

Recent Studies of Preterm Labour in Siriraj Hospital

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Preterm labor and delivery are still the leading causes of high perinatal and neonatal morbidity and mortality. Premature infants are at greater risk for short and long term complications, including disabilities and impediments in growth and mental development. Siriraj Hospital, one of the tertiary medical centers in Bangkok, had the prevalence of preterm labour about 12.89%.¹ In order to decrease the perinatal morbidity and mortality from preterm birth, many trials were initiated to inhibit, predict or prevent preterm birth.

Definition

Threatened preterm labour was defined as regular uterine contractions occurring at the frequency of at least 1 time in 10 minutes with no effacement and dilatation of the cervix between 20-37 weeks. The examination was taken for at least 30 minutes.²

Preterm labor was defined as regular uterine contractions 4 times in 20 minutes or 8 times in 60 minutes with progressive cervical dilatation greater than 1 cm and effacement at least 80%.³

Preterm birth was defined as a delivery that happened before 37 completed weeks (less than 259 days) of gestation.⁴

Trend of preterm labour in Siriraj Hospital

The trend of preterm delivery in Siriraj Hospital has been changed for 7 years. The situation of social policy, hospital contract and financial problems were the main issues for the decision of the patient of the place of delivery. Preterm birth has increased steadily in many centers which has resulted from the technique of assisted reproduction, high prevalence of complicated pregnancy and others.⁵ Siriraj Hospital is the tertiary center where the complicated cases were referred for intensive care, therefore our preterm birth rate was high.

From the study in Siriraj Hospital¹, the birth rate decreased steadily during 2002-2006, but the rate of preterm birth increased steadily from 2004 to 2008 (9.44%-12.98%). The rate of threatened preterm labour was constant between 1.20 -1.78%. (Fig 1) Low birth weight infants were mostly found among preterm births. The sepsis and chromosome abnormalities were the lowest causes of fetal death. The trend of neonatal death from prematurity had continuously declined and there was no early neonatal death in year 2008.

In the view of perinatal mortality rate, it has continuously declined and has been less than 10% in the last 10 years.⁶ Moreover it was interesting that in the year 2008, no premature baby died. This can be explained by the fact that Siriraj Hospital is the super-tertiary center where the complicated cases are referred, therefore preterm birth has consistently increased. During year 2006, there was a policy of contract insurance in which most contract pregnant women were delivered in their local hospital. This resulted in the lowest preterm birth rate in year 2004 (9.44%). Moreover the improvement in obstetric and newborn care in Siriraj Hospital has made changes in the survival rate of premature babies. The excellent equipment and well-trained neonatologists has resulted in

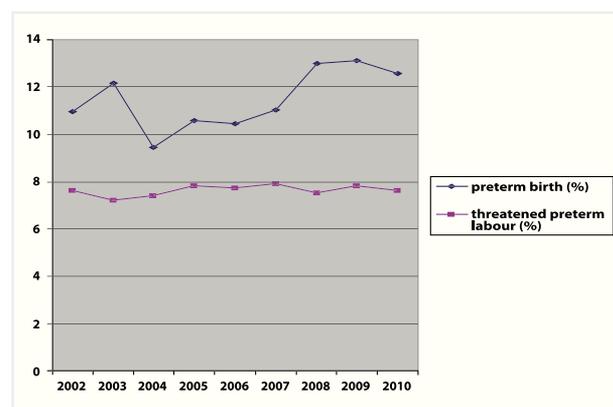


Fig 1. Trend of preterm and threatened preterm labour in Siriraj Hospital

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the best care of newborns. It is not surprising that the very high costs of newborn care around 22,925,000 Thai baht /year or 175,000 Thai bahts / case in Siriraj Hospital was recorded.⁷ (Table 1)

Risk factors for preterm labour in Siriraj Hospital

Premature infants are at greater risk for short and long term complications, including disabilities and impediments in growth and mental development. Many risk factors were identified to prevent preterm labour and delivery. Many interventions were initiated to help prevent the complications. However, many risks factors have been difficult to prove and most preterm births are delivered from the pregnant women without risk factors.

The study in Siriraj Hospital presented that no risk factor was statistically significant for preterm delivery.⁸ Previous preterm delivery is the strongest risk factor for subsequent preterm delivery.⁹ In contrary to this study was that most women with previous preterm delivery had subsequent pregnancies of normal term delivery.⁸

Maternal age, race, and marital and economic status were the risks for preterm delivery. Both teenagers and women 35 years of age or older have been reported to have elevated rates of preterm delivery.¹⁰ Education, occupation, and family income were used to define socioeconomic status. The study in Siriraj Hospital presented that risks of maternal age, socioeconomic status and pregnancy weight were not statistically significantly related to preterm delivery. However, intensive prenatal care has not been shown to decrease the risk of preterm delivery.

Multifetal pregnancy¹¹, infection or inflammation¹², maternal physical activity¹³, cigarette smoking¹⁴ and anemia (especially hemoglobin less than 9.5 g/dL)¹⁵ are related to preterm delivery. However, anemia during the third trimester which results from normal expansion of maternal plasma volume is not correlated to preterm delivery.¹⁶

Fetal factors including fetal growth restriction and congenital anomalies, both increase the risk for preterm delivery. The study of Goldenberg RL, et al¹⁷ presented that all different risk factors had no statistical significance which supported this authors study.¹⁸

Cervical insufficiency and preterm in Siriraj Hospital

Cervical insufficiency (formerly termed cervical incompetence) referred to painless cervical changes which occurred in the second trimester and resulted in recurrent pregnancy loss. Cervical insufficiency had many causes, both congenital and acquired.¹⁸ Multiple factors including structural, histological, hormonal and inflammatory causes act together and lead to pregnancy loss or preterm delivery. Women suspected of cervical insufficiency are generally treated with elective cerclage or closely monitored, with placement of an emergency cerclage if indicated.

Cervical cerclage is used for the treatment of cervical insufficiency, which is performed for a woman who had a

history of one or more recurrent pregnancy losses in the past, in the second trimester of pregnancy¹⁹. The treatment consists of a strong suture being inserted into and around the cervix early in the pregnancy, usually between 14 to 16 weeks, and then removed towards the end of the pregnancy when the highest risk of recurrent pregnancy loss has passed. There are three types of cerclage including McDonald cerclage²⁰, Shirodkar cerclage²¹ and abdominal cerclage.²² The most common techniques for cerclage were first described by McDonald and Shirodkar.

From the study in Siriraj Hospital, McDonald cerclage was performed because it is the easy procedure to perform and remove. From the study in Siriraj Hospital²³, elective cerclage results in good neonatal outcome with gestational age of delivery about 26-38 weeks which confirmed the previous study.²⁴ No evidence of neonatal asphyxia was detected. However, emergency cerclage results in poor neonatal outcome with gestational age of delivery about 25-33 weeks. The mean fetal birth weight in emergency cerclage was also lower than those in the elective cerclage group with statistical significance. The results in the present study reassured that elective cerclage has the better outcome than the emergency cerclage. If the history of recurrent pregnancy loss during second trimester was confirmed, elective cerclage should be considered instead of waiting for serial ultrasound until the cervix was shortened.

From Siriraj Hospitals study²³, the most complication of pregnancy was PPROM which was found in emergency cerclage more than elective cerclage. This result confirmed the previous studies which can be explained from the advanced cervical dilatation or prolapsed fetal membranes.²⁴ This complication has been reported in up to 65% of emergency cerclage.²⁴

Nifedipine, proluton depot and bed rest interventions for preterm labour

The recent evidence from the statistical unit, Siriraj Hospital, found that the pregnant women with threatened preterm labour who had only bed rest, turned out to have preterm labour at a rate of about 30%-50%.²⁵ After bed rest, 30% of those with threatened preterm labour were going to the advanced stage of labour and underwent delivery. If threatened preterm labour was able to be stopped, the prevalence of preterm birth could be minimized as well as perinatal mortality and morbidity be reduced. Therefore nifedipine and proluton depot were interesting to study for inhibiting contraction in threatened preterm labour compared with the bed rest group in Siriraj Hospital.

Many interventions have long been used to prevent preterm labour. Some interventions which include good antenatal care, bed rest, and intravenous fluid hydration seemed to improve outcome, but there was no strong evidence supporting those interventions in preterm labour prevention. Only fetal fibronectin in cervical mucous and cervical length are used to predict preterm birth with well supported evidence. However, threatened preterm labour which is classified as regular uterine contractions, can progress to preterm birth in about 30% of cases.^{1,2} Therefore, if this process can be stopped the chances of both preterm birth and perinatal morbidity and mortality can be reduced.

Terbutaline (bricanyl) is the first line drug which has been used intravenously or subcutaneously to inhibit preterm labour for over 20 years.²⁶ However, evidence has recently supported that the oral form of salbutamol failed to inhibit contraction.²⁶ Magnesium sulfate has not been

TABLE 1. Birth rate and costs for management of complicated preterm birth per year.

Centers	Birth rate/year	Number of complicated preterm/ year	Costs (Baht)
Sriraj Hospital	9,198	131	22,925,000 (175,000/case)
In Bangkok	117,601	1,646	288,050,000
In Thailand	813,069	11,383	1,992,025,000

approved by the FDA for inhibition contraction due to a higher risk of maternal and fetal morbidity.²⁷ Nifedipine was studied and was strongly recommended for administration to inhibit contractions.²⁸ The side effects and complications of nifedipine to mother and fetus are fewer than for beta-agonist and magnesium sulfate.²⁹ The study showed that intramuscular progesterone was associated with a reduction in the risk of preterm birth at less than 37 weeks' gestation, and of infant birth weight of less than 2500 grams in the patients who had a previous history of preterm birth.³⁰ Proluton depot and nifedipine were still the most promising medications to use with minimal side effects. There was, however, neither a study nor strong evidence which supported the use of both drugs to inhibit uterine contraction in threatened preterm labour.

From the study in Siriraj Hospital,³¹ nifedipine, proluton depot and bed rest interventions were successful in inhibiting contraction in threatened preterm labour at about 80%, 66% and 64%, respectively. There was no statistically significant difference among those interventions. However, this study had only a limited sample size. When using a post hoc power analysis at 80% to detect the success rate of intervention, each group must include at least 157 patients. Further study should be considered for precise interpretation.

However, when the time to event test was used, nifedipine took the shortest time to inhibit contraction in threatened preterm labour with a median time of 3.00 ± 0.48 hours. If the studied population was larger, the significance could be more clearly detected.

Effect of cervical length and nifedipine, and bed rest interventions for preterm labour

From the previous authors study³¹, nifedipine and bed rest interventions can be used to inhibit uterine contractions in threatened preterm labour. However, nifedipine took shorter time than bed rest to inhibit uterine contractions. This study suspected that the cervical length might influence the efficacy of both interventions.

From the recent study³², nifedipine and bed rest interventions were successful in inhibiting contraction in threatened preterm labour with a cervical length of 3 cm or greater. There was no statistically significant difference among those interventions. Therefore, bed rest intervention used first in those cases can reduce unnecessary medication which may cause side effects and complications.

When the time to event test was used, nifedipine took the shorter time to inhibit contractions in threatened preterm labour than bed rest intervention in the group of cervical length less than 3 cm. Therefore, if the cervical length is less than 3 cm, nifedipine should be used instead of bed rest intervention in order to prevent true labour.³²

CONCLUSION

Preterm labour and preterm birth have recently become the national problem. Proper interventions to predict, prevent and stop uterine contractions can reduce the preterm birth.

REFERENCES

1. Chawanpaiboon S, Sutantawibul A. preterm birth rate in Siriraj Hospital: a seven-year review (2002-2008 BE). *Thai J Obstet Gynecol.* 2009;17:204-11.
2. Chawanpaiboon S. Clinical practice guidelines: management of preterm labor. Department of Obstetrics&Gynecology, Faculty of Medicine, Siriraj Hospital. Mahidol University. 2010.
3. American Academy of Pediatrics and American College of Obstetrician and Gynaecologists. Guidelines of perinatal care, 4th ed. 1997.
4. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet.* 2008 Jan 5;371(9606):75-84.
5. Mathews, TJ, MacDorman, MF. Infant mortality statistics from the 2004 period linked birth/infant death data set. *Natl Vital Stat Rep.* 2007 May 2;55(14):1-32.
6. Titapant T, Phithakwatchara N. Trends in modes of delivery in Siriraj Hospital: A twenty-eight-year review. *Siriraj Med J.* 2007;59:271-3.
7. Coratat T. Chapter 2. Preterm birth: recent situation and effect. In: Integration of maternal and child health care system. Mother and Child Health Project Network. Ammarin Printing Publish. Edition 1/2008. 48-52.
8. Chawanpaiboon S, Sawasdimongkol S, Rongroen S, Worapitaksanond S, Phopathom K. Comparison of risk factors and outcome of delivery between preterm and term delivery: 1-year study (2008BE) at Siriraj Hospital. *Thai J Obstet Gynaecol.* 2009;17:157-64.
9. Esplin MS, O'Brien E, Fraser A, Kerber RA, Clark E, Simonsen SE, et al. Estimating recurrence of spontaneous preterm delivery. *Obstet Gynecol.* 2008 Sep;112(3):516-23.
10. Berkowitz GS, Papiernik E. Epidemiology of preterm birth. *Epidemiol Rev.* 1993;15(2):414-43.
11. ACOG Practice Bulletin #56: Multiple Gestation: Complicated twin, triplet, and high-Order multifetal pregnancy. *Obstet Gynecol* 2004;104:869.
12. Klein LL, Gibbs RS. Use of microbial cultures and antibiotics in the prevention of infection-associated preterm birth. *Am J Obstet Gynecol.* 2004 Jun;190(6):1493-502.
13. Juhl M, Andersen PK, Olsen J, Madsen M, Jørgensen T, Nøhr EA, et al. Physical exercise during pregnancy and the risk of preterm birth: a study within the Danish National Birth Cohort. *Am J Epidemiol.* 2008 Apr 1;167(7):859-66.
14. Kyrklund-Blomberg NB, Cnattingius S. Preterm birth and maternal smoking: risks related to gestational age and onset of delivery. *Am J Obstet Gynecol.* 1998 Oct;179(4):1051-5.
15. Zeisel SH, Allen LH, Coburn SP, Erdman JW, Failla ML, Freaque HC, et al. Nutrition: a reservoir for integrative science. *J Nutr.* 2001 Apr;131(4):1319-21.
16. Scholl TO, Reilly T. Anemia, iron and pregnancy outcome. *J Nutr.* 2000 Feb; 130(2S Suppl):443S-447S.
17. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet.* 2008 Jan 5;371(9606):75-84.
18. Maul H, Mackay L, Garfield RE. Cervical ripening: biochemical, molecular, and clinical considerations. *Clin Obstet Gynecol.* 2006 Sep;49(3):551-63.
19. Final report of the medical research council/royal college of obstetricians and gynaecologists multicentre randomised trial of cervical cerclage. MRC/RCOG working party on cervical cerclage. *Br J Obstet Gynaecol.* 1993 Jun;100(6):516-23.
20. MCDONALD IA. Suture of the cervix for inevitable miscarriage. *J Obstet Gynaecol Br Emp.* 1957 Jun;64(3):346-50.
21. Shirodkar VN. A new method of operative treatment for habitual abortion in the second trimester of pregnancy. *Antiseptic.* 1955;52:299-300.
22. Novy MJ. Transabdominal cervicoisthmic cerclage: A reappraisal 25 years after its introduction. *Am J Obstet Gynecol.* 1991 Jun;164(6 Pt 1):1635-41.
23. Chawanpaiboon S, Sutantawibul A, Sawasdimongkol S, Worapitaksanond S. Comparison of pregnancy outcome between elective and emergency McDonald cervical cerclage in cervical insufficiency: 3 years experience (2006-2008) in Siriraj Hospital. *Thai J Obstet Gynaecol.* 2010;18:6-11.
24. Harger JH. Cerclage and cervical insufficiency: an evidence-based analysis. *Obstet Gynecol.* 2002 Dec;100(6):1313-27.
25. Chawanpaiboon S, Wanitpongpan P, Titapant V, Kanokpongsakdi S, Wantanasiri C, Pimol K, et al. Nifedipine for inhibiting threatened preterm labour in Siriraj Hospital. *Siriraj Med J.* 2008;60:111-3.
26. Anotayanonth S, Subhedhar NV, Garner P, Neilson JP, Harigopal S. Beta-mimetics for inhibiting preterm labour. *Cochrane Database Syst Rev.* 2004 Oct 18;(4):CD004352.
27. Crowther CA, Hiller JE, Doyle LW. Magnesium sulphate for preventing preterm birth in threatened preterm labour. *Cochrane Database Syst Rev.* 2002;(4):CD001060.
28. King JF, Flendy VJ, Papatsonis DN, Dekker GA, Carbonne B. Calcium channel blockers for inhibiting preterm labour (Cochrane review). *Cochrane Database Syst Rev.* 2003;(1):CD002255.
29. Royal College of Obstetricians and Gynaecologists. Tocolytic drugs for women in preterm labour. *Clinical Guideline No. 1 (B) 2002:1-7.*
30. Dodd JM, Flenady VJ, Cincotta R, Crowther CA. Progesterone for the prevention of preterm birth: a systematic review. *Obstet Gynecol.* 2008 Jul;112(1):127-34.
31. Chawanpaiboon S, Pimol K, Sirisomboon R. Comparison of success rate of nifedipine, progesterone and bed rest for inhibiting uterine contraction in threatened preterm labour. *J Obstet Gynaecol Res.* 2011 Mar 13. DOI: 10.1111/j.1447-0756.2010.01434.x.
32. Chawanpaiboon S, Pimol K. Bacterial vaginosis in threatened preterm, preterm and term labour. *J Med Assoc Thai.* 2010 Dec;93(12):1351-5.