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Oral Micronized Progesterone in Preterm Labour: The Neonatal Outcome

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Abstract
Introduction.*. Preterm birth is leading cause of newborn death and the second leading cause of death after pneumonia in children under five years.The vaginally administered progesterone has become the most widely effective alternative in preventing preterm birth [2]. Oral Micronized Progesterone,Micronizing is a process designed to increase the half-life of progesterone and reduce its destruction in the gastrointestinal tract. Micronization decreases particle size and enhances the dissolution of progesterone[4,5.]In fact, the Cochrane survey concludes: "Further trials are still required to assess the optimal timing, mode of administration and dose of administration of progesterone therapy" [3]. Thus, the current situation with the oral route is not that of a proven absence of value, but rather of a scarcity of relevant research.**Study.** The study was a hospital based Randomised controlled study and was carried out in the department of obstetrics and Gynaecology, a tertiary hospitalZMCH, DAHOD,Titled as ORAL MICRONIZED PROGESTERONE IN PRETERM LABOUR: THE NEONATAL OUTCOME"was conducted in obstetrics and Gynaecology Department of 144 preterm labour patients,to measure neonatal outcome after giving oral micronized progesterone in cases groups.**RESULTS.**In our study we found increased birth weight in oral micronized treated group. In our study results were significant because OMP treated groups are having increase age of delivery and increased birth weight.In our study we found that APGAR score for babies,above or equail to 7/10 was 75% for cases and 37.5% for controls ,Which depicts statstically significant results between cases and controls. It reflect that Oral micronized progesterone treated group will be having better neonatal outcome and delayed period of gestation for delivery will lead to decreased perinatal death and perinal morbidity.*
CONCLUSION*. Preterm delivery continues to provide an enormous challenge in the delivery of perinatal health care. Emphasizing on the long term morbidities in preterm labour in women, a step should be taken to curtail the number of preterm labour. In developing country like ours, it is definitely better to prevent preterm labour in order to reduce neonatal morbidity and mortality as sophisticated neonatal intensive care units are not available every where.*
Keywords*: PRETERM,OMP,PROGESTERONE,MICRONISED,NEONATAL OUTCOME,BIRTH WEIGHT*

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I. Introduction

Preterm is defined as babies born alive before 37 weeks of pregnancy are completed.Currently preterm birth represents the leading cause of neonatal mortality and long-term morbidity . Preterm labor is at least partly related to an untimely decline in the progesterone effect [1]. Preterm birth is leading cause of newborn death and the second leading cause of death after pneumonia in children under five years.The vaginally administered progesterone has become the most widely effective alternative in preventing preterm birth [2]. Oral Micronized Progesterone,Micronizing is a process designed to increase the half-life of progesterone and reduce its destruction in the gastrointestinal tract. Micronization decreases particle size and enhances the dissolution of progesterone[4,5].In fact, the Cochrane survey concludes: "Further trials are still required to assess the optimal timing, mode of administration and dose of administration of progesterone therapy" [3]. Thus, the current situation with the oral route is not that of a proven absence of value, but rather of a scarcity of relevant research.

AIMS AND OBJECTIVE

1. To determine the efficacy of oral micronized progesterone in preterm labour for neonatal outcome.

II. Material And Method:

The study was carried out in the department of obstetrics and Gynaecology, a tertiary hospitalZMCH, DAHOD,The study Titled as" ORAL MICRONIZED PROGESTERONE IN PRETERM LABOUR: THE NEONATAL OUTCOME"was conducted in OBGY department of 144 preterm patients,as management of preterm labour with oral micronised progesterone.It was conducted between oral micronized progesterone treated group of preterm labour as cases(72) and without oral micronized treated progesterone group as a control(72). Out of them seventy two patients were taken as a cases for giving oral micronized progesterone and seventy two for controls for comparision. The particulars, investigations, treatment, examinations, history etc. were recorded at the relevant time. **INCLUSION CRITERIA:** Women with gestational age between 28 weeks to less than 37th completed weeks,Presenting with pain in abdomen,Four uterine contractions in 20 minutes with Cervical dilatation more than 1 cm & effacement more than 80 %,History of previous preterm birth and recurrent miscarriage.

EXCLUSIONCRITERIA

Diabetes,Hypothyroidism,Cardiacds,Severepreeclampsia,Eclampsia,antepartemhaemmrhage,Chorioamnitis,Hydroamnios,Cervical dilation greater than 3 cm, PROM, fetal distress,Women with a history of cervical insufficiency and a cerclage in place..A informed consent was taken from the subject or subject's informant willing to participate in the study and were screened for inclusion and exclusion criteria.Details of patient's history was taken and low birth weight, Low APGAR score , Bronchopulmonary dysplasia , neonatal sepsis ,assessed at the admission to Neonatal Intensive Care Unit (NICU),Perinatal mortality etc were measured. Ethical approval was obtained.**Statistical Methods:** Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number .Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis.

Statistical software: The Statistical software namely SAS 9.2, SPSS 21.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

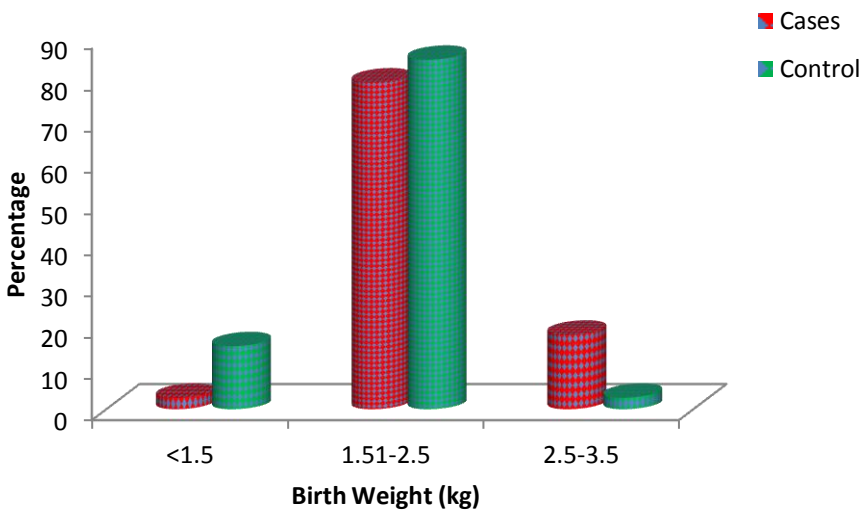
III. Results And Observation

Table 1: Birth Weight (kg) distribution in case-controls studied

Shows birth weight ranges from <1.5 kg to 3.5 kg . Table depicts that for cases 18.1% are more than 2.5 kg and for control only 2.8% above 2.5 kg. For controls 15.3% below 1.5 kg ,84.7% in between to 1.5 to 2.5kg and 2.8% were more than 2.5 kg.
These results are significant(P<0.001**, Significant, Chi-Square test)

Birth Weight (kg)	Cases	Control	Total
<1.5	2(2.8%)	11(15.3%)	13(9%)
1.51-2.5	57(79.2%)	61(84.7%)	118(81.9%)
2.5-3.5	13(18.1%)	2(2.8%)	15(10.4%)
Total	72(100%)	72(100%)	144(100%)
Mean ±SD	2.17±0.39	1.73±0.32	1.94±0.41

P<0.001**, Significant, Chi-Square test



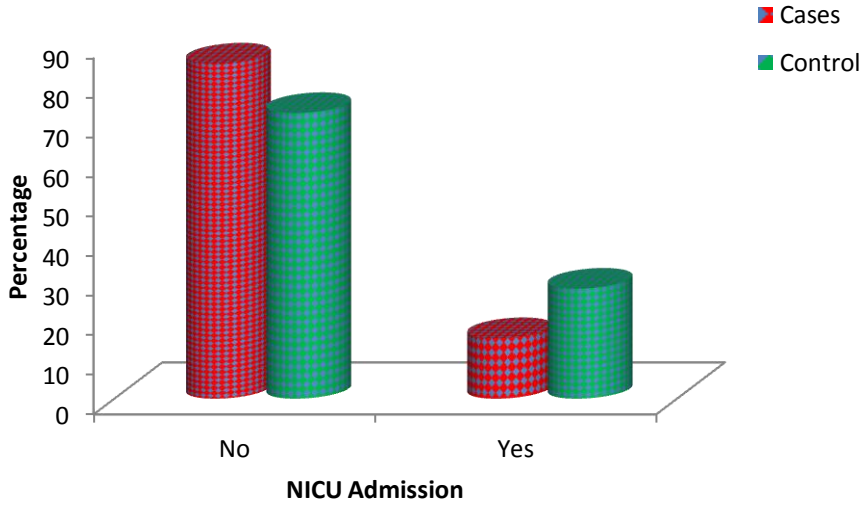
Graph

Table 2: NICU Admission in two groups studied

Below graph and table shows NICU admission in cases were 15.3% and for control 27.8%.Which was not statistically significant.(P=0.068+, Significant, Chi-Square test)

NICU Admission	Cases	Control	Total
No	61(84.7%)	52(72.2%)	113(78.5%)
Yes	11(15.3%)	20(27.8%)	31(21.5%)
Total	72(100%)	72(100%)	144(100%)

P=0.068+, Significant, Chi-Square test



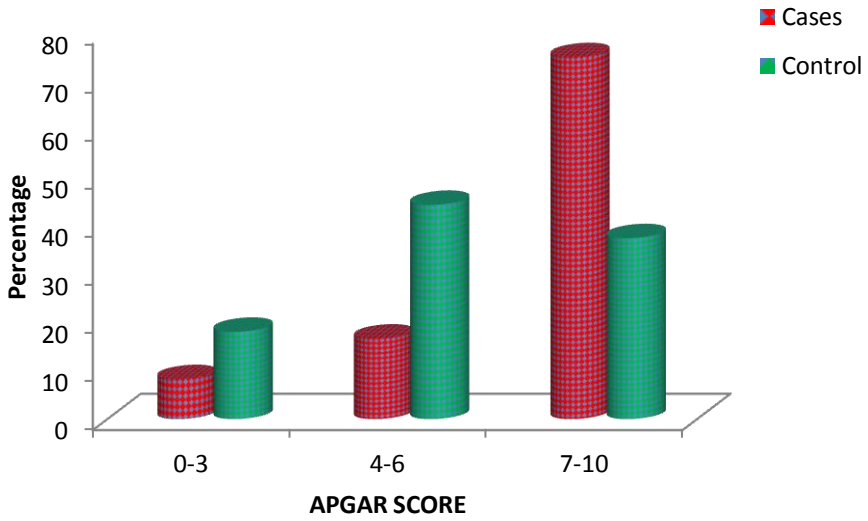
Graph

Table 3: Apgar score distribution in case-controls studied

Below graphs and table Shows APGAR score for babies that for cases 75% and for control 37.5% are above or equail to 7/10
Which depicts statistical significant.(P<0.001**, Significant, Chi-Square test),It shows that OMP treated group will be having improved APGAR score.

Apgar score	Cases	Control	Total
0-3	6(8.3%)	13(18.1%)	19(13.2%)
4-6	12(16.7%)	32(44.4%)	44(30.6%)
7-10	54(75%)	27(37.5%)	81(56.3%)
Total	72(100%)	72(100%)	144(100%)
Mean ±SD	7.54±2.12	6.13±2.35	6.83±2.36

P<0.001**, Significant, Chi-Square test



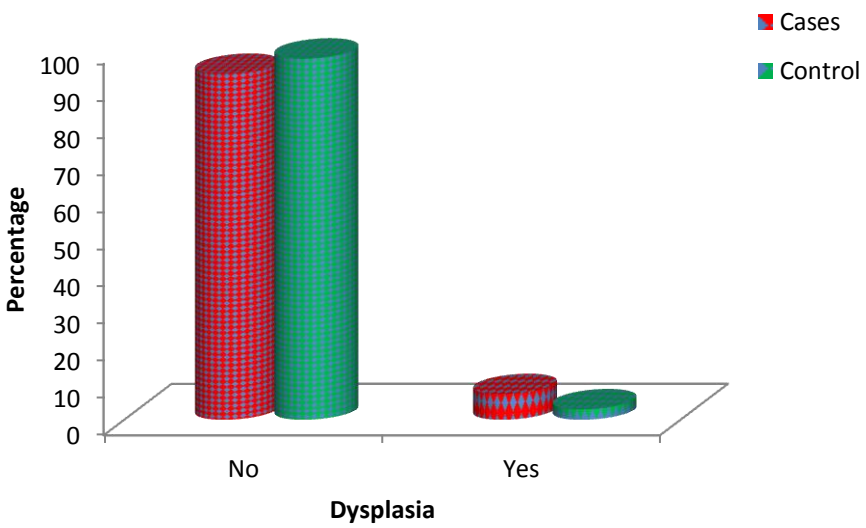
Graph

Table 4:Bronchopulmonary dysplasia incidence in case-controls studied

Shows that dysplasia was 6.9 % for cases and 2.8 % for control. (P=0.441, Not Significant, Chi-Square test)

Dysplasia	Cases	Control	Total
No	67(93.1%)	70(97.2%)	137(95.1%)
Yes	5(6.9%)	2(2.8%)	7(4.9%)
Total	72(100%)	72(100%)	144(100%)

P=0.441, Not Significant, Chi-Square test



Graph

Table 13: Complications(Neonatal sepsis)

Shows that neonatal sepsis was 1.4% in cases and 0% in control.(P=1.000, Not significant, Fisher Exact test)

	Cases (n=72)	Control (n=72)	Total (n=144)
Sepsis	1(1.4%)	0(0%)	137(95.1%)

P=1.000, Not significant, Fisher Exact test

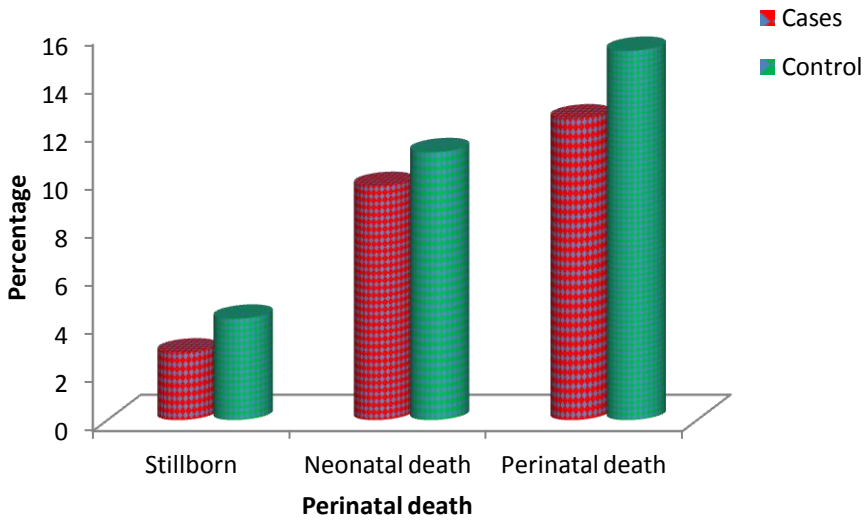
Table5: Incidence of Perinatal death

Below given graph and table Shows incidence of perinatal death in cases was 12.5% and 15.3% in control.Neonatal death was 9.7%for case and 11.1% for control.Not significant(Chi-Square test/Fisher Exact test, P value)

Stillborn was 2.8% in cases and 4.2% in controls.(Not significant,p=1.000)

Perinatal death	Cases (n=72)	Control (n=72)	Total (n=144)	P value
Stillborn	2(2.8%)	3(4.2%)	5(3.5%)	1.000
Neonatal death	7(9.7%)	8(11.1%)	15(10.4%)	0.785
Perinatal death	9(12.5%)	11(15.3%)	20(13.9%)	0.630

Chi-Square test/Fisher Exact test



IV. Discussion

In present series we found that 18.1% babies having birth weight more than 2.5 kg for cases and only 2.8% babies above 2.5 kg for control . For controls 15.3% below 1.5 kg ,84.7% in between to 1.5 to 2.5kg and 2.8% were more than 2.5 kg.These results are significant(P<0.001**, Significant, Chi-Square test).In our study we found increased birth weight in oral micronized treated group .In present study we found mean birth weight for cases 2.17±0.39 kg and 1.73±0.32kg for control(P<0.001**) .In the similar study trailed by **Meis** et al[6] found increased birth weight as compared to control group. In the study of **Chaudhary M et al**[7] also found increased birth weight in progesterone treated group compare to control group. Our study is comparable with Chaudhary M et al enrolled ninety women at 24–34 weeks of singleton pregnancy with intact membranes and arrested preterm labor were randomly allocated to receiveOMP(n=45) or placebo (n = 45) daily until 37 weeks or delivery, whichever was earlier. Outcome parameters were com- pared using Student t test, $\chi 2$ test, Fisher exact test, and log-rank $\chi 2$ test. Results: OMP significantly prolonged the latency period (33.29 ± 22.16 vs 23.07 ± 15.42 days; P = 0.013). Log-rank analysis revealed a significant difference in mean time to delivery between the 2 groups (P = 0.014). There were significantly fewer preterm births(33%vs58%;P= 0.034)and low birth weight neonates(37%vs64%;P= 0.017),and significantly higher mean birthweight(2.44±0.58vs2.14±0.47kg;P= 0.009)in the OMP group.Perinatal out comes and adverse effects were similar in the 2 groups. They concluded that Maintenance tocolysis with OMP significantly prolonged pregnancy and decreasedthe numberof preterm births.

Rai et al[8] also found increased baby birth weight in oral micronized treated group thancontrols.Rai et al found birth weight 2400 vs 1890 gm0 in their study.

Neonatal parameter

NICU admission,bronchopulmonary dysplasia and neonatal sepsis were not significant among cases and control .They were comparable each other. In our study NICU admissions in cases were15.3% and for control 27.8%(P=0.068+, Significant, Chi-Square test) . Parameter Bronchopulmonary dysplasia was present 6.9 % in cases and 2.8 % in control.

That neonatal sepsis was 1.4% in cases and 0% in control.(P=1.000, Not significant, Fisher Exact test)

In our series above mentioned parameter are not statstically significant.These results were favoured by many studies .**Mohan C. Regmi et al** [9]found similar results in their study in neonatal outcome In another **study Borna and sahabi** [10] found No significant differences between recurrent preterm labor, admission to intensive care unit and neonatal sepsis

APGAR SCORE AT 5 MINUTES.

In our study results were significant because OMP treated groups are having increase age of delivery and increased birth weight.In our study we found that APGAR score for babies,above or equail to 7/10 was 75% for cases and 37.5% for controls ,Which depicts statstically significant results between cases and controls.

(P<0.001**, Significant, Chi-Square test) Our study was favoured by Rai et al.

Rai et al[8] also found Similar results as apgar score was higher in oral micronized treated group PTB occurred in 29 (39.2%) women in the OMP group (n=74) compared with 44 (59.5%) in the control group (n=74,

P=0.002). Mean gestational age at delivery was higher in the OMP group (36.1 vs 34.0 weeks, P<0.001). Fewer preterm births occurred between 28 and 31 weeks plus 6 days in the OMP group (RR 0.20; 95% CI, 0.05-0.73, P<0.001). Neonatal age at delivery (34 vs 32 weeks, P<0.001), birth weight (2400 vs 1890 g, P<0.001), NICU stay (>24 h, P<0.001), and Apgar scores (P<0.001) were more favorable in the OMP group, and fewer neonatal deaths occurred (3 vs 7, P=0.190).

In our study incidence of perinatal death in cases was 12.5% and among control 13.9%, Incidence of Stillborn in case 2.8 % and control 4.2 % ,Incidence of neonatal death in cases 9.7 % and control 11.1 %.It reflect that Oral micronized progesterone treated group will be having better neonatal outcome and delayed period of gestation for delivery will lead to decreased perinatal death ,but not statistically significant.In our study perinatal death were not statstically significant,our results were favoured by Roberta Mackenzie et al.

Roberta Mackenzie et al[11]conducted a meta-analysis evaluating the use of progesterone for women with high risk of preterm birth. Three trials were eligible for inclusion. There was a significant reduction in risk of delivery less than 37 weeks with progestational agents. There was no significant effect on perinatal mortality or serious neonatal morbidity. The finding of present study was similar to present study.**Jay D. Iams et al**[12] studied that Women who have delivered an infant between 16 and 36 weeks' gestation have an increased risk of preterm birth in subsequent pregnancies. The risk increases with more than 1 preterm birth and is inversely proportional to the gestational age of the previous preterm birth.Period of gestation was <37 weeks in cases 33.3 % and 54.5 % in control And >37 weeks in cases was 66.7 % and control 45.5 %.(P=0.343, Not significant, Chi-Square test) Values are not statistically significant. It means in control group perinatal death were more in <37 weeks because of prematurity.In case this was less as progesterone treated group will delays gestational age of delivery.This reflect that prematurity is the most common leading factor in perinatal death.Prematurity leading perinatal death in cases was 55.6 % and control 81.8 %.Birth asphyxia and other causes in cases was 44.4 % and control was 18.2 %.(P=0.336, Not significant, Fisher Exact test)

It suggest that In micronized progesterone treated cases are as there are less chances of prematurity with compared controls.Progesterone treated groups will be having less recurrent preterm and better neonatal outcome ,because of delayed period of gestation.

Financeal support N/A
Conflict interest NA

V. Conclusion

Preterm delivery continues to provide an enormous challenge in the delivery of perinatal health care. Emphasizing on the long term morbidities in preterm labour in women, a step should be taken to curtail the number of preterm labour. In developing country like ours, it is definitely better to prevent preterm labour in order to reduce neonatal morbidity and mortality as sophisticated neonatal intensive care units are not available every where.

References

[1]. .Romero R, Yeo L, Chaemsaithong P, Chaiworapongsa T, Hassan SS. Progesterone to prevent spontaneous preterm birth. *Semin Fetal Neonatal Med*. 2014; 19: 15– 26.
[2]. Romero R, Conde-Agudelo A, El-Refaie W, Rode L, Brizot ML, Cetingoz E, et al. Vaginal progesterone decreases preterm birth and neonatal morbidity and mortality in women with a twin gestation and a short cervix: an updated meta-analysis of individual patient data. *Ultrasound Obstet Gynecol*. 2017; 49: 303– 14.
[3]. Dodd JM, Jones L, Flenady V, Cincotta R, Crowther CA. Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth. *Cochrane Database Syst Rev*. 2013;(7): CD004947.
[4]. Hargrove JT, Maxson WS, Wentz AC. Absorption of oral progesterone is influenced by vehicle and particle size. Am J Obstet Gynecol 1989;161(4):948-51.
[5]. Simon JA, Robinson DE, Andrews MC, Hildebrand JR 3d, Rocci ML, Blake RE, et al. The absorption of oral micronized progesterone: the effect of food, dose proportionality, and comparison with intramuscular progesterone. *Fertil Steril* 1993;60(1):26–33.
[6]. Meis PJ, Klebanoff M, Thom E, ,Dombroski MP ,Sibai B , Moawad AH Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med 2003 ;348(24):2379-85.
[7]. Choudhary M, Suneja A, Vaid NB, Guleria K, *Farid MM* Maintenance tocolysis with oral micronized progesterone for prevention of preterm birth after arrested preterm labor. Int J Gynaecol Obstet 2014;126(1):60-3.
[8]. Rai, Pushpanjali; Rajaram, Shalini; Goel Neerja, ,Gopalkrishnan et al Oral Micronized Progesterone for Prevention of Preterm Birth 2009. 64 (5) 285-86.
[9]. Regmi MC, Rijal P, Agrawal A, Uprety D (2012) Progesterone for Prevention of Recurrent Preterm Labor after Arrested Preterm Labor- A Randomized Controlled Trial. Gynecol Obstet 2012, 2(4):125-26
[10]. Borna S, Sahabi N. Progesterone for maintenance tocolytic therapy after threatened preterm labor: a randomized controlled trial. Aust N Z J Obstet Gynaecol 2008 ;48(1):58-63.
[11]. Mackenzie R, Walker M, Armson A, Hannah ME. Progesterone for the prevention of preterm birth among women at increased risk: a systematic review and meta-analysis of randomized controlled trials. Am J Obstet Gynecol 2006 ;194(5):1234-42.
[12]. Jay D. Iams, MD and Vincenzo Berghella, MD.Care for women with prior preterm birth. Am J Obstet Gynecol. 2010 ; 203(2): 89–100.