICATIONS FOR LSCS (n= 52)

	GROUP A (31)	GROUP B (21)
FOETAL DISTRESS	14 (45.1%)	15 (71.4%)
FAILED INDUCTION	9 (31%)	5 (23.8%)
NON PROGRESSION OF LABOUR	8 (27.6%)	1 (4.8%)

P value: 0.045 (Significant)

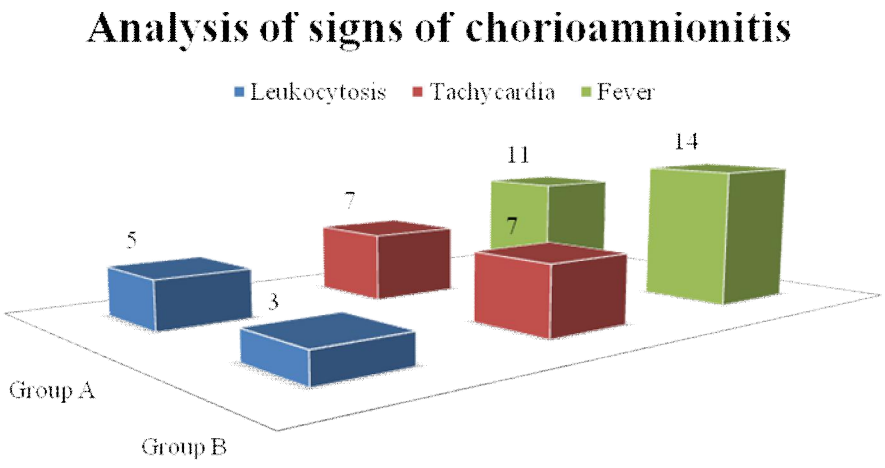


ANALYSIS OF SIGNS OF CHORIOAMNIONITIS (Table 10)

14 women in the delayed induction group had fever during the intrapartum/postpartum period while only 11 women in the immediate induction group had fever.7 patients in both groups had tachycardia while leucocytosis was slightly more in the immediate induction group.

Table 10: ANALYSIS OF SIGNS OF CHORIOAMNIONITIS

	GROUP A(100)	GROUP B(100)	P value
Maternal fever	11	14	0.521
Maternal tachycardia	7	7	1.00
Leucocytosis	5	3	0.47
Foul smelling vaginal discharge	0	0	
Uterine tenderness	0	0	

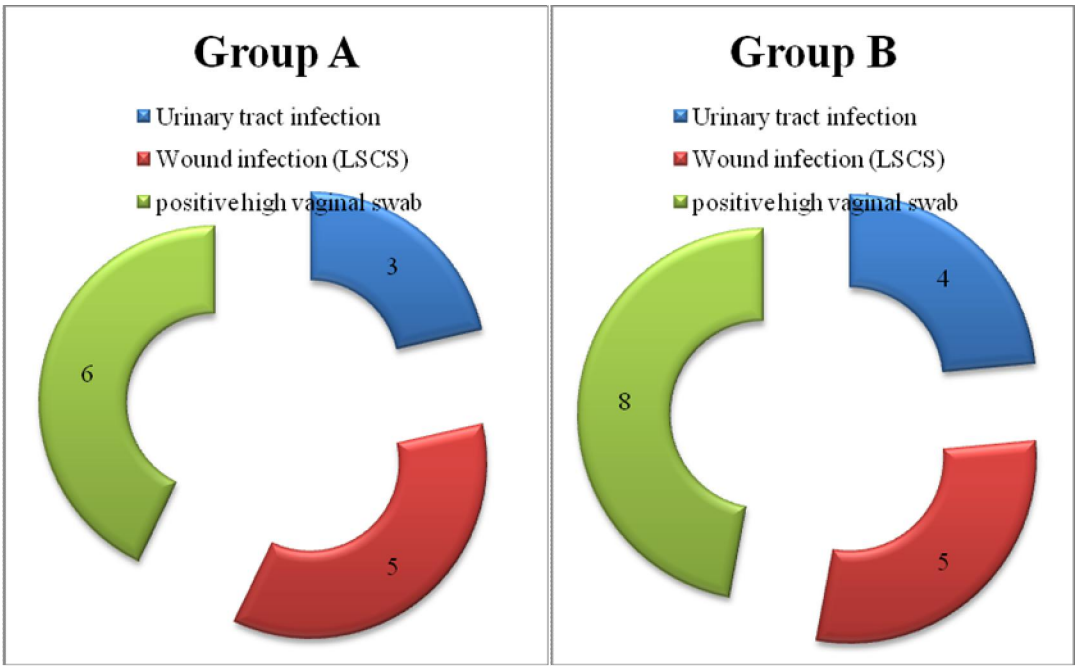


MATERNAL MORBIDITY (Table 11)

Infective morbidity was similar between the two groups (P values > 0.05 not significant).

Table 11: MATERNAL MORBIDITY

Morbidity	Group A	Group B	P Value
Urinary tract infection	3	4	0.62 (NS)
Wound infection (LSCS)	5 (16%)	5 (24%)	0.567 (NS)
Positive high vaginal swab culture	6	8	0.717 (NS)



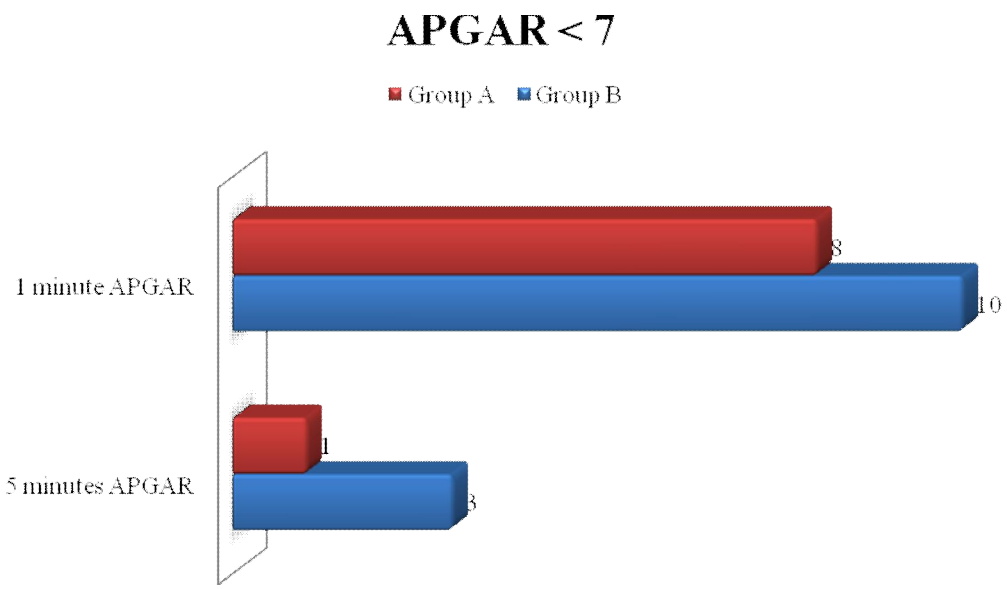
APGAR SCORE LESS THAN 7 (Table 12)

8 neonates in group A and 10 in group B had 1 minute APGAR of less than 7. 1 neonate in group A and 3 in group B had 5 minute APGAR of less than 7. There is no statistically significant difference in both.

Table 12: APGAR SCORE LESS THAN 7

ABGAR SCORE <7	GROUP A	GROUP B
1 Minute	8	10
5 Minutes	1	3

P value 0.52 (not significant)

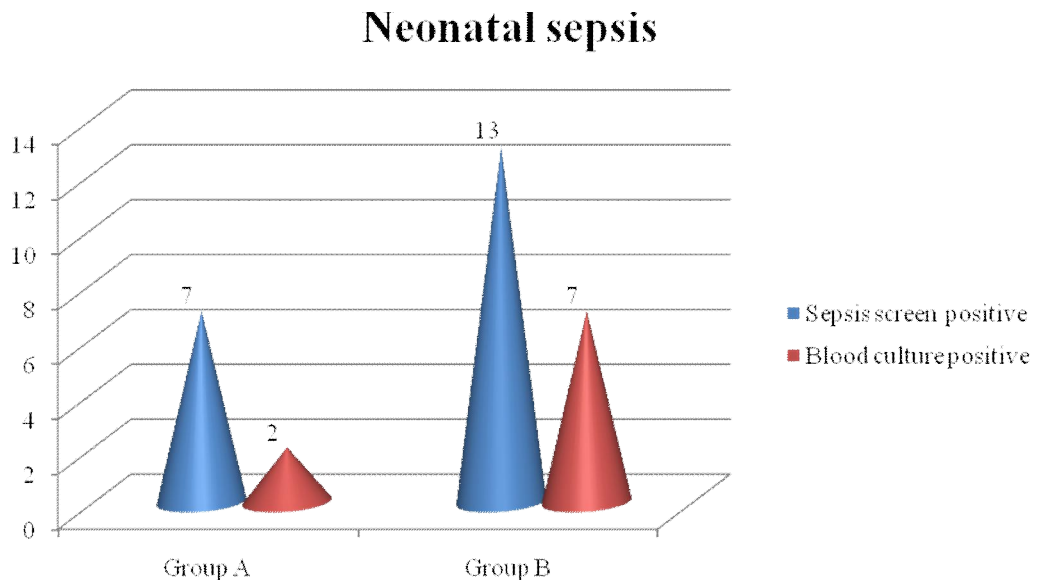


NEONATAL SEPSIS (Table 13A)

There were 7 neonates in group A and 13 in group B screened positive for sepsis. Of these 2 in group A (28%) and 7 in group B (53%) were culture positive. There was no statistically significant difference between the two groups. More number of neonates in group B had sepsis and required antibiotics.

Table 13A: NEONATAL SEPSIS

	Group A	Group B	P Value
Sepsis Screen Positive	7	13	0.157
Blood culture Positive	2	7	0.37

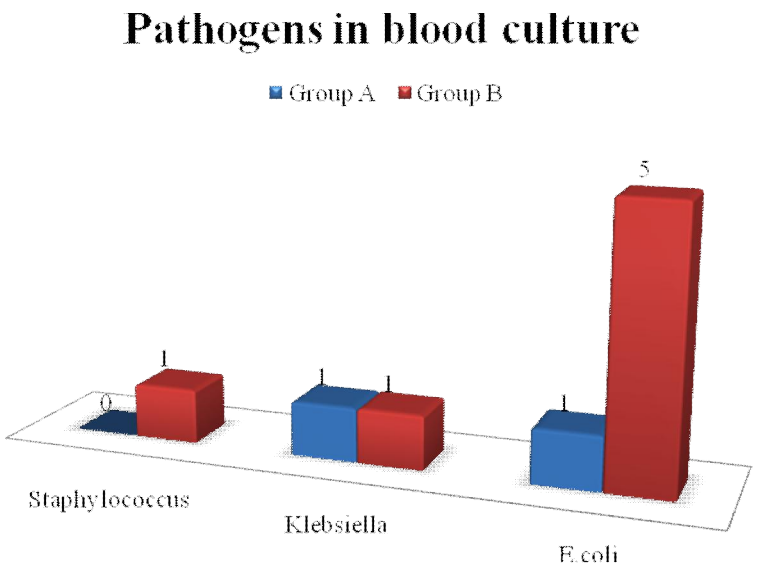


PATHOGENS IN BLOOD CULTURE (Table 13B)

E. coli was the commonly grown organism in blood culture.

Table 13B: PATHOGENS IN BLOOD CULTURE

Pathogens	Group A	Group B
Staphylococcus	0	1
Klebsiella	1	1
E.Coli	1	5

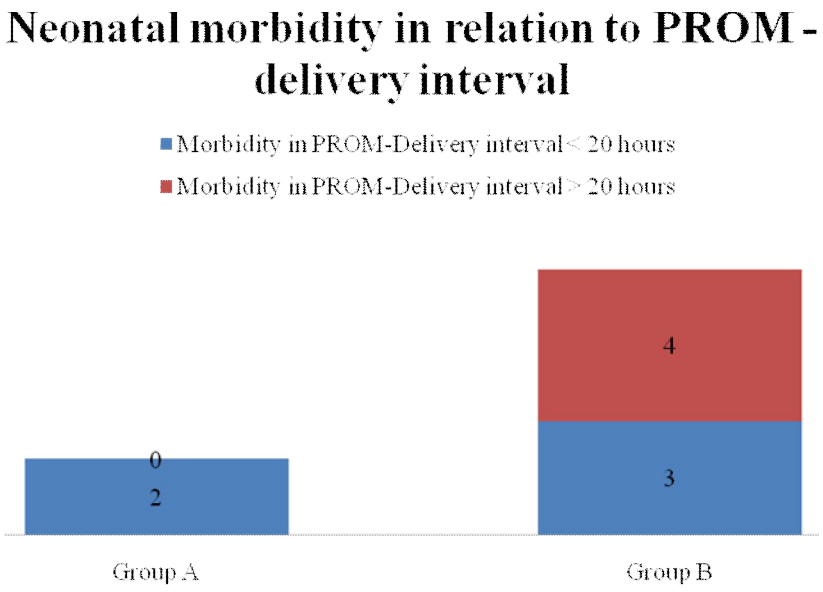


NEONATAL MORBIDITY IN RELATION TO PROM DELIVERY INTERVAL (Table 13C)

5 cases of neonatal sepsis were associated with PROM delivery interval of < 20 hrs and 4 cases with PROM delivery interval of > 20 hours. Neonatal morbidity was slightly more in group B. (statistically not significant).

Table 13C: NEONATAL MORBIDITY IN RELATION TO PROM DELIVERY INTERVAL

PROM Delivery interval	Group A	Group B	P Value
< 20 hours	2	3	0.52 (NS)
> 20 hours	0	4	

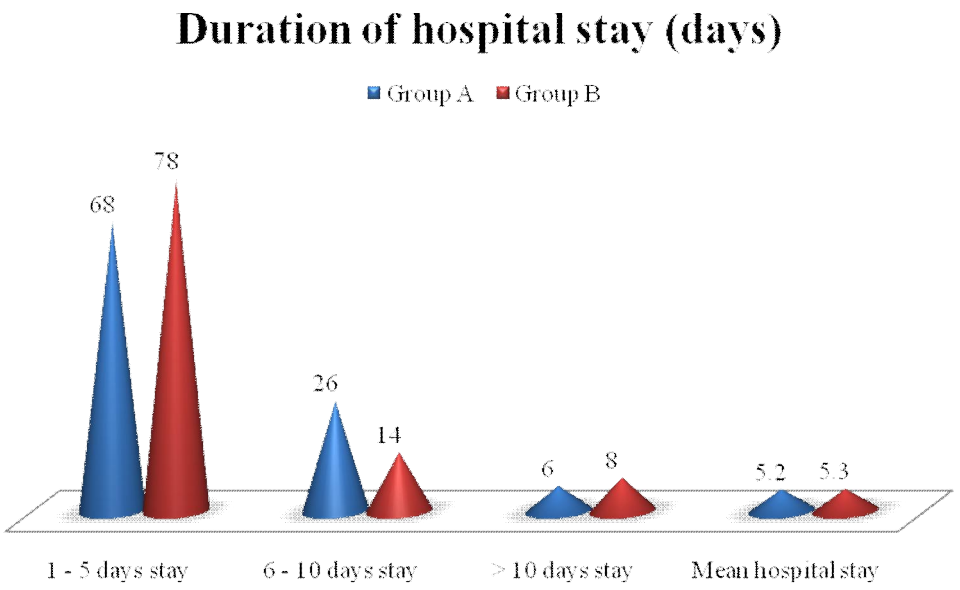


DURATION OF HOSPITAL STAY (Table 14)

68% patients in group A and 78% patients in group B got discharged within 5 days of admission. Duration of hospital stay of >10 days was slightly higher in group B when compared to group A. But it did not attain any statistical significance.

Table 14: DURATION OF HOSPITAL STAY

Duration of stay	Group A	Group B	P value
1-5 days	68	78	0.102 (not significant)
6-10 days	26	14	
>10 days	6	8	
Mean hospital stay	5.2	5.3	



DISCUSSION

DISCUSSION

Premature rupture of membranes is one of the complications of pregnancy that can lead to increased maternal complications, operative procedures, neonatal morbidity and mortality.

Premature rupture of membranes (PROM) is defined as the spontaneous rupture of amniotic membrane with a release of amniotic fluid before the onset of labour. If the membranes rupture after 37 weeks of gestation it is called term Premature Rupture of Membranes.

In this study on term PROM, the effect of immediate induction was compared to that of delayed induction after 12 hours.100 patients were studied in each group. Group A (immediate induction group) and Group B (delayed induction) were compared with regard to various parameters.

1) Number of PGE2 doses.

2) PROM-delivery interval.

3) Mode of Delivery.

4) Indications for LSCS.

5) Symptoms/signs of chorioamnionitis.

6) Maternal morbidity.

7) APGAR analysis.

8) Neonatal morbidity.

9) Duration of hospital stay.

10) Maternal and neonatal mortality.

The statistical tests used were Pearson Chi square or Fischers Chi square test. The outcome was significant if the P value was <0.05

The two groups were comparable with regard to age, parity,booking status and gestational age as seen in tables 2-5 (P value >0.05)

1. NUMBER OF PGE2 DOSES: Gestational age (P>0.05)

The results were similar to that of Krupa et al[32] which showed that significantly higher doses of PGE2 were required in immediate induction group.

38% of women entered active labour spontaneously within 12 hours of PROM.This is comparable to the following studies:

1) Dare et al: 50% (in 12 hours)

2) Krupa et al[32]: 80% (in 24 hours)

3) Poornima et al[35]: 60% (in 12 hours)

2. MEAN PROM – DELIVERY INTERVAL

Studies	Immediate induction group (in hours)	Delayed induction group (in hours)
Krupa et al[32]	13	22
Seema et al[36]	16	22
My study	14	19
Poornima et al[35]	14	18

The PROM-delivery interval was significantly shorter in the early induction group.

Bangal et al[34] and Alcalay et al[33] also inferred that mean period from rupture of membrane to delivery was shorter significantly in the induction group compared to the expectant group.

3. MODE OF DELIVERY

In this study, the caesarean section rate was significantly higher in the early induction group compared to the delayed induction group (31% vs. 21%, P value=0.049, significant). In this aspect, our inference was different from that of Krupa et al[32] and Alcalay et al[33] who showed similar rates of normal and caesarean deliveries between the two groups. The results of Poornima et al[35] were comparable to that of ours.

	Immediate induction	**Delayed induction**
Poornima et al [35]	28%	16%
This study	31%	21%

The difference in LSCS rate was largely due to the increased incidence of labour abnormalities (8% vs. 1%) and failed induction (9% vs. 5%) in the immediate induction group.

The number of operative vaginal deliveries was also higher in the early induction group (16% Vs 14%). This is also the inference of Alcalay et al[33].

4. FOETAL DISTRESS

Either non-reassuring CTG or meconium stained liquor were considered as foetal distress. Most cases were diagnosed based on CTG, while there were 3 cases of meconium stained liquor. There was slightly increased incidence of foetal distress in delayed induction group in our study (14% Vs 15%). This differed with the results of Poornima et al[35] and Alcalay et al[33] who had more foetal distress in the immediate induction group due to hyperstimulation.

5. CHORIOAMNIONITIS

The percentage of patients with symptoms & signs of chorioamnionitis was similar in both the groups (23% Vs 24%). Fever with two features (chorioamnionitis by definition) was present only in 3 of the early induction group as compared to 1 in delayed induction group.

The studies by Alcalay et al[33], Bangal et al[34] and Poornima et al[35] also showed similar incidence of chorioamnionitis in both the groups. Several studies show that chorioamnionitis is reduced with the use of prophylactic antibiotics at term[37, 38].

Fever appeared to be a nonspecific marker, while leucocytosis was more specific. No case had foul smelling vaginal discharge or uterine tenderness.

6. MATERNAL MORBIDITY

Maternal morbidity was analysed between the two groups by taking into consideration the number of patients who had urinary tract infection, LSCS site wound infection and positive high vaginal swab culture.

14% of patients in group A had some infective morbidity compared to 17% in group B ($P > 0.05$, statistically not significant). Maternal morbidity was similar in between the two groups. The study by Alcalay et al[33] has similar finding.

E. coli and enterococcus were the urinary pathogens isolated.

7. HIGH VAGINAL SWAB CULTURE AND SENSITIVITY

Candida and Group B streptococcus isolated in high vaginal swab culture was not associated with any significant morbidity. But, Hannah et al [39] in the famous multi center term PROM study states that clinical chorioamnionitis and maternal colonization with group B streptococci are the most important predictors of subsequent neonatal infection.

Of the 31 post LSCS patients in group A, 5 (17%) had wound infection. Of the 21 post LSCS patients in group B also, 5 (24%) had wound infection. P-value = 0.5 (not significant). Klebsiella, Staphylococcus, Streptococcus and E.coli were the isolated pathogens.

	GROUP A	**GROUP B**
No growth	46%	41%
Normal flora	48%	51%
Positive	6%	8%

P value: 0.717(Not significant)

8. ANALYSIS OF APGAR

An APGAR score of less than 7 was taken as significant for 1 minute and 5 minutes.(According to the study of Ehrenstein V et al, 2009, APGAR < 7 is associated with neurological disability which persisted many years postnatally).

1 and 5 minute APGAR were similar between the two groups (P-value: 0.52, not significant). One neonate in group A and three in group B had 5 minute APGAR < 7. All 4 neonates had 10 minute APGAR > 7. Only one among these 4 neonates had culture proven sepsis. All 4 neonates were discharged in a healthy state.

The study by Seema et al[36] in which APGAR < 5 was considered significant also showed that APGAR was not significantly influenced by delayed induction.

9. NEONATAL MORBIDITY

All neonates were screened for sepsis using total count, platelet count and C-reactive protein. 7% of cases had positive markers of sepsis in group A compared to 13% in group B. Of these neonates only 2 in group A & 7 in Group B were culture positive. Both were not statistically significant. All neonates were discharged in healthy condition but the culture positive babies were given IV antibiotics for 15 days. Klebsiella, E.coli and Staphylococci were the isolated pathogens. Seema et al[36] also states that neonatal infectious morbidity was similar in both groups.

10. DURATION OF HOSPITAL STAY

Duration of hospital stay was not significant between the two groups (P-value: 0.102, not significant). Duration of stay was > 5 days in 32% of cases in group A compared to 22% in Group B. This can be attributed to the increased number of LSCS in group A and our policy of discharging post LSCS patients after 8 days.

But Kirupa et al[32] states that mean hospital stay was more in expectant group compared to early induction group.

11. MATERNAL AND NEONATAL MORTALITY

There were no cases of maternal or neonatal mortality in this study.

SUMMARY

SUMMARY AND CONCLUSION

- ✓ Immediate induction was compared with that of delayed induction after 12 hours of PROM in term PROM cases.
- ✓ Both study groups were comparable with regard to age, parity, booking status and gestational age.
- ✓ During the waiting period of 12 hours 38% of cases entered active labour in the delayed induction group. So significantly lesser number of patients in the delayed induction group required induction compared to early induction group.
- ✓ Significantly higher doses of PGE2 were required in the early induction group.
- ✓ The PROM delivery interval was significantly shorter in the early induction group.
- ✓ LSCS and operative vaginal deliveries were more in the early induction group.

- ✓ Failed induction and labour abnormalities were more in the early induction group (statistically significant), while foetal distress was slightly higher in the delayed induction group.
- ✓ There was no significant difference in chorioamnionitis in both the groups. Leukocytosis was more specific marker compared to fever and maternal tachycardia.
- ✓ There was no difference in maternal and neonatal infectious morbidity between the two groups. This may be due to the use of prophylactic antibiotics.
- ✓ Neonatal outcome was equally good in both the groups.
- ✓ Though the mean hospital stay was not different, more number of patients in group A had a stay of >5 days due to increased number of LSCS.

CONCLUSION

CONCLUSION

Delayed induction after a waiting period of 12 hours stands as a reasonable option in term PROM and it decreases the number of operative deliveries without compromising on maternal and neonatal outcome.

ANNEXURE

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BIBLIOGRAPHY

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PATIENT CONSENT FORM

Title of Study

"A PROSPECTIVE STUDY ON MATERNAL AND NEONATAL OUTCOME IN TERM PREMATURE RUPTURE OF MEMBRANES: IMMEDIATE VERSUS DELAYED INDUCTION AT INSTITUTE OF OBSTETRICS & GYNAECOLOGY",

Study Centre

INSTITUTE OF OBSTETRICS & GYNAECOLOGY", Egmore, Chennai – 600 008.

PARTICIPANT NAME: AGE: I.D.NO. :

I confirm that I have understood the purpose of the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected.

I understand that investigator, the institution, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study.

I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law.

I agree not to restrict the use of any data or results that arise from this study.

I hereby consent to, undergo complete physical examination, and diagnostic tests including haematological, and micro biological examinations for me and my child.

I hereby consent to participate in this study on MATERNAL AND NEONATAL OUTCOME IN WOMEN WITH TERM PREMATURE RUPTURE OF MEMBRANES: IMMEDIATE VERSUS DELAYED INDUCTION.

Place: ..... Signature of the Patient

Date: .....

.....

Address: .....

.....

.....

Signature of the Witness: .....

Place: .....

Date: .....

Signature of the Investigator: .....

Place: .....

Date: .....

PROFORMA

NAME: I.P.No.:

AGE: Date and Time of Admission:

ADDRESS: Date of Discharge:

Booked / Unbooked:

Obstetric score:

Gestational age (by Dates): Reliable / Not Reliable:

Gestational age (by USG):

Medical Complications:

H/o Fever:

H/o Foul smelling vaginal discharge:

H/o Suggestive of

- APH:
- UTI:

Date and Time of rupture of membranes:

AT ADMISSION:

Maternal Pulse Rate: BP: Foul smelling Discharge: Y/N

Uterine Size: Uterine Tenderness:

FHR: USG (AFI): CTG - Reactive / Non Reactive

Per Speculum Examination: Draining: + / -

Clear liquor

Meconium Stained

Per Vaginal Examination: Cervix Consistency:

Position:

Dilatation:

Effacement:

Station of head:

Modified Bishop Score:

TIME OF INDUCTION:

No. of PGE2 Doses:

Augmentation with Oxytocin: Y/N

Induction - delivery interval:

TIME AND MODE OF DELIVERY:

NVD with episiotomy:

Forceps Indication:

Vacuum Indication:

LSCS Indication:

Foetal Distress at any time during labour by cardiotocography:

Meconium Stained Liquor: +/-

POSTPARTUM:

Urinary complaints:

Wound discharge:

Fever:

BABY DETAILS

Sex:

Birth Weight:

APGAR:

NICU admission / Mother's side:

Umbilical cord sepsis: Y/N

Eye discharge: Y/N

INVESTIGATIONS FOR MOTHER:

Hb, TC, DC, ESR:

Blood Sugar:

High Vaginal Swab C/S:

LSCS Wound C/S:

Urine C/S:

Endometrial Swab C/S**:**

FOR BABY:

Sepsis screen:

Total Leucocyte count:

Platelet Count:

Blood C/S:

- Duration of Hospital stay following delivery
- Condition of the patient at the time of discharge

Mother: Baby:

ABBREVIATIONS

1) AFI - Amniotic fluid index
2) APH - Antepartum hemorrhage
3) Bpm - beats per min
4) Cms - centimeters
5) CPD - Cephalo- pelvic disproportion
6) CRP - C-reactive protein
7) C/S - Culture and sensitivity
8) CSF - Cerebrospinal fluid
9) CTG - Cardiotocography
10) DC - Differential count
11) DIC - Disseminated intravascular coagulation
12) D.O.A - Date of admission
13) D.O.D - Date of discharge
14) EDD - estimated delivery date
15) FD - Foetal distress
16) Hb - Hemoglobin
17) HIV - Human Immunodeficiency Virus
18) HPE - Histopathological examination

19) HR - Heart rate

20) HVS - High vaginal swab

21) IOG - Institute Of Obtetrics and Gynaecology

22) IUGR - Intrauterine growth restriction

23) LMP - Last menstrual period

24) LSCS - Lower segment Caesarean section

25) NICU - Neonatal intensive care unit

26) No. - Number

27) NST - Non stress test

28) NVD with epi- Normal vaginal delivery with episiotomy

29) PGE2 - Prostaglandin E2

30) PROM - Premature rupture of membranes

31) PPROM - Preterm premature rupture of membranes

32) RDS - Respiratory distress syndrome

33) ROM - Rupture of membranes

34) TC - Total leukocyte count

35) UTI - Urinary tract infection

KEY TO MASTER CHART

I. B/N- Booked/Not

II. Obs. Score-Obstetric score

III. GA-Gestational age

IV. Oxy- Oxytocin

V. Y/N-Yes/No

VI. PDI-PROM-delivery interval

VII. Ind-Indication for LSCS

VIII. FI-Failed induction

IX. FP-Failure to progress

X. Sepscr-Sepsis screen (TC, platelet count, CRP)

XI. C/S-Culture and sensitivity

XII. ND- Not done

MASTER CHART

GROUP -B DELAYED INDUCTION

Sl. No	Name	Age	B/N	OBS score	GA	pge2	oxy	PDI	MOD	Ind	Apgar		Fever Y/N	TAC Y/N	TC cumm	PUS	Urine	HVS	Sep Scr +/-	Blood	STAY Days
						doses	N				1min	5min				C/S	C/S			C/S	
1	Shanthi	24	B	p	37	0	Y	15	NVD		7	8	N	N	11400	N	ND	Normal	+	No growth	3
2	Sumathy	22	B	P	40	0	Y	14	NVD		7	8	N	N	7500	N	ND	Normal	-	ND	3
3	Arthi	21	B	p	38	0	Y	18	VAC		8	9	Y	Y	11000	N	ND	No growth	-	ND	3
4	Banu	23	N	G2P1L1	37	0	Y	19	NVD		7	8	N	N	8500	N	E.coli	No growth	-	ND	3
5	Sheeba	27	B	G2P1L1	39	0	N	14	NVD		7	8	N	N	13700	N	ND	No growth	-	ND	3
6	Veni	30	B	G2P1L1	40	0	N	9	LSCS	FD	7	8	N	N	8700	N	ND	Normal	-	ND	8
7	Subbulakshmi	24	B	P	37	0	Y	12	NVD		8	9	N	N	9700	N	ND	Normal	-	ND	3
8	Kasturi	21	B	P	39	0	Y	18	NVD		7	8	N	N	13800	N	ND	No growth	-	ND	3
9	Sangeetha	32	B	G2P1L1	38	0	Y	19	LSCS	FP	5	8	N	N	9700	N	ND	Normal	-	ND	8
10	Vasumathy	22	N	P	40	0	Y	14	NVD		7	8	N	N	8500	N	ND	Normal	-		3
11	Baby	21	B	P	38	0	Y	18	NVD		7	8	N	N	15000	N	ND	No growth	-	ND	3
12	Surya	25	B	G2P1L1	41	0	N	8	NVD		8	9	N	N	16900	N	Entero	Normal	+	E..coli	15
13	Kavitha	22	B	P	38	0	N	15	NVD		8	9	N	N	9400	N	ND	No growth	-	ND	3
14	Kartiga	25	B	G2P1L0	38	0	Y	17	LSCS	FD	6	8	Y	N	16700	N	ND	Enterococ	+	E.coli	15
15	Kannagi	21	B	P	39	0	Y	16	NVD		7	8	N	N	13000	N	ND	Normal	-	ND	3
16	Muniamma	23	B	G2P1L1	40	0	Y	15	OUT		7	8	N	N	9850	N	ND	No growth	-	ND	3
17	Valli	18	B	P	38	0	N	10	NVD		7	8	N	N	8300	N	ND	No growth	-	ND	3
18	Balamma	27	B	G2P1L0	38	0	N	19	NVD		7	8	N	N	13800	N	ND	No growth	-	ND	3
19	Shanmugi	29	B	P	37	0	Y	18	NVD		7	8	N	N	9500	N	ND	Normal	-	ND	4
20	Beena	28	B	P	39	0	N	13	NVD		7	8	N	N	8400	N	ND	Candida	-	ND	3
21	Srinithi	25	B	P	38	0	N	12	NVD		8	9	N	N	7500	N	ND	No growth	-	ND	3
22	Menaka	29	N	G2P1L1	40	0	Y	14	LSCS	FD	7	8	N	N	9400	Klebs	ND	No growth	+	No growth	8
23	Megala	22	B	P	41	0	Y	13	NVD		7	8	N	N	6300	N	ND	Normal	-	ND	3
24	Roopa	21	B	P	38	0	Y	15	LSCS	FD	4	6	Y	Y	7490	E.coli	ND	Normal	-	ND	8
25	Rukmani	20	B	P	37	0	Y	16	NVD		7	8	N	N	9300	N	ND	No growth	-	ND	3
26	Valliamma	27	B	P	39	0	N	11	NVD		8	9	N	N	9500	N	E.coli	Normal	-	ND	3
27	Sherlin	29	B	G2P1L1	40	0	N	14	NVD		8	9	N	N	9250	N	ND	Normal	-	ND	3
28	Muskan	21	B	P	41	0	Y	17	LSCS	FD	7	8	N	N	11600	N	ND	Normal	-	ND	4
29	Mariamma	24	B	P	38	0	Y	14	NVD		7	8	N	N	7900	N	ND	No growth	-	ND	3
30	Manimegalai	26	N	P	37	0	Y	13	NVD		8	9	Y	N	7350	N	ND	Normal	-	ND	3
31	Noorjahan	22	B	P	39	0	Y	28	LSCS	FD	7	8	N	N	7200	N	ND	Normal	-	ND	9

Sl. No	Name	Age	B/N	OBS score	GA	pge2	oxy	PDI	MOD	Ind	Apgar		Fever	TAC	TC	PUS	Urine	HVS	Sep	Blood	STAY Days
						doses	N				1min	5min	Y/N	Y/N	cumm	C/S	C/S		Scr +/-	C/S	
32	Dilshath	21	B	P	40	0	Y	18	NVD		8	9	N	N	8540	N	ND	Normal	-	ND	3
33	SahayaMary	35	B	G2P1L1	38	0	N	13	VAC		7	8	N	N	8300	N	ND	GBS	-	ND	3
34	Anitha	28	B	P	37	0	N	9	VAC		7	8	N	N	8700	N	ND	Normal	-	ND	3
35	Prema	28	B	G2P1L1	39	0	Y	16	LSCS	FD	6	7	N	N	8200	Staph	ND	Normal	-	ND	15
36	Pushpa	29	B	G2P1L0	40	0	Y	15	NVD		8	9	N	N	9400	N	ND	Normal	+	Staph	4
37	Mariamma	24	B	P	39	0	Y	14	NVD		8	9	N	N	7800	N	ND	Normal	-	ND	3
38	Vanitha	23	B	P	38	0	Y	13	NVD		7	8	N	N	7350	N	ND	No growth	-	ND	3
39	Vanishree	22	B	P	38	1	N	20	NVD		8	9	Y	N	9400	N	ND	No growth	-	ND	4
40	Gomathy	28	B	G2P1L1	39	1	N	19	nvd		8	9	Y	Y	8300	N	ND	No growth	-	ND	4
41	Sangeetha	23	B	P	37	1	N	18	NVD		7	8	N	N	7400	N	ND	Normal	-	ND	4
42	Margaret	28	B	G2P1L1	40	1	N	18	NVD		7	8	N	N	7100	N	ND	No growth	-	ND	4
43	Shivani	29	B	G2P1L0	39	1	N	16	NVD		7	8	N	N	8400	N	ND	Normal	-	ND	4
44	Sowmya	28	B	G2P1L1	39	1	N	17	NVD		7	8	N	N	8200	N	ND	Normal	-	ND	4
45	Pushpa	22	B	P	40	1	Y	20	LSCS	FD	4	6	N	N	8900	N	ND	GBS	-	ND	8
46	Caroline	21	B	P	38	1	N	17	LSCS	FD	7	8	N	N	8550	N	ND	No growth	-	ND	8
47	Rani	19	B	P	39	1	Y	22	NVD		7	8	N	N	14900	N	ND	Normal	+	No growth	4
48	Parameswari	29	N	G2P1L1	37	1	N	17	NVD		7	8	N	N	9300	N	ND	No growth	-	ND	4
49	Punitha	21	B	P	40	1	N	15	LSCS	FD	7	8	N	N	8500	N	ND	Normal	-	ND	8
50	Pankajam	30	B	G2P1L1	37	1	Y	23	NVD		7	8	N	N	6900	N	ND	Normal	-	ND	4
51	Maragatham	22	B	P	38	2	N	24	NVD		8	9	N	N	9700	N	ND	Normal	-	ND	4
52	Vani	21	B	P	40	1	Y	21	NVD		7	8	N	N	9450	N	ND	No growth	-	ND	4
53	Nalini	26	B	G2P1L1	41	2	N	23	OUT		7	8	N	N	9370	N	ND	No growth	-	ND	4
54	Alamelu	26	B	P	39	1	Y	22	VAC		7	8	N	N	9470	N	ND	Normal	-	ND	4
55	Yogalakshmi	28	B	G2P1L1	37	2	N	24	LSCS	FD	6	8	Y	Y	16800	E.coli	ND	No growth	+	E.coli	15
56	Sumathy	29	B	G2P1L0	38	1	Y	20	NVD		7	8	N	N	12700	N	ND	No growth	-	ND	4
57	Senthamarai	21	B	P	40	1	N	19	NVD		7	9	Y	N	6750	N	ND	No growth	-	ND	4
58	Tamilselvi	22	B	P	41	2	N	26	LSCS	FI	7	8	N	N	8500	N	ND	No growth	-	ND	9
59	Leela	21	B	P	39	1	N	19	NVD		7	8	N	N	9500	N	ND	Normal	-	ND	4
60	Parimala	28	B	G2P1L1	37	1	Y	20	NVD		8	9	N	N	9700	N	ND	Normal	-	ND	4
61	Lalitha	21	B	P	38	2	N	24	NVD		8	9	N	N	9300	N	ND	Normal	-	ND	4
62	Mercy	26	B	P	40	2	N	25	LSCS	FI	8	9	Y	N	10500	N	ND	No growth	-	ND	9

Sl. No	Name	Age	B/N	OBS score	GA	pge2	oxy	PDI	MOD	Ind	Apgar		Fever Y/N	TAC Y/N	TC cumm	PUS	Urine	HVS	Sep Scr +/-	Blood	STAY Days
						doses	N				1min	5min				C/S	C/S			C/S	
63	Arputham	30	N	G2P1L1	38	1	Y	23	NVD		7	9	N	N	9400	N	ND	Normal	-	ND	4
64	Arka	21	B	P	39	2	N	24	LSCS	FD	4	6	Y	Y	13500	N	ND	No growth	+	E.coli	15
65	Bhavani	22	B	G2P1L1	40	1	N	18	NVD		7	8	N	N	7800	N	ND	CANDIDA	-	ND	4
66	Amudha	21	B	P	37	1	Y	18	VAC		7	8	N	N	9300	N	ND	No growth	-	ND	4
67	Priya	20	B	P	39	2	Y	28	OUT		7	8	Y	N	11100	N	ND	No growth	-	ND	4
68	bhuvana	21	B	P	40	2	Y	30	NVD		8	9	N	N	13900	N	ND	No growth	+	No growth	4
69	gayathri	26	B	P	37	1	Y	22	NVD		8	9	N	N	9400	N	ND	Normal	-	ND	3
70	Sowmya	28	B	P	40	2	Y	27	NVD		7	8	N	N	9200	N	ND	Normal	-	ND	4
71	srividhya	23	B	P	38	2	N	26	LSCS	FI	7	8	N	N	8450	N	ND	No growth	+	Staph	15
72	Kanimoli	26	B	P	39	1	N	20	NVD		7	8	N	N	8200	N	ND	No growth	-	ND	4
73	Viji	21	B	P	40	1	Y	20	OUT		7	8	N	N	8600	N	ND	Normal	-	ND	4
74	Meera	20	B	P	39	1	Y	21	NVD		8	9	N	N	8300	N	ND	Enterococ	-	ND	4
75	Kannagi	19	B	P	39	2	N	24	NVD		7	8	N	N	8750	N	ND	Normal	-	ND	4
76	Sivasankari	26	B	G2P1L1	38	1	Y	22	NVD		7	8	N	N	9540	N	ND	Normal	-	ND	4
77	vidhya	20	B	P	40	1	N	19	NVD		8	9	N	N	8400	N	ND	Normal	-	ND	4
78	Boomika	20	B	P	41	2	N	26	LSCS	FI	6	7	Y	Y	9950	N	ND	No growth	+	Kleb	15
79	Suseela	21	B	P	39		Y	20	NVD		8	9	N	N	8300	N	ND	Normal	-	ND	4
80	Bavani	24	B	P	39	1	Y	23	NVD		8	9	N	N	7950	N	ND	Normal	-	ND	4
81	sheela	2`	N	P	38	1	N	20	NVD		7	8	N	N	8500	N	ND	No growth	-	ND	4
82	Shalini	30	B	G2P1L1	40	1	Y	24	NVD		8	9	N	N	9600	N	ND	Normal	-	ND	4
83	Gomathy	21	B	P	39	1	Y	21	NVD		7	8	N	N	8400	N	ND	Normal	-	ND	4
84	Tennarasi	23	B	P	38	1	Y	22	NVD		7	8	N	N	9600	N	ND	No growth	-	ND	3
85	Annammal	24	B	G2P1L1	37	1	N	20	OUT		7	8	N	N	9250	N	ND	Normal	-	ND	4
86	Kasiamma	29	B	p	40	2	N	24	LSCS	FI	7	8	Y	N	14600	N	ND	No growth	-	ND	8
87	Thenmoli	21	B	P	41	1	N	19	NVD		8	9	N	N	13670	N	ND	No growth	+	No growth	4
88	Ramani	20	B	P	37	2	Y	28	LSCS	FD	7	8	N	N	12450	N	ND	Normal	-	ND	8
89	Nageswari	25	B	P	38	1	N	16	VAC		8	9	N	N	14760	N	Entero	Normal	-	ND	8
90	Yuvarani	27	B	P	39	1	N	19	VAC		7	8	N	N	9800	N	ND	Normal	-	ND	4
91	seema	30	B	G2P1L1	41	1	Y	18	LSCS	FD	8	9	N	N	9450	N	ND	Normal	-	ND	8
92	surya	21	B	P	40	1	N	17	NVD		7	8	N	N	7800	N	ND	No growth	-	ND	3
93	Ravanamma	23	B	P	39	1	Y	19	NVD		7	8	N	N	8540	N	ND	Normal	-	ND	3

Sl. No	Name	Age	B/N	OBS score	GA	pge2	oxy	PDI	MOD	Ind	Apgar		Fever Y/N	TAC Y/N	TC cumm	PUS	Urine	HVS	Sep Scr +/-	Blood	STAY Days
						doses	N				1min	5min				C/S	C/S			C/S	
94	Catherine	21	B	P	38	1	Y	22	NVD		8	9	N	N	9400	N	ND	Normal	-	ND	4
95	Sweetlin	20	B	P	39	2	Y	26	VAC		7	8	Y	Y	14800	N	ND	No growth	-	ND	4
96	Reena	21	B	P	40	1	N	17	LSCS	FD	6	8	N	N	9740	TREPT	ND	Enterococ	+	No growth	15
97	Sherlin	27	B	G2P1L1	38	1	Y	23	NVD		7	8	N	N	11800	N	ND	GBS	-	ND	4
98	Tulasi	21	B	P	40	1	Y	20	VAC		7	8	N	N	7600	N	ND	No growth	-	ND	4
99	nithya	22	B	P	39	1	N	18	NVD		7	8	N	N	8450	N	ND	No growth	-	ND	3
100	Mariamma	20	B	P	38	1	Y	20	NVD		7	8	N	N	9350	N	ND	Normal	-	ND	4