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Study of fetal wellbeing and pharmacological therapy for preterm labour patients at a tertiary hospital

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Abstract
Background: Preterm labour and delivery before 37 weeks of gestation is a principal contributor to perinatal mortality and morbidity. 75% of infant mortality is related to preterm labor. Our study aims at studying foetal wellbeing and pharmacological therapy for preterm labour patients at a tertiary hospital.
Material and Methods: Present study was prospective, observational study, conducted in pregnant women of 18-40 yrs., with gestational age 24-37 weeks, and had preterm labour.
Results: In the present study, 50 mothers were included. Mean age of the mothers was 29.7 ± 5.1 years, majority were from 21 to 35 years age group (84%), had GA of 32-37 weeks (56%), were primigravida (50%). It was observed that patients significantly high proportion of mothers had cervical encerclage with cervical length >2.5 cm as compared to those with cervical length >3 cm (p value < 0.05). 80% of the patients received betamethasone and 10% received dexamethasone. Nifedipine (38%) and Ixosuprine (20%) were used as tocolytic. The most commonly used antibiotic were erythromycin (38%), ceftriaxone (36%) and Amoxiclav (8%). Pregnancy was prolonged by up to 5 days in majority of mothers (84%). LSCS was performed in 48% and rest had preterm vaginal delivery. Of the 52 live births, majority had APGAR score of 7-10 (67.4%). In 15 neonates with APGAR score less than 6, NICU admission was required. Neonatal deaths were observed in 19% of the live births. Mean birth weight of the neonates was 1605 ± 564 gms, majority had 1500-2499 gms (50%). Neonatal complications were observed in 56% of the live births. The most common neonatal complication was respiratory distress syndrome (27%).
Conclusion: The results of the present study show that prolongation of pregnancy is safe in mothers presenting with preterm labor.

Keywords: Preterm labor, antenatal care, preterm birth, low birth weight

Introduction

Preterm labour and delivery before 37 weeks of gestation is a principal contributor to perinatal mortality and morbidity [1]. 75% of infant mortality is related to preterm labor. Preterm labor not only inflicts financial and emotional distress on the family, it may also lead to permanent disability (physical or neurological damages) in infants. The economic cost of preterm birth is high in terms of neonatal intensive care and ongoing health care and educational needs [2, 3].

Despite advances in perinatal medicine in recent decades the problems of preterm delivery continues to frustrate satisfactory reproductive outcomes with little progress having been made in identifying and reducing the frequency of preterm birth [4]. Due to continued innovation in neonatal intensive care facilities and obstetric interventions, fetal survival is now possible even at 20 weeks gestation in developed countries.

However, a real reduction in preterm delivery rates will only take place through an improvement in understanding of the physiology of preterm labour, identification of patients at risk, prediction and prevention of its occurrence, early detection of its onset and effective management [4]. Our study aims at studying foetal wellbeing and pharmacological therapy for preterm labour patients at a tertiary hospital.

Material and Methods

Present study was prospective, observational study, conducted in department of Obstetrics and Gynecology, at a tertiary hospital in Mumbai, India. Study duration was of 2 years (December 2018- to November2020). Study approval was obtained from institutional ethical committee.

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Inclusion criteria
All pregnant women of 18-40 yrs., with gestational age 24-37 weeks, had preterm labour, giving their consent for the study.

Exclusion criteria
1. Patients with induced preterm labour for medical or surgical indications.
2. Pregnant women with major fetal congenital anomalies incompatible with life
3. Intrauterine fetal demise

Study was explained to patients in local language & written consent was taken for participation & study. Patients were subjected to a detailed history with respect to age, parity, previous pregnancy outcomes and to identify the presence of any risk factors in this pregnancy including presence of GDM, anemia, hypertension or any medical disease. They were evaluated by history taking, clinical examination, and ultrasonography. ACOG criteria for preterm labour was used to document preterm labor and threatened preterm labor *viz.*, at least 4 contractions in a time period of 20 minutes or 8 contractions in a time period of 60 minutes with progressive change in the cervical score in the form of effacement of 80% or more and cervical dilatation greater than 1 cm.

All women with preterm labor were subjected to ultrasonography to assess the placenta location, fetal maturity estimated fetal weight, cervical length, status of os, amniotic fluid index and they will also be investigated for presence of infection by complete hemogram, and urine and high vaginal swab culture. All women > 34 weeks received 2 doses of betamethasone 12 mg 24hrs apart.

Obstetrical outcomes were recorded in terms of gestational age at the time of delivery, mode of delivery vaginal, assisted vaginal delivery / caesarean delivery & complications if any. Fetal outcomes were recorded in terms of APGAR score at birth, Fetal Weight & NICU admission.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.05 was considered as statistically significant.

Results
In the present study, 50 mothers were included. Mean age of the mothers was 29.7 ± 5.1 years, majority were from 21 to 35 years age group (84%), had GA of 32-37 weeks (56%), were primigravida (50%). There were 40 single pregnancies and 10 twin pregnancies.

Table 1: General characteristics

Characteristics	No. of patients	Percentage
Maternal age (years)		
<20	2	4
21-35	42	84
>35	6	12
Gestational Age (weeks)		
< 28	8	16
28-32	14	28
32-37	28	56
Gravid status		
Primigravida	25	50
G2	14	28
≥ G3	11	22
Pregnancy type		
Single	40	80
Twins	10	20

In present study, common past history was of first trimester MTP/SA (22%), second trimester MTP/SA (6%), History of PROM (6%) and history of preterm labor (6%). History of tobacco chewing (14%), history of alcohol (2%) and smoking (2%) before pregnancy also noted. Past history of hypothyroidism (18%), Pregnancy induced hypertension (12%), GDM (10%) were noted. Anatomical factors such as fibroid (6%), bicornuate uterus (6%) and septate uterus (2%) were noted. Surgical history of Dilation and curettage (18%), previous LSCS (14%) and hysterolaparoscopy (6%) were noted.
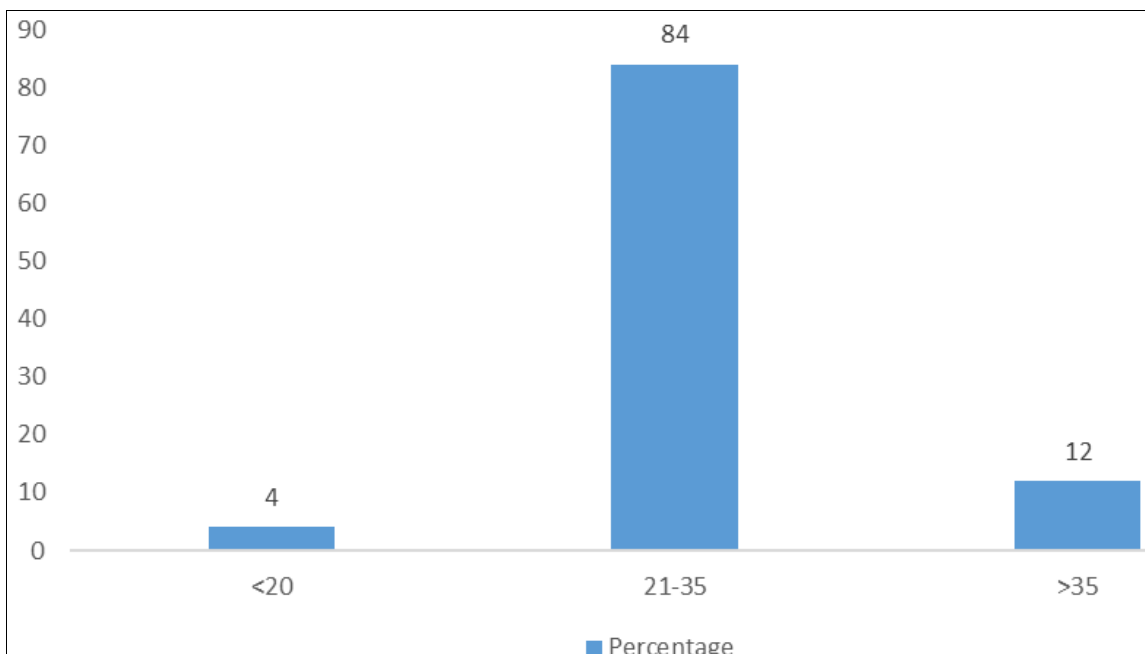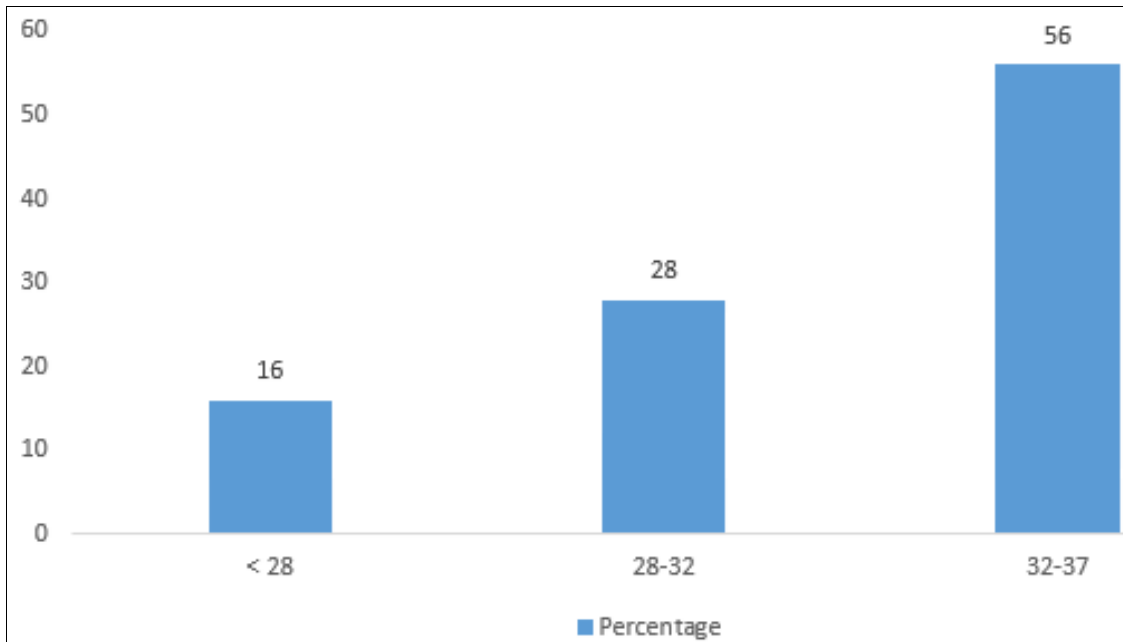

Fig 1: Maternal age (Years)
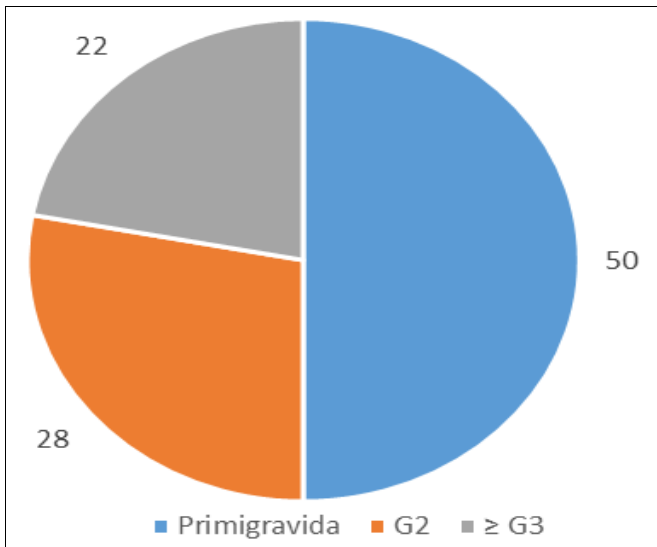
Fig 2: Gestational age (Weeks)

Fig 3: Gravid status
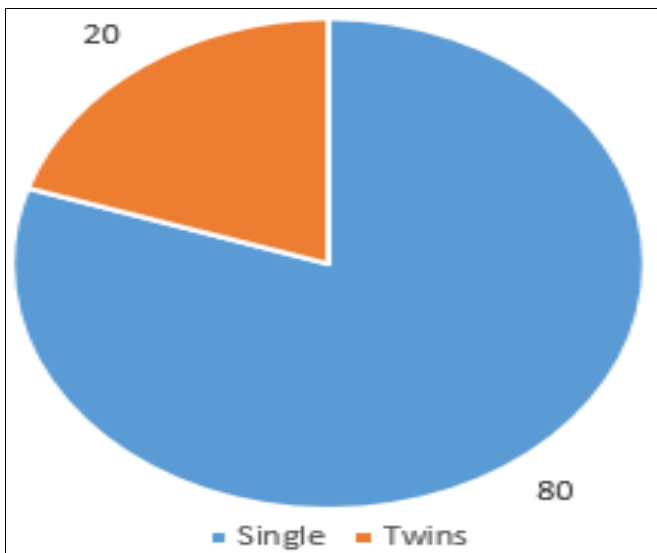
Fig 4: Pregnancy type

Table 2: Significant past history

Frequency	Past history	Percent
	Obstetric history	
11	1st trimester (MTP/ Spontaneous Abortion)	22
3	2nd trimester (MTP/ Spontaneous Abortion)	6
3	History of Premature Rupture of Membrane	6
3	History of Preterm Labor	6
	Substance use	
7	Tobacco chewing	14
1	Alcohol intake before pregnancy	2
1	Smoking before pregnancy	2
	Past medical history	
9	Hypothyroidism	18
6	Pregnancy induced hypertension	12
5	Gestational Diabetes Mellitus	10
2	Thalassemia minor	4
1	Overt diabetes mellitus	2
1	Polycystic ovarian disease	2
1	Systemic lupus erythematosus	2
	Anatomical factors	
3	Fibroid	6
2	Bicornuate uterus	4
1	Septate uterus (resection done)	2
	Surgical history	
9	Dilation and curettage	18
7	Previous LSCS	14
3	Hysterolaparoscopy	6
1	H/O myomectomy	2
1	Op laparoscopy i/v/o ectopic pregnancy	2
1	Septal resection	2
1	Exploratory laparotomy	2

It was observed that patients significantly high proportion of mothers had cervical encerclage with cervical length >2.5 cm as compared to those with cervical length > 3 cm (p value < 0.05). In addition, significantly higher proportion of mother took progesterone who had cervical length < 2.5 cm as compared to those with cervical length > 3 cm. (p value < 0.05).

Table 3: Cervical length, H/O Cervical encerclage and use of progesterone

	Cervical length (cm)			Total	p value
Cervical encerclage	< 2.5 (N=5)	2.5 to 3 (N=21)	> 3 (N=24)		
No	2 (40%)	14 (66.70%)	23 (95.80%)	39 (78%)	< 0.05
Yes	3 (60%)	7 (33.30%)	1 (4.20%)	11 (22%)	
Progesterone					
No	1 (20%)	7 (33.30%)	17 (70.80%)	25 (50%)	< 0.05
Yes	4 (80%)	14 (66.70%)	7 (29.20%)	25 (50%)	

It was found that 32% of the patients had upto 5 pus cells, 68% had more than 5 pus cells per high power field. The most common organisms observed in high vaginal swab reports were candida (16%), E. coli (14%) and Mycoplasma hominis (12%).

Table 4: Maternal microbiological profile

Microbiological profile	Frequency	Percent		
Urine Pus cells per hpf				
Upto 5	16	32		
More than 5	34	68		

Vaginal Swab				
Candida	8	16		
E. coli	7	14		
Mycoplasma hominis	6	12		
Group B streptococcus	4	8		
Enterococcus faecalis	3	6		
Klebsiella pneumonia	2	4		
Pseudomonas	1	2		
Ureaplasma urealyticum	1	2		

80% of the patients received betamethasone and 10% received dexamethasone. Nifedipine (38%) and Ixosuprine (20%) were used as tocolytic. The most commonly used antibiotic were erythromycin (38%), ceftriaxone (36%) and Amoxiclav (8%).

Table 5: Distribution of mothers according to the treatment given to them

Treatment given	Frequency	Percent
Steroids		
Betamethasone	40	80
Dexamethasone	5	10
Tocolytics		
Nifedipine	19	38
Ixosuprine	10	20
Magnesium sulphate	4	8
Atosiban	1	2
Antibiotics		
Erythromycin	19	38
Ceftriaxone	27	36
Amoxiclav	4	8
Total	50	100

Pregnancy was prolonged by up to 5 days in majority of mothers (84%).

Table 6: Distribution of mothers according to days pregnancy was prolonged

Days pregnancy was prolonged	Frequency	Percent
Up to 5	42	84
6 to 10	3	6
11 to 15	4	8
More than 15	1	2
Total	50	100

LSCS was performed in 48% and rest had preterm vaginal delivery. Post-partum complications such as fever (6%), retained placenta and post-partum hemorrhage in 4% each were noted.

Abnormal placental position noted in 12% of the cases.

Table 7: Distribution of mothers according to their obstetric outcome

Obstetric outcome	Frequency	Percent
Mode of delivery		
Lower section cesarean section	24	48
Preterm Vaginal Delivery	26	52
Maternal complications		
Fever	3	6
Retained placenta	2	4
Post-partum hemorrhage	2	4
Episiotomy site gape	1	2
Placental position		
Normal	44	88
Abnormal	6	12

We observed that among still born, 75% had gestational age at delivery of less than 28 weeks (p value < 0.01). In addition, we found that 87.5% of the still born had birth weight of less than 1000 gm (p value < 0.01).

Table 9: Association of gestational age and birth weight with birth status

	Birth type		Total (N=60)	P Value
Gestational age at Delivery (weeks)	Live birth (N=52)	Still birth (N=8)		
< 28	3 (5.8%)	6 (75%)	9 (15%)	< 0.01
28 to 32	15 (28.8%)	1 (12.5%)	16 (26.7%)	
32 to 37	34 (65.4%)	1 (12.5%)	35 (58.3%)	
Birth weight (gm)				
Less than 1000	2 (3.8%)	7 (87.5%)	9 (15%)	< 0.01
1000 to 1499	16 (30.8%)	1 (12.5%)	17 (28.3%)	
1500 to 2499	30 (57.7%)	0	30 (50%)	
≥ 2500	4 (7.7%)	0	4 (6.7%)	

Of the 52 live births, majority had APGAR score of 7-10 (67.4%). In 15 neonates with APGAR score less than 6, NICU admission was required. Neonatal deaths were observed in 19% of the live births. Mean birth weight of the neonates was 1605 ± 564 Gms, majority had 1500-2499 Gms (50%). The mean length of NICU stay was 14.19 ± 9.64 days. Neonatal complications were observed in 56% of the live births. The most common neonatal complication was respiratory distress syndrome (27%).

Table 10: Neonatal outcome

Neonatal outcome	Frequency	Percent
APGAR (N=52)		
4 to 6	17	32.6
7 to 10	35	67.4
Birth weight		
Less than 1000	9	15
1000 to 1499	17	28.3
1500 to 2499	30	50
≥ 2500	4	6.7
Mean ± SD	1605 ± 564 (540 to 2870)	

Neonatal complications		
Respiratory distress syndrome	14	27
Neonatal jaundice	5	10
Hypoglycemic episodes	4	8
Transient Tachypnea of Newborn	4	8
Meconium aspiration	1	2
Mild birth asphyxia	1	2
Neonatal outcome		
Discharge	21	81
Neonatal death	5	19
Total NICU admission	26	100
mean length of NICU stay	14.19 ± 9.64 days, (2 to 40 days)	

Discussion

Preterm delivery is defined by the World Health Organization as delivery before 37 complete weeks' gestation [2]. Preterm births account for 60–80% of all perinatal mortality and up to 75% of neonatal and infant morbidity. In the present study, mean age of the mothers was 29.7 ± 5.1 years, ranging from 20 to 43 years. It was observed that 84% of the patients were in the age group of 21 to 35 years. In another study, Beevi et al., [5] noted that the maternal age groups 22 to 30 years was the most common.

In study by Manuck et al, [6] mothers who received tocolysis had mean gestational age at delivery of 28.9 ± 2.7 weeks. In their study only 1.7% of the mothers delivered at 34 weeks of gestation or more. Median cervical dilatation at admission was 5 cm, ranging from 4 to 5.5 cm. In their study, 23.6% of the mothers included had a history of previous preterm delivery and the incidence of preterm PROM was 47.2%.

In present study, tocolytics were given in 54% of the cases, the most commonly used was Nifedipine (38%) and Ixosuprine (20%). Oral nifedipine is a slow-release calcium-channel blocker, prevents calcium uptake in the myometrial cell, hence preventing it from contracting [7].

LSCS was performed in 48% and rest had preterm vaginal delivery. The indications for which LSCS was done were GA less than 32 weeks, Twin gestations, ART, previous history of LSCS, Bad obstetric history and precious pregnancy. In another similar study, Jamal and Srivastava[8] observed a labor induction rate of 23.4% and Caesarean delivery was performed in 146 (33.5%) cases, thus indicating a high induction and caesarean rates in such pregnancies. Manuck et al reported cesarean rate of 25.8% in mothers presenting with preterm labor. In another study by Jaju[9], pregnancy outcomes were normal in all the patients with the majority (47 [94.0%]) being vaginal deliveries.

In another study by Beevi et al, [5] the incidence of neonatal sepsis is 34.3% (36) and 54(51%) babies needed NICU care. There were 16 (15.2%) neonatal deaths in this study and all had features of sepsis. In a similar study by Aggarwal et al., [10] mean birth weight of the neonates was 2266.76 ± 726.9 gm. Their mean APGAR score at 1 and 5 minutes was 8 and 9 respectively. In their study, 32% of the neonates required NICU care, of which 8% required ventilatory support. The authors reported that out of 25 neonates, three developed RDS, five developed sepsis and there was an overall 8% perinatal mortality. Jamal and Srivastava [8] reported that 48.9% neonates were admitted to NICU for > 24 hours, though the observed rate of still birth was 4.2%, the number of early neonatal death was quite high, i.e., 17.4%. Nonetheless, 190 (29.6%) cases had to be admitted to intensive care for observation for around < 24 hours. In addition, the authors reported that 47.7% had birth weight of more than 2 kgs, while 32.8% had 1.5 to 2 kgs and 19.5% had less than 1.5 kgs.

In another study by Manuck et al, [7] NICU admission rate was 94%, and mean birth weight was 1357 ± 491 gms. The authors

reported major neonatal morbidity in 41.6%, which included him diagnosis of at least one of the following before discharge: bronchopulmonary dysplasia, grade III or IV intraventricular hemorrhage, periventricular leukomalacia, necrotizing enter colitis, stillbirth, or neonatal death. The median length of NICU admission was 42 days, ranging from 27 to 73 days.

Jaju[9] reported that the mean fetal birth weight was 2.7 ± 0.3 kg. The median (range) Apgar score at 1 minute and 5 minutes were 7.0 (2.0) and 9.0 (1.0), respectively. Only one infant (1 [2.0%]) required NICU admission on day 4 post birth due to hyper-bilirubinemia, who was in NICU for 3 days. There were no cases of congenital anomaly or fetal infection. The authors reported that the mean fetal birth weight was 2.6 ± 0.4 kg in group 1(GA less than 32 weeks at baseline) and 2.7 ± 0.3 kg in group 2 (GA more than 32 weeks at baseline). The median (range) Apgar scores at 1 and 5 minutes were 7.0 (2.0) and 9.0 (1.0) in group 1 and 2, respectively [9].

Preterm delivery may lead to different serious neonatal complications such as respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP) and perinatal death. Long-term morbidities include cerebral palsy (CP), developmental delay (DD), mental retardation, behavioral problems and early demise [11-14].

The main treatment options of women in threatened PTL include cervical cerclage, antibiotics, tocolysis, antenatal corticosteroids (CS) and progesterone treatment. Provider initiated preterm birth can be minimized by early detection of risk factors and prompt intervention to minimize their effects [13-45]. Above all, early booking and promotion for institutional deliveries with NICU set up, should be promoted. Furthermore, future multicentric trials may be conducted to assess the effectiveness of maintenance tocolysis.

Conclusion

The results of the present study show that prolongation of pregnancy is safe in mothers presenting with preterm labor. It is recommended that specialized antenatal care for the patients, who are thought to be at risk of preterm birth, should be performed that can bring down the incidence to some extent. Screening for genital infections, for urinary tract infections and treating them can also achieve the target for diminishing the rates.

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