

COMPARE THE PERINATAL/EARLY NEONATAL MORBIDITY AND MORTALITY IN WOMEN WITH PPRM RECEIVING BED REST WITH THE WOMEN RECEIVING ACTIVITY DURING PREGNANCY

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Abstract

Background: Preterm premature rupture of membranes (PPROM) i.e. rupture of membranes before 37 weeks of gestation. It can lead to significant perinatal morbidity and is associated with 18-20% of perinatal deaths. Perinatal morbidity results due to infection, cord compression, placental abruption and prematurity. Management of PPRM is a challenging problem and it depends on the gestational age and fetal status. **Methodology-** The study was carried out in the Department of Obstetrics & Gynaecology, UCMS & GTB Hospital, Delhi from November 2013 to 30 July 2016. A total of 60 patients were included in the study and were randomized in 1:1 ratio with the help of centralized computer randomization (Group-1: Bed rest group Group-2: Activity group). Detailed history pertaining to risk factors were taken. Diagnosis of PPRM was confirmed by sterile speculum examination. All the patients were managed as per hospital protocol and admitted till delivery. Maternal demographic and obstetrics data and neonatal outcomes were compared between groups using independent t-test, Fisher's exact test, and Chi-square test. **Result-** Neonatal outcome included G.A., NICU stay, birth weight, Apgar 1 min and 5 min, neonatal morbidity like RDS, sepsis, NEC, and neonatal mortality. The mean NICU stay in bed rest group was 6 days 3 hour±6 days 1 hour and in activity group was 4 days 22 hour±5 days 1 hour (p-value=0.56). Neonatal mortality occurred 6 cases in bed rest group and 12 cases in activity group. **Conclusion-** There is no

significant effect of bed rest on early neonatal parameters like G.A. (gestational age) at the time of delivery, birth weight, Apgar (1 min. & 5 min.), and NICU stay. Composite neonatal morbidity like RDS, sepsis, NEC (necrotizing enterocolitis) is not affected by activity. There was increased neonatal mortality in activity group, however this was not statistically significant.

Keywords- PPRM, morbidity, mortality, neonatal, bed rest

Introduction

Preterm premature rupture of membranes (PPROM) i.e. rupture of membranes before 37 weeks of gestation occurs in 3% of pregnancies and is responsible for 1/3rd of preterm births.¹ It can lead to significant perinatal morbidity and is associated with 18-20% of perinatal deaths.² Perinatal morbidity results due to infection, cord compression, placental abruption and prematurity. It is also associated with maternal morbidity due to chorioamnionitis (37%), postpartum endometritis (11%) and sepsis (1%).³⁻⁶ The majority of pregnancies with PPRM (56%) deliver within one week of membrane rupture. In a randomized trial of PPRM at 24-32 weeks, group B streptococcal negative patients managed expectantly with prophylactic antibiotics, the median time to delivery was 6.1 days.^{7,8} The mean time to delivery in our institution was 6.7 days.⁹ Management of PPRM is a challenging problem and it depends on the gestational age and fetal status. Termination of pregnancy is advised in gestation <24 weeks and >34 weeks. However, in gestation between 24-34 weeks, expectant treatment is offered.⁴⁻⁶ During expectant management, patients are hospitalized and admitted till delivery for maternal & fetal monitoring. The aim expectant management is to prolong the pregnancy. and improve the neonatal outcome without compromising maternal health. The recommended treatment is antibiotic course and steroid coverage for lung maturity.^{4,5} The management generally include bed rest in cases of PPRM, though the guidelines do not mention about the antepartum bed rest, however the general practice is to put the patients on bed rest.⁴⁻⁶ Fox NS, et al. study enquired the practice patterns regarding bed rest in women with PPRM and found that 87% of practitioners would recommend bed rest.¹⁰ Bed rest, though currently prescribed in regarding the PPRM, preterm labor, other pregnancy complications, and hypertension in pregnancy, but no benefits have been observed.¹¹

On the other hand bed rest represents significant change in lifestyle and causes the risk of thromboembolism, muscle atrophy and emotionally distressing both to the patients and her family.¹² According to the recent meta-analysis by Maloni JA, et al. and the Cochrane review there is no evidence that bed rest is useful in prevention of preterm birth.¹²⁻¹³ The Cochrane review have been published in 2005, the role of bed rest in preterm labor and author concluded that there is no evidence, either supporting or refuting the use of bed rest in prevention of preterm birth.¹³ As there was no prospective study with role of bed rest in cases of PPRM at that time, the present study was planned. Despite the widespread use of bed rest there are one studies evaluating the use of bed rest in pregnancies complicated by PPRM. Bed rest versus activity trial (BRAT) in PPRM, is the only randomized trial, was started in 2013.¹⁴

The above study was conducted to compare the perinatal/early neonatal morbidity and mortality in women with PPRM receiving bed rest with the women receiving activity during pregnancy.

Materials And Methods

Study place- The study was conducted out in the Department of Obstetrics & Gynaecology, UCMS & GTB Hospital, Delhi from November 2013 to 30 July 2016.

Study design- Randomized controlled clinical study.

Inclusion criteria- Pregnant women between 26-34 week's gestation with PPRM, showing Vertex presentation, having Singleton pregnancy and ready to give consent.

Exclusion criteria- Women with multiple gestation, malpresentation, having any maternal or fetal indication for immediate delivery, active Herpes simplex genital infection, refusal to give consent.

Sample size-60 patients were included in the study which were further randomized in 1:1 ratio with the help of centralized computer randomization.

Group-1: Bed rest group

Group-2: Activity group

Data Analysis-Maternal demographic and obstetrics data and neonatal outcomes were compared between groups using independent t-test, Fisher's exact test, and Chi-square test. Data was analyzed using SPSS. 21 version and entered in Microsoft Excel sheet.

Ethical Consideration- Prior ethical clearance was taken from the Institutional Ethical Committee. A written informed consent was taken from all the patients.

Detailed history pertaining to risk factors were taken. Diagnosis of PPRM was confirmed by sterile speculum examination. If pooling of fluid in the posterior vaginal fornix was not seen then actim PPRM test or AFI on ultrasonography was used to substantiate the diagnosis. Maternal examination was done for signs of chorioamnionitis, i.e. maternal pyrexia, tachycardia, uterine tenderness, offensive vaginal discharge. All the patients were managed as per hospital protocol and admitted till delivery. They were given erythromycin 250 mg qid for 10 days, betamethasone (12 mg) IM stat, and the same dose was repeated after 24 hours. TPR was recorded 6 hourly for first 48-72 hrs, and twice a day. There after BPS was done twice weekly. Mother was observed for signs of clinical chorioamnionitis. Patients were randomized into two groups by computer generated randomized table in 1:1 ratio.

Group I: Patients were put on bed rest i.e. patients spent majority of their days in their hospital bed usually in reclined or lying position. Subjects abstained from walking or engaging in any extraneous activity including lifting or spending any extended period of time out of bed. Subjects were allowed to use the bathroom privilege.

Group II: Patients were allowed activity and did minimum one hour walking per day in addition to the toilet privileges like women walked to fetch her meals/to get ultrasound done etc. Subjects were permitted more activity as desired.

Maternal and fetal monitoring was done till the time of delivery.

Result**Table 1: Comparison of baseline characteristics in both groups**

Parameters	Bed rest n=30	Activity n=30	p- value
Age (years) (mean±SD.)	25.20±3.70 (median=24)	25.40±4.02 (median=25)	0.84
Parity	0	10 (33.33%)	0.05
	1	15 (50%)	
	2	5 (16.67%)	
	≥3	0%	

In bed rest group, the age of subjects ranged from 20 to 35 years and in activity group, ranged from 20 to 41 years. The mean age in bed rest group was 25.20±3.70 years and in activity group was 25.40±4.02 years. The difference was statistically non-significant (p-value= 0.84). Parity was non equally distributed in both groups. In bed rest group 10 women were nullipara while in activity group 18 (60%) cases were nulliparous women. There was only one grand multipara which was in activity group. The difference was statistically non-significant (p=0.05)

Table 2: Comparison of baseline parameters (pregnancy related) in both groups

Parameters	Bed rest (n=30) Mean±SD.	Activity (n=30) Mean±SD.	p- value
Time from L.P.V. To D.O.A. (hours)	36±72.57	41.03±88.13	0.49
POG (D) (days)	220.53±19.09 (median=224)	212.47±12.05 (median=214)	0.05
POG (USG) (days)	216.63±16.60	212.70±13.84	0.32

(POG (D)- period of gestation, D- by date last menstrual period, USG- by ultrasonographically first trimester scan, D.O.A.- day of admission, L.P.V.- leaking per vagina)

In bed rest group the time from L.P.V. to D.O.A. ranged from 3 to 394 hours, and in activity group ranged from 2 to 389 hours. The mean of time from L.P.V to D.O.A. in bed rest group was 36±72.57 hours & in activity group was 41.03±88.13 hours. The difference was statistically non-significant (p-value=0.49) In all cases period of gestation was calculated from dates of L.M.P. corresponded to the POG determined from first antenatal USG. Period of gestation (by dates) ranged from 26 weeks 3 days to 33 weeks 4 days in bed rest group and from 26 weeks 6 days to 33 weeks 4 days in activity group. The mean of period of gestation by dates in bed rest group was 220.53±19.09 days (31.50±2.72 weeks) & in activity group was 212.47±12.05 days (30.35±1.72 weeks). The difference was statistically non-significant (p-value=0.05) .

Table 3: Comparison of mode of delivery in both groups

Parameters		Bed rest n=30	Activity n=30	p- value
Mode of delivery	NVD	26 (86%)	24 (80%)	0.49
	LSCS	4 (13.33%)	6 (20%)	

(NVD= Normal vaginal delivery, LSCS= Lower segment caesarean section)

NVD cases contained spontaneous labor pains and induction of labor pains followed by normal vaginal delivery occurred. Majority of subjects went into spontaneous labor. Percentage of normal vaginal delivery in bed rest and activity group was 26 (86%) and 24 (80%) respectively. Caesarean section cases contained emergency LSCS and elective LSCS. In bed rest group 4 (13.33%) LSCS occurred i.e. 2 elective LSCS and 2 emergency LSCS. In activity group 6 (20%) LSCS occurred i.e. 2 elective LSCS and 4 emergency LSCS. Difference of mode of delivery was statistically non-significant (p-value= 0.49)

Table 4: Comparison of fetal outcomes in both groups

Parameters		Bed rest (mean±SD.) n=30	Activity (mean±S.D.) n=30	p- value
G.A. (days)		228.23±15.19	227.00±12.64	0.73
Birth weight (kg)		1.68±0.42	1.61±0.37	0.52
Apgar (1 min.)		8.20±1.71	7.90±1.92	0.52
Apgar (5 min.)		8.60±1.50	8.43±1.41	0.66
NICU admission	No	6 (20%)	6 (20%)	1.00
	Yes	24 (80%)	24 (80%)	1.00
NICU Stay (hours)		147.13±145.23	118.43±121.19	0.56
RDS		21 (70%)	24 (80%)	0.37
Sepsis		3 (10%)	3 (10%)	1.00
NEC		0%	1 (3.33%)	1.00
Neonatal mortality	Early	4 (13.33%)	11 (36.67%)	0.24
	Late	2 (6.67%)	1 (3.33%)	
	Total	6 (20%)	12 (40%)	

(G.A.= Gestational age, NICU= Neonatal intensive care unit, RDS= Respiratory distress syndrome, NEC= Necrotizing Enterocolities)

Neonatal outcome included G.A. At the time of delivery, NICU stay, birth weight, Apgar 1 min and 5 min, neonatal morbidity like RDS, sepsis, NEC, and neonatal mortality.

Baby weight in bed rest group was slightly more than activity group. The mean of baby birth weight in bed rest group was 1.68±0.42 and in activity group was 1.61±0.37 (p-value=0.52)

The mean of Apgar in 1 min in bed rest group was 8.20 ± 1.71 and in activity group was 7.90 ± 1.92 (p -value=0.52). Apgar score at 5 min in both group was approximately equal. The mean of Apgar in 5 min in bed rest group was 8.60 ± 1.50 and in activity group was 8.43 ± 1.41 , there was no statistical difference between both groups (p -value=0.66).

24 (80%) babies in each group required NICU admission.

NICU stay in bed rest group was longer than activity group. The mean NICU stay in bed rest group was 147.13 ± 145.23 hours (6 days 3 hour \pm 6 days 1 hour) and in activity group was 118.43 ± 121.19 hours (4 days 22 hour \pm 5 days 1 hour) (p -value=0.56).

Percentage of RDS in bed rest and activity group was 21 (70%) and 24 (80%) respectively (p -value=0.37). Sepsis occurred in babies equal in number in both groups i.e. 3 (10%) (p -value=1.00). Necrotizing enterocolitis occurred one baby only in activity group i.e. 1 (3.33%) (p -value=1.00).

Neonatal mortality occurred in 18 cases (6 cases in bed rest group and 12 cases in activity group). Total early neonatal mortality (<7 days) was 15 cases and late neonatal mortality was 3 cases in both groups. Though neonatal mortality was high in activity group it was not found to be statistically significant (p -value= 0.24). Early neonatal death in bed rest and activity group was 4 (13.33%) and 11 (36.67%) respectively. Late neonatal death in bed rest and activity group was 2 (6.67%) and 1 (3.33%) respectively. Difference was not significant statistically (p -value=0.24).

Comparison of analysis of neonatal mortality in both groups

Neonatal mortality cases were further analyzed as per-

(a) baby birth weight

(b) gestational age interval

Table 5 (a): Comparison of analysis of neonatal mortality in both groups (by birth weight)

Parameters	Bed rest	Activity	p- value
≤ 1.5 kg	6/9 (66.67%)	9/13 (69.23%)	0.24
> 1.5 kg	0/21 (0%)	3/17 (17.65%)	
total	6/30 (20%)	12/30 (40%)	

Analysis of neonatal mortality was done according to baby birth weight in both groups. In both groups majority of neonatal mortality occurred in baby weight less than or equal to 1.5 kg. Difference was statistically non-significant (p - value= 0.24)

Table 5 (b): Comparison of analysis of neonatal mortality in both groups (by period of gestation at the time of delivery)

Parameters	Bed rest	Activity	p- value
26- 28	1/1 (100%)	0 (0%)	0.24
28- 30	4/5 (80%)	4/4 (100%)	
30- 32	1/3 (33.33%)	6/13 (46.15%)	
32- 34	0/17 (0%)	2/10 (20%)	
>34	0/4 (0%)	0/3 (0%)	
Total	6/30 (20%)	12/30 (40%)	

Neonatal mortality was done according to period of gestational age at the time of delivery. In both groups majority of neonatal mortality occurred in gestational age ≤ 32 weeks. Difference was statistically non-significant (p-value=0.24)

Table 6: Comparison of antepartum & postpartum events in both groups

Parameters		Bed rest n=30	Activity n=30	p- value
APE & PPE	Chorio	0%	1 (3.33%)	0.40
	Abruption	2 (6.67%)	0%	
	PPFI	0%	0%	
	Total	3 (10%)	3 (10%)	

(Chorio= Chorioamnionitis, APE& PPE= Antepartum & postpartum events, PPFI= Postpartum febrile illness)

Percentage of choriomnionitis only present in activity group i.e.1 (3.33%). Placental abruption occurred during intrapartum followed by normal vaginal delivery occurred. Percentage of placental abruption only present in bed rest group i.e. 2 (6.67%). Postpartum febrile illness in both group was not found. Difference of antepartum and postpartum event was statistically non- significant (p-value=0.49)

Discussion

In above study, age ranged from 20 to 41 years which was similar to Bigelow CA, et al.¹⁵ study. Also, parity in both groups were non equally distributed. 10 (33.33%) women were nullipara in bed rest group and 18 (60%) women were nulliparous in activity group. Bigelow CA, et al. study also found that majority of subjects in both groups were nulliparous.¹⁵

In above study, period of time from L.P.V. to D.O.A was comparable in both groups and difference was not significant statistically. Period of gestation (by dates) were comparable in both groups.

Majority of subjects had normal vaginal delivery in both groups i.e. (bed rest-86%, activity-80%) and less number of subjects had LSCS in both groups i.e. (bed rest-13.33%, activity-20%). These observations compared with Bigelow CA, et al study and in their study found that number of NVD and LSCS cases in bed rest group was 10 (56%) cases and 8 (44%) cases respectively and number of NVD and LSCS cases in activity group was 5 (29%) cases and 12 (71%) cases respectively.¹⁵

Fetal outcomes were compared between both groups and found that difference was not statistically significant. Mean of birth weight was compared with both groups and found approximately similar. These observations compared with Bigelow CA, et al study and in their study mean birth weight in bed rest and activity group was 1.796.4(\pm 632.4) and 1.494.7(\pm 761.1) kg (p=0.80).¹⁵ Apgar 1 min and Apgar 5 min compared with both groups and found difference was not statistically significant. These parameters compared with Bigelow CA et al. study and found similar observations.¹⁵ Observation showed that, NICU stay in bed rest group was longer as compared to activity group but their difference was statistically non-significant. In our study, in each group, 24 (80%) babies required NICU admission. In our study, number of RDS babies compared with both groups and found that difference was not statistically significant. Number of RDS babies in both groups in our study were seen more

than Bigelow CA et al study {bed rest group 6 (33%) cases, activity 8 (47%) cases respectively ($p=0.80$).¹⁵ Number of sepsis was seen in 3 (10%) neonate in each group in our study and we found that there was not significant difference between two groups. Similar results were found with Bigelow CA et al study wherein they also found that likely develop of neonatal sepsis.¹⁵ Necrotizing enterocolitis was only present in one case in activity group in our study difference was not found to be statistically significant between two groups. Bigelow CA et al.¹⁵ study found higher incidences of necrotizing enterocolitis in activity group i.e. 4 (24%) though it was not significant.¹⁵

In above study, we found higher neonatal mortality in activity group as compared to bed rest group. Further analysis showed that mortality was high in babies less than or equal to 1.5 kg and gestational age less than 32 weeks in both groups. Difference between neonatal mortality was not significant statistically ($p=0.24$). We found that, number of neonatal mortality in our study more than Bigelow CA, et al. study [activity-2 (12%) ($p=0.80$)].¹⁵

In the above study, antepartum events were compared in both groups and found difference was not significant statistically. Postpartum event postpartum febrile illness was not found in any group. Bigelow CA et al. in their study also reported likely to develop postpartum sepsis i.e. endometritis in only one case (6%) in activity group.¹⁵ Bigelow CA et al. had used pedometer for measurement of activity though they did not find it useful.¹⁵ In our study we did not used pedometer for subjects because of cost factor. As there was no objective measurement of activity in group-II this is limitation of our study.

In above study, activity did not have a significant effect on maternal and fetal outcomes like latency period, gestational age at delivery, or neonatal outcomes. Bigelow CA et al.¹⁵ in their study, also found that similar observations were seen in ABOVE study.

Conclusion

From the above study it can be stated that there is no significant effect of bed rest on early neonatal parameters like G.A. (gestational age) at the time of delivery, birth weight, Apgar (1 min. & 5 min.), and NICU stay. Composite neonatal morbidity like RDS, sepsis, NEC (necrotizing enterocolitis) is not affected by activity. There was increased neonatal mortality in activity group, however this was not statistically significant.

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