# INCIDENCE AND RISK FACTORS OF PRETERM DELIVERY AT RAMATHIBODI HOSPITAL: 2005-2006

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## ABSTRACT

Preterm delivery is the most important cause of infant mortality and mobility. The first part of this study is a historical cohort study with the objective to determine the incidence of preterm delivery among mulliparous women at Ramathibodi hospital during 1 January – 30 December 2005. The second part is a case – control study with the objective to determine risk factors of preterm delivery. During the study period, there were 2,542 pregnant women who came to register for the first time. For those who failed to follow-up an attempt to contact was made by mail or telephone.Overall, 68.6 % of women who registered had known outcomes of pregnancy (59.9% delivery, 8.7% abortion). Descriptive statistics were percentage, mean and standard deviation. Analytical statistics including odds ratio with 95% confidence intervals, chi – square test, and logistic regression analysis were used to determine risk and association between factors and preterm delivery. SPSS$^+$ PC program was used for statistical analysis.

The results of the study showed that the incidence of preterm delivery was 12.48%. Most preterm deliveries occurred at gestational ages of34-36weeks(7.16%). About 1-2% occurred at gestational ages of less than 28 wks(2.23%), 28-30wks(1.12%) and 31-33wks(1.97%). The case control study included 190 cases of preterm delivery and 190 cases of control. The controls were selected from pregnant women who came to register on the same day just after the test cases and delivered at full term. From univariate analysis, the significantly associated factors were maternal height≤155 cms, mean weight gain≥1kg/wk, civil employment, hemoglobin<10g% and medical complication before delivery. However from multiple logistic regression analysis only premature rupture of membranes and maternal height were factors significantly associated with preterm delivery.

In conclusion, incidence of preterm delivery at Ramathibodi hospital is comparable to other studies. Risk factors of preterm delivery are found to be difficult to change or are resistant to intervention. However, these finding could be applied to screen pregnant women, to advise them on and prepare services to prevent and care for preterm delivery.

KEY WORDS: INCIDENCE / RISK FACTORS / PRETERM

59 pp.

อุบัติการณ์ และ ปัจจัยเสี่ยงที่มีความสัมพันธ์กับการเกิดภาวะ คลอดก่อนกำหนดที่โรงพยาบาลรามาธิบดี
(INCEDENCE AND RISK FACTORS OF PRETERM DELIVERY AT RAMATHIBODI HOSPITAL)

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บทคัดย่อ

การคลอดก่อนกำหนดยังคงเป็นปัญหาที่สำคัญที่สุดที่ทำให้ทารกแรกเกิดตายและเจ็บป่วย ส่วนแรกของการศึกษาครั้งนี้เป็น การศึกษาแบบ historical cohort study ซึ่งวัตถุประสงค์เพื่อ ศึกษาอุบัติการณ์ของการเกิดภาวะคลอดก่อนกำหนดของหญิงตั้งครรภ์ที่โรงพยาบาลรามาธิบดี ช่วงวันที่ 1 มกราคม ถึง 30 ธันวาคม 2548 ส่วนที่สอง เป็นการศึกษาแบบ case control ซึ่งมีวัตถุประสงค์เพื่อศึกษาปัจจัยเสี่ยงต่อการเกิดภาวะคลอดก่อนกำหนด ในช่วงที่ทำการศึกษามีหญิงตั้งครรภ์มาลงทะเบียนครั้งแรกในการฝากครรภ์จำนวน 2,542 ราย และในจำนวนนี้มีที่ไม่ทราบการคลอดและการแท้งได้มีการติดตามโดยการส่งจดหมายและโทรศัพท์ไปสอบถามเพิ่มเติม สรุปโดยรวม พบผลร้อยละ 68.6 ทราบผลการคลอดและแท้ง โดยร้อยละ 65.7 ทราบผลการคลอด และ ร้อยละ 8.7แท้ง บุตรก่อนอายุครรภ์ 20 สัปดาห์ สถิติที่ใช้ ได้แก่ สถิติพรรณนา ประกอบไปด้วย ร้อยละ ค่าเฉลี่ย ส่วนเบี่ยงเบนมาตรฐาน และสถิติวิเคราะห์ ประกอบด้วย odds ratio, 95% confidence interval, chi –square และmultiple logistic regression เพื่อหาปัจจัยเสี่ยงที่มีความสัมพันธ์กับภาวะ คลอดก่อนกำหนดโดยใช้โปรแกรม SPSS $^{+}$ PC ในการวิเคราะห์ข้อมูล

ผลการศึกษาพบว่า อุบัติการณ์ของการเกิดภาวะ คลอดก่อนกำหนดในโรงพยาบาลรามาธิบดี เท่ากับ ร้อยละ 12.48 ส่วนใหญ่ร้อยละ 7.16 เกิดที่อายุครรภ์ระหว่าง 34-36 สัปดาห์ , อายุครรภ์น้อยกว่า 28 สัปดาห์ ร้อยละ 2.23 อายุครรภ์ระหว่าง 28-30 สัปดาห์ ร้อยละ 1.12และอายุครรภ์ระหว่าง 31-33 สัปดาห์ ร้อยละ1.97 สำหรับการศึกษาแบบ case control ประกอบด้วยหญิงตั้งครรภ์ที่มีและไม่มีภาวะคลอดก่อนกำหนด จำนวน 190 คนเท่าๆกัน สตรีที่ไม่มีภาวะคลอดก่อนกำหนดเลือกจากหญิงตั้งครรภ์ที่มาฝากครรภ์ในวันเดียวกันและต่อหลังจากหญิงตั้งครรภ์ที่มีภาวะคลอดก่อนกำหนด การศึกษาหาความสัมพันธ์ของแต่ละตัวแปรพบว่า หญิงตั้งครรภ์ที่มีความสูงน้อยกว่า155เซนติเมตร,หญิงตั้งครรภ์ที่ประกอบอาชีพข้าราชการ, หญิงตั้งครรภ์ที่มีน้ำหนักเพิ่มระหว่างตั้งครภ์เฉลี่ยมากกว่าหรือเท่ากับ 1 กิโลกรัมต่อสัปดาห์, หญิงตั้งครรภ์ที่มีระดับฮีโมโกลบินเมื่อมาฝากครรภ์ครั้งแรกน้อยกว่า 10 กรัมเปอร์เซ็นต์และหญิงตั้งครรภ์ที่มีการเจ็บป่วยทั้งก่อนและขณะตั้งครรภ์ มีความสัมพันธ์กับการเกิดภาวะคลอดก่อนกำหนดอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) แต่จากการศึกษาความสัมพันธ์แบบ multiple logistic regressionพบว่าหญิงตั้งครรภ์ที่มีความสูงน้อยกว่า 155 เซนติเมตรและหญิงตั้งครรภ์ที่มีภาวะถุงน้ำคร่ำแตกก่อนเจ็บครรภ์ ที่มีความสัมพันธ์กับการเกิดภาวะคลอดก่อนกำหนดอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$)

โดยสรุป อุบัติการณ์การเกิดภาวะ คลอดก่อนกำหนด ในโรงพยาบาลรามาธิบดี ใกล้เคียงกับการศึกษาอื่นๆ ปัจจัยเสี่ยงที่มีความสัมพันธ์กับภาวะ คลอดก่อนกำหนด ยังเป็นปัจจัยที่ป้องกันและแก้ไขได้ยากแต่อาจจะนำไปจำแนกหญิงตั้งครรภ์ ให้คำแนะนำ และเตรียมการดูแลและป้องกันรักษาการเกิดภาวะ คลอดก่อนกำหนด ได้

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# CHAPTER I
# INTRODUCTION

## Background and Significance of the Study

Preterm delivery is an important maternity and child health problem in the developing countries(1). Preterm birth accounts for up to 75 to 80% of all neonatal morbidity and mortality. Preterm infants have many problems in short-term and long-term life(2). In addition, Preterm birth leads devastating effects on emotion of parents, finance of families, and responsibility of society if the children are neglected. Therefore, preterm birth is an unwanted birth outcome. The incidence of preterm birth varies throughout the world In Thailand, the incident of preterm delivery nation wide is not available because had most of the birth weight is reported without the gestational age. However, some institutions had reported statistics of preterm delivery. For example, Thannirandorn W(3) at King Chulalongkorn Memorial Hospital, had a rate of preterm delivery of approximately 9.4% Titapant V.(4) in Maharaj Nakorn Chiangmai Hospital reported the rate of singleton pregnancy with preterm delivery was12 %. In Siriraj Hospital, the rate of singleton pregnancy with preterm delivery was 6.85%(4) .

According of the World Health Organization and American Academy of Pediatrics(5) the definition of the premature infant is that any infant was born before 37 weeks of gestational age.. In America, the incidence of prematurely in 1983 was 9.2% and the result of the infant's death rate was as high as 7.5% in 1984(6).

Preterm birth is responsible for causing almost two thirds of infant deaths(7). Preterm infants are at a higher risk of death because their vital organ systems are immature enough to be able to make an uncomplicated transition to extra uterine life especially, the respiratory system. The most significant problem is related to lung immaturity. It results in the inability of neonate to perform the vital respiratory functions.Preterm infants born at 25 to 30 weeks" gestation tend to have more complications, higher mortality rate, and more costly hospital charges .The life-long effects include major health problems such as cerebral pulsy, mental retardation, and

sensory and cognitive disabilities which lead to difficult adaptation to an increasingly complex environment. Moreover, parents are usually emotionally unprepared for the birth of a preterm infant They would have a feeling of guilt, anger, and depression that is the signs of grief for the expected healthy, full- term infant .This may cause an ineffective maternal role adaptation that brings about inappropriate childrearing, child neglect and abuse that could become problems of the society.

Because of these importances of preterm delivery to the neonates, the mothers and the society, I would like to study the incidence of preterm birth by apply a historical cohort research design. Risk factors of preterm delivery were also determined by case control study in Ramathibodi Hospital where the statistic is rather complete.

**Objective to Study:**

1. Incidence of preterm delivery among pregnant women who came to register at antenatal booking unit Ramathibodi hospital.
2. Factors associated with preterm delivery. Factors included in this study were maternal age, maternal height, parity, years since last child, occupational, education level, history of abortion, history of hypertension, premature rupture of membrane, ante partum bleeding, medical complication, hemoglobin level at first visit and mean weight gain.

**Hypothesis:**

Factors which had significant association with preterm delivery were maternal age, maternal height, parity, years since last child, occupational, education level, history of abortion, history of hypertension, premature rupture of membrane, ante partum bleeding, medical complication, hemoglobin level at first visit and mean weight gain.

**Scope of this study**

The subject of this study were confined to mothers came to register at Ramathibodi Hospital and had received antenatal care and followed up at Hospital or Public Health Centers during pregnancy and know out come of labor

**Definition and meaning of terminology used in this study**

Maternal height (cm.) means height in centimeters recorded at first attendance to the antenatal clinic.

Antenatal care means how and frequency of pregnant women coming to be attend at the Hospital or Public Health Centers for examination and advice.

Weekly weight gain during pregnancy (kg/wk.) means weight gain during pregnancy (kg) divided by duration of gestational age in weeks that calculated at the beginning of pregnancy to the last of antenatal care.

Gestational age at delivery means number of weeks calculated from the first day of the last menstrual period to the day of delivery .

Preterm delivery means the delivery of infant from $22^{th}$ – $36^{th}$ weeks of gestation (or 140-258 day).

Full-term delivery means the delivery at $37^{th}$ – $42^{nd}$ weeks of gestation (or 259-294 days) and full-term infants examined and signed of term infants.

Birth weight (grams) means the first weight of the newborn weighed without other immediately after delivery.

# CHAPTER II
# REVIEW OF LITERATURES

Preterm delivery is an important determinant of infant mortality and morbidity because the survivals of the neonate that birth should not occur until the fetal organ system that are essential for postnatal survival are sufficiently mature. Many previous studies about factors associated with gestational age at delivery have been published. Most of them have been conducted in other countries.

In this chapter, concepts and theories on the preterm delivery were presented. The presentation will be organized into different topics as follow:

1. Categorization of the newborns.
2. Considerations surrounding preterm delivery
3. Causes of preterm birth
4. Identification of women at risk for spontaneous preterm labor
5. Related research of risk factors of preterm delivery

**Categorization of the newborns**.

Preterm or premature delivery is the terms used to define neonates who are born too early. With respect to gestational age, a newborn may be preterm, term, or post term. With respect to size, a newborn may be normally grown or appropriate for gestational age, small in size or small-for-gestational age, or overgrown and consequently large-for-gestational age. In recent years, the term small-for-gestational age has been widely used to categorize newborns whose birth weight is usually below the $10^{th}$ percentile for gestational age. Other frequently used terms have included fetal growth restriction or intrauterine growth restriction. The term large-for-gestational age has been widely used to categorize newborns whose birth weight is above the $90^{th}$ percentile for gestational age, and the term appropriate-for-gestational age designates newborns whose weight is between the $10^{th}$ and $90^{th}$ percentiles. Thus, infants born

before term can be small- or large-for-gestational age but still fit the definition of preterm(8).

In the United States in 2001, almost 28,000 infants died in their first year of life. Preterm delivery, which is defined as delivery before 37 completed weeks, was implicated in approximately two thirds of these deaths. Overall, infant mortality has continued to decline from 1990 to 2000, albeit at a slower rate than in earlier decades. The causes of infant mortality have also declined from 1990 to 2000, except for those associated with preterm birth or low birth weight. Importantly, singleton preterm births in this country have increased only in white non-Hispanic women. Despite this, preterm births in this country remain highest in black women(8).

**Considerations Surrounding Preterm Delivery**

**Estimating Survival.** Aside from survival, appreciable physical and intellectual compromise afflicts extremely low-birthweight infants. At what gestational age should obstetrical interventions be practiced?

Improved survival of extremely low-birthweight infants has understandably lowered the “threshold of viability”. John EB (9) reported outcomes from an inborn cohort of the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network for 1993 and 1994. Death, severe neonatal morbidities, or both were common before 26 weeks, and they were almost universal before 24 weeks. Thus, gestations from 23 to 25 weeks pose the greatest dilemma for providers of obstetrical and newborn care and for their patients(10).

**What is the best management scheme?** This question of course cannot be answered, except possibly on an individual basis. Approaches to preterm labor and delivery currently are guided in large part by expectations for survival of the neonate. Perceptions of the potential for survival, however, are often confused by imprecisely know gestational age. The most accurate estimates of gestational age are made from last menses, obstetrical parameters, and ultrasonographical examination. They are considered to be the “best care” outcomes. Perinatal mortality and morbidity decrease

markedly from 24 to 26 weeks gestation. Survival increases from approximately 20 percent at 24 weeks up to 25 weeks, or an increase of almost 4 percent each day(10).

However, most survival data are based on birthweight, which may vary appreciably between 24 and 26 weeks. Neonates born between 24 and 26 weeks can vary in weight from 435 g to 1640 g (11). Although survival is possible for newborns weighing 500 to 750 g, many survivors are growth restricted and therefore of more advanced maturity(12). For example, survival of a 380-g neonate has been reported, but the gestational age was confirmed to be 25 weeks (13). Neonatal morbidity and mortality are primarily influenced by gestational age and thus maturity, and less so by birthweight**.**

Evans N(14)described the appreciable selection bias in preterm survival studies. The Neonatal Research Network data reflect an important bias – all neonates were delivered in tertiary university centers and only liveborn infants were included. These rates also exclude deaths after 120 days.

**Long Term Outcomes.** The high rate of significant neonatal morbidity in these very immature neonates and the diminished likelihood of a normal life must be weighed against the apparent triumph of survival. A number of investigators have reported long-term outcomes in survivors born at the frontier of viability.

Doyle LW(15) did a follow-up study of neonates born at 24 to 26 weeks. They reported the only 20 percent were totally free on impairment at 5 years or more. Vohr BR(16) assessed outcomes at 18 to 22 months in 1151 survivors from the NICHD Neonatal Research Network centers who were born in 1993 and 1994. Their birthweight was 400 to 1000 g. Only 50 percent had a normal neurodevelopmental and sensory assessment, and those with lower birthweights had markedly worse outcomes as predicted by chronic lung disease, grades 3 and 4 intraventricular hemorrhage, and periventricular leukomalacia. Wood NS (17) reported similar results in the EPI Cure Study Group of the United Kingdom. They evaluated 283 infants who were born at or before 25 weeks who survived to 30 months of age. Only 1 of 138 infants born during the 22$^{nd}$ week had *no* neurological disability, compared with 11 of 241 (5 percent) of those born during the 23$^{rd}$ week; 45 of 382 (12 percent) of those born during the 24$^{th}$

week; and 98 of 424 (23 percent) of those born during the 25th week. Stoll J (18) found that these extremely low-birthweight newborns compared with similarly matched uninfected neonates had increased associated risks of poor neurodevelopmental and growth outcomes in early childhood.

Hack M (19) concluded that the limits of viability have been reached and that the continuing toll of major morbidity is of serious concern. In analyzing data collected from three different time periods by the NICHD Neonatal Research Network, Fanaroff AA (20) found that newborn outcomes at the threshold of viability – 24 or 25 weeks or 501 to 750 g – did not improve from 1993 to 1994 compared with 1999 to 2000. This followed a dramatic improvement in both mortality and morbidity between 1987 and 1988 and 1993 to 1994. Similarly, Horbar JD (21) studied outcomes in 118,448 very-low-birthweight newborns in the Vermont-Oxford Trials Database from 1991 through 1999. There were no additional improvements in mortality or morbidity after 1995, ending a decades-long trend of improving outcomes.

**Lower limit of survival: Counseling Considerations.** Perinatal care at the threshold of viability, defined as 25 or fewer weeks of gestation, has been reviewed by the American College of Obstetricians and Gynecologists (10). It concluded that "parents can be counseled that infants delivered before 24 weeks are not likely to survive, and those who do are not likely to survive intact. Disabilities in mental and psychomotor development, neuromotor function, or sensory and communication function are present in approximately one half of survivors." Maternal-fetal transport to a tertiary care center prior to delivery should be considered when possible. Importantly, all members of the health care team should maintain a consistent theme with family members regarding neonatal assessment and prognosis, as well as recommendations and plans for care(10).

Amon B(22) surveyed obstetricians to determine their clinical opinions regarding intrapartum management of the extremely preterm fetus requiring delivery. According to their survey results, cesarean delivery was not performed at less than 24 weeks. Almost 90 percent of respondents were willing to perform cesarean delivery for fetal distress or breech presentation at 26 weeks or 750 g fetal weight. Doron

MW(23) analyzed delivery room decisions by neonatologists to provide or withhold resuscitation between 23 and 26 weeks' gestation. They concluded that resuscitation of these extremely preterm neonates may provide time to gather additional information about neonatal prognosis and an opportunity for decision making regarding continued care.

The decision not to perform cesarean delivery or use intrapartum monitoring does not necessarily imply that the fetus is "nonviable" or "written off**."** Kitchen WH (24) analyzed the outcomes of liveborn neonates weighing 500 to 999 g and found that although 50 percent of newborns survived and only 7 percent were severely disabled, these outcomes were unrelated to the use of cesarean delivery or electronic fetal monitoring.

**Upper limit for adverse outcomes from preterm delivery .** Survival of larger preterm newborn now approaches that for term newborns . This raises the question: Is there a birthweight or gestational age threshold after which attempts to delay delivery are unwarranted? DePalma RT (25) found that the threshold for neonatal mortality at Parkland Hospital was 1600 g, and it was 1900 g for neonatal morbidity. He concluded that aggressive attempts to prevent births for fetuses whose weight estimates exceeded 1950 g is the $10^{th}$ percentile for 34 weeks and the $50^{th}$ percentile for 32 weeks Nation wide, the survival rate for newborns at 34 weeks is within 1 percent of those born at or beyond 37 weeks.

**Economic impact of preterm birth.** Resources used to care for low-birthweight newborns is one measure of the financial burden of preterm birth(26). In the United States, Lewit EM(27) found that more than a third of the dollars expended for infant health care during the first year of life is spent on the 7 percent of neonates born who weigh less than 2500 g. Additional expenditures for developmental handicaps during the remainder of childhood should also be considered.

**Cause of preterm birth**

A wide spectrum of causes and demographic factors have been implicated in preterm birth.

**Medical and obstetrical complications.** The NICHD Maternal-Fetal Medicine Units Network (12)has analyzed the causes of delivery before 37 weeks. The report by Kimberlin DF(28) showed that 28 percent of these preterm singleton births were indicated as being due to several factors; about a half were for preeclampsia; a fourth for fetal growth restriction, placental abruption, or fetal death. The remaining 72 percent were due to spontaneous preterm labor, with or without prematurely ruptured membranes.

**Threatened abortion.** Vaginal bleeding in early pregnancy is associated with increased adverse outcomes. Weiss JL (29) reported data on vaginal bleeding at 6 to 13 weeks in nearly 14,000 women. Both light bleeding (described as spotting) and heavy bleeding (similar to menses) were associated with subsequent pregnancy loss prior to 24 weeks, preterm labor, and placental abruption.

**Lifesytle factors.** Cigarette smoking, inadequate maternal weight gain during pregnancy, and illicit drug use play important roles in both the incidence and the outcome of low-birthweight neonates (8). Some of these effects are undoubtedly due to restricted fetal growth, but Hickey CA(30) linked prenatal weight gain specifically with preterm birth.Other maternal factors implicated include young or advanced maternal age; poverty; short stature; Vitamin C deficiency; and occupational factors such as prolonged walking or standing, strenuous working conditions, and long weekly work hours (31). Santiago P(32) found no increased incidence of recurrent preterm birth in women with a history of preterm birth and whose work during their current pregnancies was outside the home or required physical exertion.

Psychological and physical stress have seldom been formally studied but seem intuitively important. Both stress and higher levels of maternal serum cortisol have been associated with spontaneous preterm birth (33). Neggers Y(34) found a significant link between low birthweight and preterm birth in women injured by physical abuse , however Casts A (36) reported that maternal depression was not associated with birth prior to 35 weeks.

**Genetic factors.** The recurrent, familial, and racial nature of preterm birth has led to the suggestion that genetics may play a causal role (37). The gene for decidual relaxin is one candidate. Fetal mitochondrial trifunctional protein defects or polymorphism in the interleukin-1 gene complex, $\beta_2$-adrenergic receptor, or tumor necrosis factor-$\alpha$ (TNF-$\alpha$) may also be involved in preterm membrane rupture (38). Studies to evaluate gene-environment interactions are also needed. For example, when Bytautiene E(39) induced an allergic reaction in pregnant guinea pigs that resulted in preterm delivery, He found that the rate was reduced three-fold by pretreatment with an antihistamine and cromolyn sulfate.

**Chorioamionitis.** Infection of the membranes and amnionic fluid caused by a variety of microorganisms has emerged as a possible explanation of some cases of ruptured membranes, preterm labor, or both. Bacteria are recovered by transabdominal amniocentesis from as many as 20 percent of women in preterm labor without overt clinical infection and with intact fetal membranes (40). Viral products have also been recovered (41). Infection is not limited to amnionic fluid. In studies done at cesarean delivery in 609 women with intact membranes, Hauth JC(42) confirmed that recovery of organisms from the chorioamnion was significantly increased with spontaneous preterm labor.

The pathway for bacteria to enter amnionic fluid with intact membranes is unclear. Gyr TN(43) have shown that Escherichia coli can permeate living membranes; thus, He are not an absolute barrier to ascending infection. Another pathway for bacterial initiation of preterm labor may not require bacteria in the amnionic fluid. Cox SM(44) found that the cytokine network of cell-mediated immunity can be activated within the decidual tissue that lines the presenting fetal membranes. In this scheme, bacterial products such as endotoxin stimulate decidual monocytes to produce cytokines, which in turn stimulate arachidonic acid and then prostaglandin production. Prostaglandins $E_2$ and $F_{2\alpha}$ act in a paracrine fashion to stimulate adjacent myometrium to contract (45).

**Identification of Women at Risk for Spontaneous Preterm Llabor**

**Risk scoring system**. There has been considerable interest in risk-scoring system to identify women at greatest risk for preterm birth. In their review, Hueston WJ (46) found no benefits of this programmatic approach. Mercer BM(47)concluded that risk assessment failed to identify most women who deliver preterm neonates. In another study, Kaltreider DF (48)randomly assigned 619 Medicaid-eligible black women with a modified risk assessment score for preterm delivery of 10 or higher to receive augmented or customary prenatal care. Mean birthweight and the incidences of preterm delivery and low-birthweight newborns were similar in both groups as well as in the general obstetrical population (49).

**Prior preterm birth.** Prior preterm delivery strongly correlates with subsequent preterm labor. The study of the incidence of recurrent preterm birth in nearly 16,000 women delivered at Parkland Hospital Copper RL(50) found that the risk of recurrent preterm delivery for women whose first delivery was preterm was increased threefold compared with that of women whose first neonate was born at term. More than a third of women whose first two newborns were preterm subsequently delivered a third preterm newborn. The majority (70 percent) of the recurrent births in this study occurred within 2 weeks of the gestational age of the prior preterm delivery. Importantly, the causes of prior preterm delivery (i.e., preterm labor with intact membranes, preterm membrane rupture, or indicated delivery) also recurred. Although women with prior preterm births were clearly at risk for recurrence, they contributed only 10 percent of the total preterm births. Expressed in another way, 90 percent of the preterm births at Parkland Hospital could not be predicted based on a history of preterm birth(51).

**Incompetent cervix.** Cervical incompetence is a clinical diagnosis characterized by recurrent, painless cervical dilatation and spontaneous midtrimester birth in the absence of spontaneous membrane rupture, bleeding, or infection (47).

**Cervical dilatation.** Asymptomatic cervical dilatation after midpregnancy has gained attention as a risk factor for preterm delivery, although some clinicians consider it to be a normal anatomical variant, particularly in parous women. Recent

studies, however, have suggested that parity alone is not sufficient to explain cervical dilatation discovered early in the third trimester. Cook SM (49) longitudinally evaluated cervical status with transvaginal ultrasonography between 18 and 30 weeks in both nulliparous and parous women who all subsequently gave birth at term. Cervical length and diameter were identical in both groups throughout these critical weeks(48) .Approximately 25 percent of women whose cervices were dilated 2 or 3 cm delivered prior to 34 weeks. Many of these women had experienced the same complication in earlier pregnancies. Other investigators have verified cervical dilatation as a predictor of increased risk of preterm delivery (50), (51)

Although women with dilatation and effacement in the third trimester are at increased risk for preterm birth, it has not been established that detection improves pregnancy outcome. Beechen RE (52) randomly assigned 2719 women to undergo routine cervical examinations at each prenatal visit and compared them with 2721 women without examinations. Knowledge of antenatal cervical dilatation did not affect any pregnancy outcome related to preterm birth or the frequency of interventions for preterm labor. The investigators also reported that cervical examinations were not related to preterm membrane rupture. It seems therefore that prenatal cervical examinations are neither beneficial nor harmful.(53)

**Signs and symptoms.** In addition to painful or painless uterine contractions, symptoms such as pelvic pressure, menstrual-like cramps, watery vaginal discharge, and pain in the low back have empirically associated with impending preterm birth. Such symptoms are thought by some to be common in normal pregnancy and are therefore often dismissed by patients, clinicians, and nurses. The importance of these signs and symptoms as a harbinger of labor has been emphasized by some but not all investigators Copper RL(53)found that the signs and symptoms signaling preterm labor, including uterine contraction, appeared only within 24 hours of preterm labor.

**Ambulatory uterine monitoring**. Uterine activity monitoring has received considerable interest. An external tocodynamometer is belted around the abdomen and connected to an electronic waist recorder. Uterine activity is transmitted via telephone daily. Women are educated concerning signs and symptoms of preterm labor, and

clinicians are kept apprised of their progress(54).The 1985 approval of this monitor by the U.S. Food and Drug Administration prompted its widespread clinical use. Subsequently, the American College of Obstetricians and Gynecologists (26) concluded that the use of this expensive, bulky, and time-consuming system does not reduce the rate of preterm birth. Studies that followed confirmed this conclusion. In the Collaborative Home Uterine Monitoring Study, sham transducers were used in 655 women and outcomes compared with those of 637 women with functioning monitors. The rate of preterm birth was similar in both groups. Doron MW(23) analyzed data from almost 35,000 hours of daily home monitoring form 306 women. They verified that contraction frequency increased with gestational age but that no pattern efficiently predicted preterm birth(60).

In a study by Dyson DC(54), women were randomly assigned to receive weekly contact with a nurse or to use home contraction monitoring. There were no differences in the rate of preterm delivery before 35 weeks or in the incidence of birthweights less than 1500 g or less than 2500 g. Moreover, women who used home monitoring had a significant increase in the number of unscheduled visits and women with twins had increased use of tocolytic therapy.

**Fetal fibronectin**. This glycoprotein is produced in 20 different molecular forms by a variety of cell types, including hepatocytes, fibroblasts, and endothelial cells, and by fetal amnion. Present in high concentrations in maternal blood and in amnionic fluid, it is thought to play a role in intercellular adhesion during implantation and in the maintenance of placental adhesion to the decidua (54). Fetal fibronectin is detected in cervicovaginal secretions in women who have normal pregnancies with intact membranes at term, and it appears to reflect stromal remodeling of the cervix prior to labor.Lockwood CJ (55) reported that fibronectin detection in cervicovaginal secretions prior to membrane rupture was a possible marker for impending preterm labor. This report stimulated considerable interest in the use of fibronectin assays for the prediction of preterm birth. Fetal fibronectin is measured using an enzyme-linked immunosorbent assay, and values exceeding 50 ng/mL are considered positive. Contamination of the sample by amnionic fluid and maternal blood should be avoided (56). A positive value for cervical or vaginal fetal fibronectin assay, even as early as 8

to 22 weeks, has been found to be a powerful predictor of subsequent preterm birth (57). In a randomized trial, a negative fibronectin assay in women with threatened preterm labor was associated with fewer admissions and decreased hospital stay (58).Subsequent studies of cervicovaginal fibronectin have allowed better assessment of its positive and negative predictive value. Dyson DC(54) found that in 404 pregnancies, a positive assay result at 22 to 34 weeks had a positive predictive value for delivery within 1 week of 30 percent or within 2 weeks of 41 percent. The negative predictive value was 98 and 96 percent, respectively. The less informative positive predictive value likely results from factors such as cervical manipulation and infection(53), which can stimulate fetal fibronectin release (57). These findings may implicate infection in the initiation of preterm labor in some women.

**Intervention with Positive Fibronectin Assay.** Because the positive predictive value along with evidence that a positive fibronectin assay may suggest infection, Goldenberg RL. (57)studied the effectiveness of antimicrobial treatment to reduce the incidence of preterm birth. Of 16,317 women screened for fetal fibronectin between 21 and 26 weeks, 6.6 percent had a positive result. In women given antimicrobial treatment or placebo, no differences were observed in rates of spontaneous preterm birth before 37 weeks (14.4 versus 12.4 percent), before 35 weeks (6.9 versus 7.5 percent), or before 32 weeks (4.3 versus 2.2 percent).

**Bacterial vaginosis**. It is not an infection but rather a condition in which the normal, hydrogen peroxide-producing lactobacillus-predominant vaginal flora is replaced with anaerobes, Gardnerella vaginalis, Mobiluncus species, and Mycoplasma hominis (57)Using Gram staining, relative concentrations of the bacterial morphotypes characteristic of bacterial vaginosis are determined and graded as the Nugent score.

Bacterial vaginosis has been associated with spontaneous abortion, preterm labor, preterm ruptured membranes, chorioamnionitis, and amnionic fluid infection (57).Bacterial vaginosis may precipitate preterm labor by a mechanism similar to that proposed for amnionic fluid infection (54) . In 3600 Danish women, however, when bacterial vaginosis was detected before 24 weeks, it was not related to preterm

membrane rupture before 37 weeks or to low birthweight (53).Conflicting reports may relate to the imprecise diagnosis of bacterial vaginosis (42). Women with bacterial vaginosis whose vaginal secretions contained sialidase, but not prolidase, had a significantly increased risk of preterm delivery (55). Finally, therapy modifies the conditions, and treatment with metronidazole decreased cervical concentrations of interleukin-1β, -6, and –8 (41).

**Environmental factors** It appear to be important in the development of bacterial vaginosis. Exposure to chronic stress, ethnic differences, and frequent or recent douching have all been associated with increased rates of the condition (31)**.**Despite this, prospective studies of women who regularly douched reported no relationship with preterm birth (40)**.** A gene-environment interaction was identified by Hauth JC(42). Women with bacterial vaginosis who had a susceptible TNF-α genotype had a ninefold increased incidence of preterm birth. Hoffman JD(37) have reviewed bacterial vaginosis and the role of genetic epidemiology in the prevention of preterm birth.From all of these studies there seems no doubt that adverse vaginal flora, such as in bacterial vaginosis, is associated with spontaneous preterm birth. Unfortunately, to date, screening and treatment have not been shown to prevent preterm birth .

**Lower genital tract infection**. Some investigators have implicated a number of other genital infections as a cause of preterm labor. Weiss JL(29) evaluated 2929 women at 24 and 28 weeks for Trichomonas or Candida species. Women who had one or both of these organisms were not at greater risk for preterm birth. Conversely, Cook CM(49) found that the neonates of women with Trichomonas had increased risk of having low-birthweight, a 30-percent increased risk of preterm birth, and a twofold risk of perinatal deat. Based on this report, Kaltreider DF(48) evaluated 617 asymptomatic women with trichomoniasis in midtrimester. Preterm birth was significantly greater in women randomly assigned to receive metronidazole compared with that of those receiving placebo (19 versus 11 percent).Chlamydia trachomatis likely does not play a role in increased preterm delivery. American College of

Obstetricians and Gynecologists(10),has found no association of preterm birth in women with midtrimester chlamydial infectio. Similarly, Evans N(14) found similar incidences of preterm delivery in women with and without chlamydial or trichomonal infection. In the Vaginal Infections and Prematurity Study, 414 women with chlamydial infection were randomly selected to receive either erythromycin or placebo. **N**eggers Y(34) found similar incidences of preterm birth. Currently, screening and treatment to prevent preterm birth in women with either C. trachomatis or Trichomonas vaginalis is not recommended.Finally, other studies implicate nonspecific markers of infection in increasing the risk of preterm birth. In a study of 3160 asymptomatic women, Kimberlin DF(28) found that a midtrimester vaginal Gram-stained smear with an increased polymorphonuclear:epithelial cell ratio was predictive of birth before 35 week. Hauth JC(42) reported that nonpregnant women with interpartum chronic endometritis, characterized by plasma cells, were 2.5 times more likely to deliver before 35 weeks in a subsequent pregnancy.

**Peridontal disease**. Oral bacteria, especially Fusobacterium nucleatum and Capnocytophaga species, have been associated with upper genital tract infection in pregnant women(42).Gyr TN (48) found that women with periodontitis had a sevenfold risk of preterm birth compared with that of controls. Reddy U(41) confirmed this in a prospective trial of more than 1300 women assessed at midpregnancy for periodontal inflammation. In each gestational age category, periodontal disease was associated with increased preterm delivery . Indeed, 24 of the 28 women who delivered before 32 weeks and periodontitis; this is fourfold increase compared with that of women without disease. Gyr TN(43) observed that women who delivered spontaneous before 32 weeks were significantly more likely to have severe periodontal disease than controls. Beechen RE(52)found that preterm new-borns of mothers with periodontal disease were 23 percent smaller than those of mothers without disease. Genc MR(38). have suggested that this may be related to decreased maternal antibody titers.

**Related researches of risk factors of preterm delivery**

## 1. Maternal general characteristics

### 1.1 Socioeconomic status

Socioeconomic categories commonly used include income and education. Poor and uneducated women tend to be unhealthy before pregnancy, especially its refer to malnourishment and its associated with preterm delivery.

Van Den Berg B(58)found that mothers who have high socioeconomic status had 13.8% of preterm delivery,while the mothers who have low socioeconomic status had 29.3% of preterm delivery .

Baird D(59)studied mothers in high social class and found that thy had the lowest rates of prematurity .

Ericson A(60) who studied pregnant woment in Sweden, divided the population into 3 groups i.e., high, medium, and low socioeconomic status and found that has relative risk of preterm delivery in each group was 1.0, 1.3 and 1.8 respectively.

Arbuck TE (61)found that maternal education and family income were associated with preterm delivery .

Kaltreider DF(62) found that maternal age, race and education had significant association with preterm delivery .

### 1.2 Maternal age

Lowson JB(63)suggested that the optimal age for pregnancy should be between 20 and 30 years old. His study indicated that maternal age is an important factor for physiological and gynecological maturity.

Baird D(59)found that primigravida mothers younger than 20 years of age had a highest rate of prematurity because of they lacked gynecological immaturity.

Zlatnik FJ(64)reported similar findings. The uterus may somehow be structurally or functionally less able to carry a fetus to term and the uterine vasculature are less well – developed in those young women.

Lowson JB(63) studied mothers of younger (<20 years old) or older (>30years old) groups and suggest that both may encounter special problems. It is possible that ovarian function is not stabilized when the mother is too young and her physical growth has not fully developed .Her reproductive system is not well prepared for pregnancy so that the hormonal effect on her reproductive organs is deficient. This factor may result in complicated pregnancy as well as preterm delivery.

### 1.3 Maternal occupation

Creasy RK(7)studied heavy physical work, maternal emotions and stressful life events which were once belived to be potent sources of harm to the fetus during pregnancy. He found that the incidence of preterm delivery was 4.3% among professional and business groups and 10.9% among in Semi and unskilled manual workers.

Mamelle N(65)Investigated the relationship between prematurity and occupational fatigue of mothers. The latter had been quantified by the index based on the 5 sources of fatigue (posture, work on industrial machine, physical exertion, mental stress, and environment). A significant relative risk between 1.6 and 19. Is found for each source, when any one of these sources increases from low to high, so that each fatigue source can be considered as a prematurity risk factor.

Holmes T(66) studied based on the assumption that anxiety or stress is increased by changes in an individual's lifestyle and environment. He demonstrated that the occurrence of stress 6 months before delivery, or during the $2^{nd}$ and $3^{rd}$ trimester, is associated with an increased number of pregnancy complication.

## 2. Maternal nutritional status and food intake

### 2.1 Food intake

Food is essential to life and growth. Without an adequate supply of food and nutrients an organism cannot grow and develop normally and eventually dies. Pregnancy makes many demands on the prospective mother, especially her nutritional needs. During pregnancy two factors that determine energy requirements are changes

in the mother's usual physical activity and an increase in her basal metabolism to support the work required for growth of the fetus and the accessory tissue. The goal of weight management during pregnancy should be to promote optimum nutrition for the mother and child. Correlation between energy intake and weight gain in 489 pregnant women(10).

Beechen RE(67)studied the relationship between caloric intake and weight gain during pregnancy there was a positive correlation, but the coefficient was statistically significant only for caloric intake in the second trimester, This result was similar to the report by Thompson AM(68) for intakes from $20^{th}$ – $28^{th}$ weeks of gestation. In the third trimester, when many women in this study were restricted caloric intake, the correlation with total weight gain was smaller and statistically in significance.

### 2.2 Maternal height

Baird D(59)studied maternal height among primigravidas in Aberdeen, Scotland and classified their height into 3 groups :-

1. 64 inches and over (tall)
2. 63 inches to 61 inches (medium)
3. <61 inches (small)

It was found that incidence of preterm delivery was 4.9, 7.7 and 12.1 percent, in each group respectively. The stunted growth of mothers give rise to a high rate of prematurity.

Grant JP(6)studied pregnancy of teenage mothers (13-19 years)and found that they had a higher incidence of prematurity and diminished birth size. Teenage mothers tend to be of small stature and weight. The size and gestational age at delivery of their infants are in proportion to their smaller size (small stature and weight) .

### 2.3 Pre-pregnancy weight and weight gain

Maternal pre-pregnancy weight and weight gain, which refers to maternal nutritional status during pregnancy, associated positively with preterm delivery. Several anatomic, physiological and biochemical changes occur during a normal pregnancy. The purpose of these changes is to create an internal environment which is conductive to the healthy development of the fetus and to prepare the mother for labor, birth, and lactation. These changes in physiology form the basic for the nutrient requirements of the pregnant woman. Fetal health is significantly influenced by the efficiency of nutrient transport by the placenta. The rapid growth of the fetus increases the need for all nutrients.The mother's weight gain and the week of delivery were compared, a positive correlation appeared.

Berkowitz GS(72) studied influence of weight gain during pregnancy. Duration of gestation and infant size at birth were examined among women beginning pregnancy with underweight and with normal weight, 654 prenatal and postpartum care in a major hospital located in St. Paul, Minnesota, USA and delivered single infants between the year 1969 and 1976. Pre-pregnancy weight status was calculated as a percentage of normal weight, defined as the midpoint of the weight range given for a women's height and age in the Metropolitan Life Insurance table. Women's height and age in the Metropolitan Life Insurance table. Women weighing less than 80% of standard weight were designated as very underweight, those weighing from 80 to 90% as moderately underweight, and those weighting from 90 to 120% as normal weight. It was found that Pre –pregnancy weight status was not associated with the amount of weight gained during pregnancy and that underweight women who gained as the same amount of weight as normal weight women delivered infants at a younger gestational age and of lower birth weight and length.The relationship of antenatal weight gain to pregnancy outcome in 362 pairs of underweight women (<90% Metropolitan Relative Weight, MRW) and normal weight women, underweight women had more preterm infants (8.8% and 9.4% respectively, $P<0.01$). Mean antenatal weight gain of underweight women ($9.3 \pm 3.2$ kgs.) was significantly higher than that of normal weight momen ($8.4 \pm 3.1$ kgs) ($P < 0.001$)

Women who are overweight prior to pregnancy are at an increased risk of complications such as toxemia, pre-eclampsia and diabetes mellitus. The maternal complications observed during pregnancy may lead to preterm delivery significantly. In Jamaica, a study showed a relationship between obesity in mothers and complication during pregnancy (diabetes mellitus and pre-eclampsia), which followed by poor fetal outcome and short gestational age .

In several studies, the adequate weight gain is of critical importance to women beginning in pregnancy, it reflects the good outcome.

Baird D(59)found that the lowest rate of prematurity was found in association with a weight gain of about 1 pound per week between the twentieth and thirty-sixth week of pregnancy. This rate of weight increase is also associated with the lowest perinatal mortality.

Pepiernik E(51)found a significant association between preterm birth and maternal weight gain of less than 5 kg. (11 lb) at 32 weeks gestation.

Berkowitz GS(72)found that the odds ratio for inadequate weight gain" adjusted for pregnancy duration was 4.28 (95% confidence interval 2.3, 8.0) .

The average weight increase is estimated to be approximately 12 kg, of which about 3.5 kg (29%) represent the weight of the fetus at term; the uterus, amniotic fluid, and placenta account for about 2 kg and the breast for 1 kg. One and one-half kg are due to fluid retention and 4 kg. due to fat deposit. For practical purposes, it has been said that during the $2^{nd}$ and $3^{rd}$ trimesters of pregnancy a woman should put on 0.4 kg/wk(49).

Hediger ML(69)found that a low weekly rate of gain (less than 0.23 kg) after 20 weeds' gestation was associated with preterm birth.

Abrams B(70)studied the relationship between maternal weight gain and preterm delivery in 2163 women between 1978-1986. Categories of rate of weight gain were define as follows :

1. Low rate of gain = less than 0.27 kg/week
2. Average rate of gain = 0.27 – 0.52 kg/week
3. High rate of gain = more than 0.52 kg/week.

It was found that 37.3% of the preterm mothers gained less than 0.27 kg/week, compared with only 24.2% of the term group ($p<0.002$) Women with a low rate of gain were more than twice as likely to experience a preterm delivery as those with a high gain (higher than 0.52 kg/week); the odds ratio was 2.54 (95% confidence interval 1.49, 4.88). The mean weekly weight gain of preterm mothers ($0.33 \pm 0.19$ kg/week) was significantly ($p = 0.002$) lower than that of full – term mothers ($0.39 \pm 0.17$ kg/week). This difference in weight gain appeared e after 20 week' gestation .

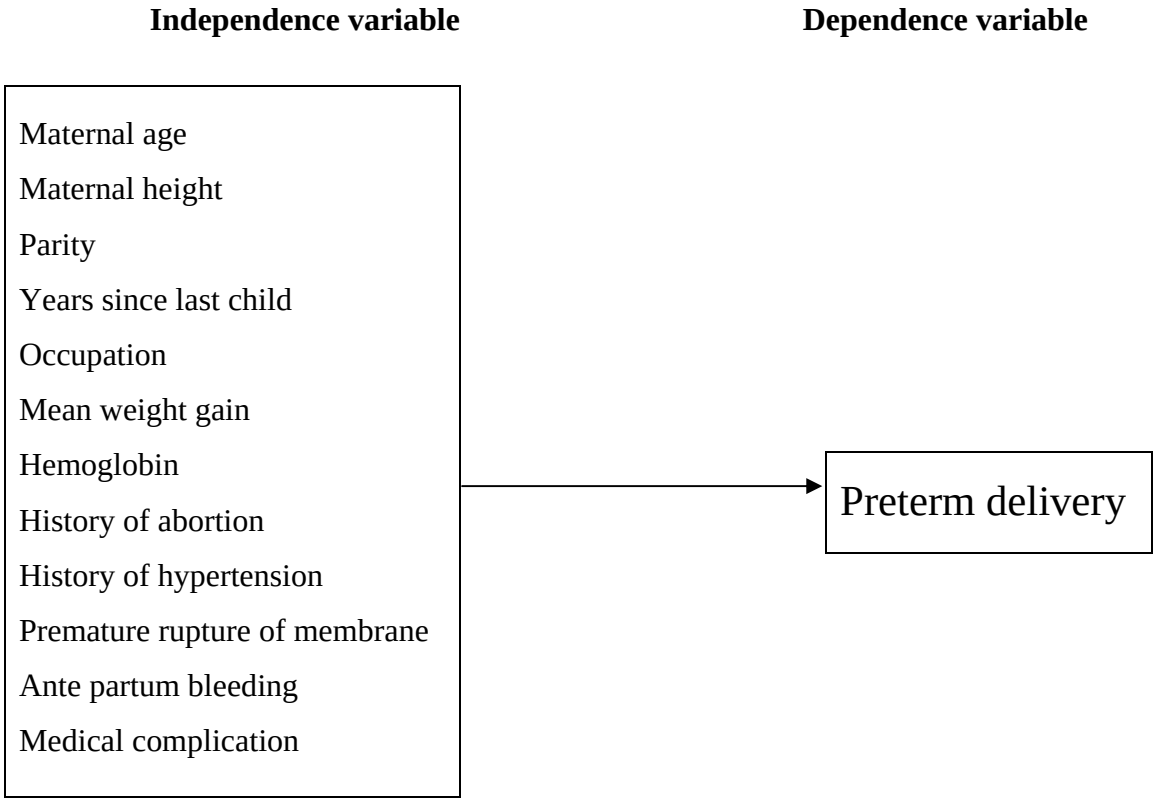
Hediger ML(69)studied a cohort of 1790 teenagers and found that an inadequate weight gain (less than 400 g/week) during the late second and third trimesters significantly increased the risk of preterm delivery.

## 2.4 Hemoglobin and hematocrit levels

Hemoglobin and hematocrit levels decrease during pregnancy because the fetus will act as a parasite, depleting the mother of iron. If, however, at any point in the pregnancy the hemoglobin falls below 11 gm% or the hematocrit below 33%, the diagnosis is anemia .

Kaltredir DF(62)found that if hemoglobin and hematocrit dropped to less than 9 gm% and 31% respectively, preterm delivery and low birth weight infants accurred.

# CONCEPTUAL FRAMEWORK



# CHAPTER III
# MATERIALS AND METHODS

## Research Design

This study compared of two parts of study. The first part of this study is historical cohort study with the objective to determine the incidence of preterm delivery among mulliparous women who came to register for the first time at antenatal booking unit Ramathibodi hospital during 1 January – 30 December 2005. The second part is case – control study with the objective to determine risk factors of preterm delivery.

## Target Population

In the first part of study all the pregnant women who came to register from the first time at antenatal booking unit Ramathibodi hospital during 1 January – 30 December 2005. The name and hospital numbers of all pregnant were in the computerized records of the hospital.

The second part of the study was a case control study. The cases were pregnant women who outcome of deliveries were know and who were preterm delivery which was recorded in the computerized medical statistics of the hospital. The inclusion criteria of cases and controls were:

Cases:

1. The pregnancy women who came to register at antenatal booking unit for first time at Ramathibodi hospital during 1 January 2005 – 30 December 2005
2. They were pregnant women.
3. Outcome of delivery was known.

They were diagnosed preterm delivery from medical statistics of Ramathibodi hospital or self report in women who delivered in other hospital.

Control:

The inclusion criteria of the controls were the same as cases except that they were full term labor and they registered at antenatal booking unit just after the cases.

**Sample Size Estimation**

To collect all pregnant women who came to registered at antenatal booking unit Ramathibodi hospital on day to day basis, we included total cases of 1 year (during 1st January to 30th December 2005) to be our sample which totally were 2,542 cases.

**Instrument**

The instrument of this study was data record form which constructed by the researcher according to the objectives. Data was collected from computerized, records of antenatal booking unit, medical records and statistics from medical statistics unit of Ramathibodi hospital.

**Data Collection Procedure**

The steps of data collection were as follow:

Submitting the research proposal for approval on human rights related to researches involving human subjects, based on the declaration of Helsinki form

1. Ethical research committee of Faculty of medicine Ramathibodi hospital. It received approval on 15 January 2007.
2. Outcome of delivery or abortion were recorded from medical statistics unit of Ramathibodi hospital, computerized medical records form and delivery log book at the delivery unit, Ramathibodi hospital.
3. Those women, whose outcome of delivery and abortion were not known, were following by mail and telephone. Three weeks period was allowed for their response. If there was no response, they were classified as loss to follow up.

**Method Of Data Analysis**

1. Descriptive statistic: number and percentage
2. Analysis statistical:

- Univariate analysis; odds ratio, 95% confidence interval and p– value was used to compare each of the independent risk factors associated with preterm delivery
- Multivariable analysis by logistic regression.
- $SPSS^{+}$ PC program was used for statistical analysis.

# CHAPTER IV
# RESULTS

This study compared of 2 parts. The first part is a historical cohort study of incident a preterm delivery among mulliparous women in Ramathibodi hospital. The second part is a case control study with the objective to risk factors association with preterm delivery.

The studied results were present as follow:

Objective 1. Incidence of preterm delivery at Ramathibodi hospital

During 1 January – 30 December2005 there were 5,288 pregnant women who came to register for the first time at antenatal care booking unit Ramathibodi hospital. Among these women, there were 2,542 pregnant women. This pregnant woman were followed, 1,461cases (57.47%) delivered their baby in Ramathibodi hospital and 221 cases (8.7%) of abortion before twenty weeks of gestational. Eight hundred sixty pregnant (33.83) women who lost to follow up were followed by telephone or mail. Sixty-three cases (7.33%) responded. Sixty two cases responded outcome of there delivery and one case of abortion.

In conclusion among 2,542 cases of pregnant women who registered at booking unit Ramathibodi hospital, outcomes of pregnancy were knows in1,745 cases (68.64%), 1,523 cases of delivery (59.91%) and 222 cases (8.73%) of abortion. The numbers of loss to follow up were 797 cases (31.35%).

Among 1,523 cases of women delivery whose outcomes of deliveries were knows, there were 190cases of preterm delivery (before 37 week of gestation). Incidence of preterm delivery among pregnant women whose came to register the delivery at Ramathibodi hospital was 12.48%. The distribution of gestational age of this preterm delivery was show in Table I. Most of preterm delivery occurred between 34-36 of gestation age (7.16%). There were 2.23% of case occurred before 28 weeks of gestational age.

**Table 1** Classification in sample side preterm delivery

| : Classification | Number | % |
|---|---|---|
| -<28 wks | 34 | 2.23 |
| -28-30 | 17 | 1.12 |
| -31-33 | 30 | 1.97 |
| -34-36 | 109 | 7.16 |
| Total | 190 | 12.48 |

Objective 2 Factors associated with preterm delivery by case – control study

In this case - control study, Comparison between of 190 cases of preterm deliveries and 190cases of full term deliveries was record.

1) Univariate Analysis

By using uinvariate analysis of chi-square test with odds ratio and 95% confidence intervals, factors which were found to be significantly associated with preterm delivery were maternal age, maternal height, occupational, education, history of hypertension, history present of illness, history of abortion, ante partum bleeding, premature rupture of membrane, haemoglobin, parity, duration after last child and mean weight gain as show in table 2.

**Maternal age**

The lowest risk of preterm delivery was found among pregnant women of <=20 years of age which was used as a reference group. When compare with reference group, the highest risk was found among women of 35 years or more had the odds ratio with 95% confidence intervals of 2.58(1.08 – 6.14) which was not statistically significant.

**Maternal height**

The lowest risk of preterm delivery was found among pregnant women of height≥161 centimetres who were used as reference group. When compare with reference group, the highest risk was found among pregnant women of height ≤145centimetres which had the odds ratio with 95% confidential interval of 2.78(1.11-2.36) which was statistically significant.

**Parity**

The lowest risk of preterm delivery was found among the first pregnant women who were used as reference group. When compare with reference group, the highest risk was found among the second and over pregnant women which had the odds ratio with 95% confidential interval of 1.84(1.08-3.10) which was statistically significant.

**Years since last child**

The lowest risk of preterm delivery was found among duration after last child =0 of pregnant women who were used as reference group. When compare with reference group, the highest risk was found among duration after last child was one year or over of pregnant women which had the odds ratio with 95% confidential interval of 1.48 (0.72-3.04) which was not statistically significant.

**Education**

The lowest risk of preterm delivery was found among diploma or higher who was used as reference group. When compare with reference group, the highest risk was found among which had the odds ratio with 95% confidential interval of 0.79 (0.49-1.28) which was not statistically significant.

Occupational

The lowest risk of preterm delivery was found among enterprenant who was used as reference group. When compare with reference group, the highest risk was found among civil servilant which had the odds ratio with 95% confidential interval of 3.79 (1.50-9.60) which was statistically significant.

**Mean weight gain**

The lowest risk of preterm delivery was found among pregnant women of mean weight gain <0.5 which was used as reference group. When compare with reference group, the highest risk was found among pregnant women of mean weight gain 2 or more had the odds ratio with 95% confidential interval of 3.81 (2.09-6.96) which was statistically significant.

**Hemoglobin**

The lowest risk of preterm delivery was found among pregnant women hemoglobin was >10g% which was used as reference group. When compare with reference group women who had haemoglobin <10g% more had the odds ratio with 95% confidential interval of 1.75 (1.07-2.86) which was statistically significant

**History of abortion**

The lowest risk o of preterm delivery was found among pregnant women who had not history of abortion which was used as reference group. When compare with reference group women who had history of abortion had the odds ratio with 95% confidential interval of 0.85 (0.44-1.63) which was not statistically significant

History of hypertension

The lowest risk of preterm delivery was found among pregnant women who had not history of hypertension which was used as reference group. When compare with reference group, the highest risk was found among pregnant women who had history of hypertension which had the odds ratio with 95% confidential interval of 1.45 (0.79-2.65) which was not statistically significant.

**Premature rupture of membranes**

The lowest risk of preterm delivery was found among pregnant women who had premature rupture of membrane which was used as reference group. When compare with women who had premature rupture of membrane had the odds ratio with 95% confidential interval of 1.49(0.96-2.31) which was not statistically significant

**Ante partum bleeding**

The lowest risk of preterm delivery was found among pregnant women who had ante partum bleeding which was used as reference group. When compare with women who had ante partum bleeding had the odds ratio with 95% confidential interval of 2.06(0.69-6.31) which was not statistically significant

**Medical complication**

The lowest risk of preterm delivery was found among pregnant women who had present of illness which was used as reference group. When compare with women who had had present of illness the odds ratio with 95% confidential interval of 2.07(1.24-3.46) which was statistically significant. Medical complication included diabetic milieus, heart, hypertension, lung, hepatitis.

**Table2:** Odds ratio and 95% Confidence interval of risk factors

| Factor | Case (n=190) | | Control (n=190) | | OR | 95%CI |
|---|---|---|---|---|---|---|
| | No | % | No | % | | |
| 1.Maternalage(years) | | | | | | |
| ≤20 | 11 | 35.5 | 20 | 64.5 | 1.00 | Ref. |
| 20-24 | 29 | 51.8 | 27 | 48.2 | 1.95 | 0.79-4.82 |
| 25-29 | 58 | 46.4 | 67 | 53.6 | 1.57 | 0.70-3.56 |
| 30-34 | 48 | 51.6 | 45 | 48.4 | 1.94 | 0.84-4.50 |
| ≥35 | 44 | 58.7 | 31 | 41.3 | 2.58* | 1.08-6.14 |
| | | | $X^2$=2.14 | df=4 | p-value=0.14 | |
| 2.Maternalheight(cm.) | | | | | | |
| ≤145 | 41 | 63.1 | 24 | 36.9 | 2.78* | 1.11-5.36 |
| 146-150 | 16 | 60 | 11 | 40 | 2.36* | 1.30-4.30 |
| 151-155 | 51 | 59.3 | 35 | 40.7 | 2.37* | 1.30-4.30 |
| 156-160 | 47 | 42.7 | 63 | 57.3 | 1.21* | 1.22-4.30 |
| ≥161 | 35 | 38 | 57 | 62 | 1.00 | Ref. |
| | | | $x^2$=16.01 | df=4 | p-value=0.01 | |
| 3.Parity | | | | | | |
| 1 | 113 | 48.9 | 118 | 51.1 | 1.00 | Ref. |
| 2 | 51 | 63.8 | 29 | 36.3 | 1.84* | 1.08-3.10 |
| 3 | 26 | 37.7 | 43 | 62.3 | 1.88 | 0.61-5.78 |
| | | | $x^2$=15.32 | df=2 | p-value=0.01 | |
| 4. Years since last child | | | | | | |
| 0 | 129 | 46.1 | 151 | 53.9 | 1.00 | Ref. |
| ≥1 | 10 | 52.6 | 9 | 47.4 | 1.31 | 0.51-3.30 |
| | | | $x^2$=2.87 | df=1 | p-value=0.24 | |
| 5.Education level | | | | | | |
| High school or lower | 81 | 51.6 | 76 | 48.4 | 1.00 | Ref. |
| Diploma or higher | 67 | 58.3 | 48 | 41.7 | 1.31 | 0.81-2.13 |
| | | | $x^2$=1.58 | df=1 | p-value=0.67 | |

**Table2:** Odds ratio and 95% Confidence interval of risk factors (Conts.)

| Factor | Case (n=190) | | Control (n=190) | | OR | 95%CI |
|---|---|---|---|---|---|---|
| | No | % | No | % | | |
| 6.Occupation | | | | | | |
| Laborers | 25 | 41.7 | 35 | 58.3 | 1.49 | 0.85-2.60 |
| House wife | 73 | 54.9 | 60 | 45.1 | 1.63 | 0.99-2.69 |
| Merchant | 17 | 53.1 | 15 | 46.9 | 1.24 | 0.60-2.57 |
| Civil employment | 20 | 74.1 | 7 | 25.9 | 3.79* | 1.50-9.60 |
| Entrepreneur | 55 | 43 | 73 | 57 | 1.00 | Ref. |
| | | | x2=11.885 | df = 4 | p-value = 0.02 | |
| 7.Mean weight gain (kilogram per weak) | | | | | | |
| ≤0.5 | 21 | 28 | 84 | 72 | 1.00 | Ref. |
| 0.51-1.0 | 10 | 45.5 | 12 | 54.5 | 2.02 | 0.79-5.16 |
| 1.01-1.5 | 22 | 47.8 | 24 | 52.2 | 2.36* | 1.09-5.08 |
| 1.51-2.0 | 46 | 54.8 | 38 | 45.2 | 3.11* | 1.61-6.04 |
| ≥2.01 | 89 | 59.7 | 60 | 40.3 | 3.81* | 2.09-6.96 |
| | | | x2=21.20 | df=4 | p-value=0.01 | |
| 8.Hemoglobin (g%) | | | | | | |
| <10 | 157 | 53 | 139 | 47 | 1.75* | 1.07-2.86 |
| ≥10 | 33 | 39.3 | 51 | 60.7 | 1.00 | Ref. |
| | | | x2=4.95 | df = 1 | p-value = 1.03 | |
| 9. History of abortion | | | | | | |
| Yes | 26 | 53.1 | 23 | 46.9 | 1.15 | 0.63-2.1 |
| No | 164 | 53 | 167 | 50.5 | 1.00 | Ref. |
| | | | x2=0.21 | df = 1 | p-value = 0.65 | |
| 10.History of hypertension | | | | | | |
| Yes | 21 | 42 | 29 | 58 | 1.45 | 0.79-2.65 |
| No | 169 | 51.2 | 161 | 48.8 | 1.00 | Ref. |
| | | | x2=1.47 | df = 1 | p-value = 0.23 | |

**Table2:** Odds ratio and 95% Confidence interval of risk factors (Conts.)

| Factor | Case (n=190) | | Control (n=190) | | OR | 95%CI |
|---|---|---|---|---|---|---|
| | No | % | No | % | | |
| 11. Premature rupture of membranes | | | | | | |
| Yes | 50 | 43.1 | 66 | 56.9 | 1.49 | 0.96-2.31 |
| No | 140 | 53 | 124 | 47 | 1.00 | Ref. |
| | | | x2=3.18 | df=1 | p-value = 0.08 | |
| 12. Ante partum bleeding | | | | | | |
| Yes | 5 | 33.3 | 10 | 66.7 | 2.06 | 0.69-6.13 |
| No | 185 | 50.7 | 180 | 49.3 | 1.00 | Ref. |
| | | | x2=1.74 | df=1 | p-vaule = 0.19 | |

**Table 3** The association between preterm delivery and risk factor by Univariate analysis

| Factor | Case (n=190) | | Control (n=190) | | OR | p-value | 95%CI |
|---|---|---|---|---|---|---|---|
| | No | % | No | % | | | |
| 1.Maternalage(years) | | | | | | | |
| ≥35 | 31 | 54.4 | 31 | 41.3 | 1.55 | 0.94 | 0.93-2.58 |
| <35 | 146 | 47.9 | 159 | 52.1 | | | |
| 2.Maternalheight(cm.) | | | | | | | |
| ≤155 | 120 | 59.4 | 82 | 40.6 | 2.26 | 0.01* | 1.50-3.41 |
| >155 | 70 | 39.3 | 108 | 60.7 | | | |
| 3.Parity | | | | | | | |
| 1 | 113 | 48.9 | 118 | 51.1 | | | |
| ≥ 2 | 77 | 51.7 | 72 | 48.3 | 1.12 | 0.60 | 0.74-1.69 |
| 4. Years since last child | | | | | | | |
| ≥1 | 10 | 52.6 | 9 | 53.9 | 1.3 | 0.58 | 0.51-3.30 |
| 0 | 129 | 46.1 | 151 | 47.7 | | | |

**Table 3** The association between preterm delivery and risk factor by Univariate analysis (Conts.)

| Factor | Case (n=190) | | Control (n=190) | | OR | p-value | 95%CI |
|---|---|---|---|---|---|---|---|
| | No | % | No | % | | | |
| 5.Education level | | | | | | | |
| Diploma or higher | 67 | 58.3 | 48 | 41.7 | 1.31 | 0.28 | 0.81-2.13 |
| High school or lower | 81 | 51.6 | 76 | 48.4 | | | |
| 6.Occupation:civil employment | | | | | | | |
| Yes | 20 | 74.1 | 7 | 25.9 | 3.08 | 0.01* | 1.27-7.46 |
| No | 170 | 48.2 | 183 | 51.8 | | | |
| 7.Mean weight gain (kilogram per weak) | | | | | | | |
| ≥1 | 135 | 57.9 | 98 | 42.1 | 2.34 | 0.01* | 1.53-3.59 |
| <1 | 53 | 37.1 | 90 | 62.9 | | | |
| 8.Hemoglobin(g%) | | | | | | | |
| <10 | 157 | 53 | 139 | 47 | 1.75 | 0.03* | 1.07-2.86 |
| ≥10 | 33 | 39.3 | 51 | 60.7 | | | |
| 9.History of abortion | | | | | | | |
| Yes | 26 | 53.1 | 23 | 46.9 | 1.15 | 0.65 | 0.63-2.1 |
| No | 164 | 53 | 167 | 50.5 | | | |
| 10. History of hypertension | | | | | | | |
| Yes | 21 | 42 | 29 | 58 | 1.45 | 0.23 | 0.79-2.6 |
| No | 169 | 51.2 | 161 | 48.8 | | | |
| 11. Premature rupture of membranes | | | | | | | |
| Yes | 50 | 43.1 | 66 | 56.9 | 1.49 | 0.08 | 0.96-2.31 |
| No | 140 | 53 | 124 | 47 | | | |

**Table 3** The association between preterm delivery and risk factor by Univariate analysis (Conts.)

| Factor | Case (n=190) | | Control (n=190) | | OR | p-value | 95%CI |
|---|---|---|---|---|---|---|---|
| | No | % | No | % | | | |
| 12. Ante partum bleeding | | | | | | | |
| Yes | 5 | 33.3 | 10 | 66.7 | 2.06 | 0.18 | 0.69-6.13 |
| No | 185 | 50.7 | 180 | 49.3 | | | |
| 13. Medical complication | | | | | | | |
| Yes | 28 | 35.9 | 50 | 64.1 | 2.07 | 0.01* | 1.24-3.46 |
| No | 162 | 53.6 | 140 | 46.4 | | | |

## 2. Logistic regression analysis

By logistic regression analysis using significant dichotomous variables from univariate analysis to enter in to the equation. The results showed that only three risk factors had significantly association with preterm delivery. There were premature rupture of membrane (OR=2.33,95%CI=1.22-4.44) and maternal height(OR=2.22, 95%CI=1.14-4.33). Other factors including, ante partum bleeding, mean weight gain≥1, maternal age≥35, civil employment, history of hypertension, hemoglobin<10g%, history of abortion, medical complication, years since last child≥1,parity≥2, education level=diploma or higher showed no statistically significant association with preterm delivery (Table4).The overall chisquare of the model was 13.868 p<0.01.

**Table 4** Association between risk factors and preterm delivery by multiple logistic regression

| Risk factor | β | SE (β) | Exp. (β) | P-value | 95%CI |
|---|---|---|---|---|---|
| 1.Maternalheight≤155(cm.) | .948 | 0.32 | 2.57 | 0.008 | 1.37-4.81 |
| 2.Prematureruptureofmembranes | 0.780 | 0.312 | 2.181 | 0.012 | 1.183-4.022 |

# CHAPTER V
# DISCUSSION

The objective of this study to determine the incidence of Preterm delivery among mulliparous women who came to register for the first time at antenatal booking unit Ramathibodi hospital during 1 January – 30 December 2005. The second part is case – control study with the objective to determine risk factors of preterm delivery. The discussion will be divided in to two sections as follow:

**Part I.** Research methodology
**Part II.** Research results

## Part I. Research methodology

### 1. Research design

The research design of this study comprised of two parts of study. The first part of the study was a historical cohort study which is appropriate for study of incidence rate. For historical cohort study cases were identified and their experience up to the present is obtained. This is a less common type of study because detailed record are often not available. This lack of data make it difficult to be sure about an individual's level of exposure or even whether they did or did not develop the disease under study.

However, if good data is available a retrospective cohort study can be extremely effective and relatively inexpensive. Detailed records are kept and updated annually. Advantages of historical cohort study are allowing complete information on the subject's exposure, including quality control of data, and experience there after. Provide a clear temporal sequence of exposure and disease, give an opportunity to study multiple out comes related to a specific exposure patterns, permit calculation of incidence rates (absolute risk) as well as relative risk, methodology and results are easily understood by non-epidemiologists and enable the study of relatively rare exposures. The disadvantages of historical cohort study were not suited for the study

of rare diseases because a large number of subjects is required, exposure patterns, expensive to carry out because a large number of subjects is usually required, baseline data may be sparse because the large number of subjects does not allow for long interviews. In Ramathibodi hospital, it was possible to identify pregnant women who came to register to deliver their babies and follow up of their outcomes was also relatively complete. Only 32.4% were loss to follow up after contact by mail or phones were attempted.

The second part of the study was a case control study which is appropriate for study of risk factors or preterm delivery. The advantages of cases-control study were that at permits the study of rare diseases, or with long latency between exposure and manifestation. The study can be launched and conducted over relatively short time periods, relatively inexpensive as compared to cohort studies. Study of multiple potential causes of disease is also possible. For disadvantages of case-control study were information on exposure and past history is primarily based on interview and may be subject to recall bias. Validation of information on exposure is difficult, or incomplete, or even impossible. The case control study concerned with one disease only, generally incomplete control of extraneous variables and choice of appropriate control group may be difficult.

**Population**

The populations of this research were pregnant women who came to register for first time at antenatal booking unit at Ramathibodi hospital during 1 January 2005 – 30 December 2005. They were followed up to the end of pregnancy and data was kept in the hospital data base. For those who loss to follow up, contact by phone or mail was done. Loss to follow up in this study was 32% which was acceptable.

**Sample size**

The sample size of this study was to collect all pregnant women who came to registered at antenatal booking unit Ramathibodi hospital on day to day basis, we included total cases of 1 year (during 1$^{st}$ January to 30$^{th}$ December 2005) to be our sample which totally were 2,542 cases.

**Data collection**

The instrument of this study was data record form which created by the researcher. Data was collected from computerized records of booking medical records and statistics from medical statistics unit of Ramathibodi hospital

**Part II. Research results**

**Objective 1. Incident of preterm delivery at Ramathibodi hospital**

Incidence of preterm delivery among pregnant women in Ramathibodi hospital was 12.48%. Most of the occurred at gestational ages of 34-36 weeks(7.16%). About 1-2% occurred at gestational ages of less than 28 wks(2.23%), 28-30wks(1.12%) and 31-33wks(1.97%).. The incidence of preterm delivery in this study was comparable with other study although using different research designs.

The true incident of preterm delivery is not as well document as might be expect, owing in past to lack of differentiation of growth-restricted from preterm infants. (6)In the United States, data from study of birth certificates for most regions revealed the incidence of preterm birth to be 9.4% in1981. This figure rose to10.7% in 1989 and to 11% in 1995. Therefore, the overall preterm birth rate is approximately 10-11% and probably varies among different populations, depending on risk factors present.

In Thailand, the number of preterm delivery for the overall country is not available because infant birth weight is reported without the gestational age. However, some institution report statistics of preterm delivery. There are, for example, King Chulalongkorn Memorial Hospital, with a rate of preterm delivery of approximately 9.4% (3).Maharaj Nakorn Chiangmai Hospital, with a rate of singleton pregnancy with preterm delivery of 12% (4), In Siriraj Hospital the rate of singleton pregnancy with preterm delivery of 6.85%(4) .

**Objective 2. The result of association between risk factors and preterm delivery:**

**2.1 Logistic Regression Analysis**

Several factors predisposing to the development of preterm delivery have been identified. They are important because we can use these factors in screening

patients at high risk for special care and attention. Also, the presence or absence of predisposing factors can be helpful in differential diagnosis.

**Premature rupture of membrane**

The study confirmed the association between premature rupture of membrane and risk factor of preterm delivery. After controlling the other effects, the result showed that premature rupture of membrane is an important risk factor for preterm delivery, with adjusted odds ratio of 2.24 ( 95%CI=1.21-4.17).

Several more studies confirmed the long-suspected association premature rupture of membrane and preterm delivery. Infection of the membranes and amniotic fluid caused by a variety of micro organisms has emerged as a possible explanation of some cases of ruptured membranes, preterm labor, or both. Bacteria are recovered by transabdominal amniocentesis from as many as 20 percent of women in preterm labor without overt clinical infection and with intact fetal membranes .Viral products have also been recovered .Reddy U (41)reported that infection is not limited to amniotic fluid. In studies done at caesareans delivery in 609 women with intact membranes, Recovery of organisms from the chorioamnion was significantly increased with spontaneous preterm labor. Recovery of pathogens was also inversely correlated with gestational age. The pathogenesis of upper genital tract infection and preterm birth will be studied the future. The pathway for bacteria to enter amniotic fluid with intact membranes is unclear. Escherichia coli can permeate living membranes; thus, they are not an absolute barrier to ascending infection. Another pathway for bacterial initiation of preterm labor may not require bacteria in the amnionic fluid. The cytokine network of cell-mediated immunity can be activated within the decidual tissue that lines the presenting fetal membranes. In this scheme, bacterial products such as endotoxin stimulate decidual monocytes to produce cytokines, which in turn stimulate arachidonic acid and then prostaglandin production. Prostaglandins $E_2$ and $F_{2\alpha}$ act in a paracrine fashion to stimulate adjacent myometrium to contract.

In Thailand, this finding is in accordance with Suvaree S.(71) was studied factor associated with preterm delivery in pregnant women at Ramathibodi hospital in 1988-1990, Pregnant women who had premature rupture of membrane also had preterm delivery with adjust odds ratio of 1.1( 95%CI=7.1-17.3) .

Preterm Premature rupture of membrane is a condition which its etiology is still not known. As discussed above, infection by various mechanisms may be a cause but no definite standards or treatment was setup about vaginal infection and discharge.

Thus, preterm premature rupture of membrane is difficult to predicted and prevented. One strategy is to screen it in pregnant women. Vaginal or cervical swab should be as a routine which would cost financial burden to the society.

**Maternal height**

The study showed that maternal height equal to and less than 155 cms is association with preterm delivery with adjust odds ratio of 2.57 ( 95%CI=1.37-4.81) .

Baird D(59) found that the incidence of preterm delivery was 4.9, 7.7 and 12.1 percent, respectively. The stunted growth of mothers give rise to a high rate of prematurity

Grant JP(6)studied pregnancy of teenage mothers (13-19 years)and found that they had a higher incidence of prematurity and diminished birth size. Teenage mothers tend to be of small stature and weight. The size and gestational age at delivery of their infants are in proportion to their smaller size (small stature and weight).

**2.2 Univariate analysis**

By using univariate analysis of chi-square test with odds ratio and 95% confidence intervals, factors which were found to be significantly associated with preterm delivery included maternal age equal to more than35years, occupation of civil employment, hemoglobin level less than 10 %, parity equal to more than two, mean weight gain equal to more than 1 kg. per week and medical complication. But the results showed that there were not significantly association with preterm delivery by logistic regression analysis.

**Maternal age**

The study showed that the lowest risk of preterm delivery was found among pregnant women equal to or less than 20 years , the highest risk was found among women of 35 years or more who had the odds ratio with 95% confidence intervals of 2.58(1.08 – 6.14) which was statistically significant. This finding is in contrast with

study of Lowson JB(63)who mentioned that mothers of younger (<20 years old) or older (>30 years old) groups may encounter special problems. It is possible that ovarian function is not stabilized when the mother is too young and her physical growth has not fully developed. Her reproductive system is not well prepared for pregnancy so that the hormonal effect on her reproductive organs is deficient. This factor may result in complicated pregnancy as well as preterm delivery.

The study of Zlatnik FJ(64)found that primigravida mothers younger than 20 years of age had a highest rate of prematurity because of gynecological immaturity. The uterus may somehow be structurally or functionally less able to carry a fetus to term and the uterine vasculature are less well – developed in those young women. Van den Berg B(58)evaluated a population of 17,000 indigent women and found that younger (<17 years old) or older (>30 years old) were significantly related to preterm delivery.

**Occupation**

The study showed that the highest risk was found among civil employment which had the odds ratio with 95% confidential interval of 3.18 (0.96-10.54) which was statistically significant. In Thailand, this finding is in contrast with TitapanV(4)whose study of heavy physical work, maternal emotions and stressful life events which were once believed to be potent sources of harm to the fetus during pregnancy. The incidence of preterm delivery was 4.3% among professional and business groups and 10.9% among in semi and unskilled manual workers.

In other countries, Mamelle N(65)studied the relationship between prematurity and occupational fatigue of mothers, the latter having been quantified by the index based on the 5 sources of fatigue (posture, work on industrial machine, physical exertion, mental stress, and environment). A significant relative risk between 1.6 and 19. Is found for each source, when any one of these sources increases from low to high, so that each fatigue source can be considered as a prematurity risk factor.

Holmes T(66)found that anxiety or stress is increased by changes in an individual's lifestyle and environment. It demonstrated that the occurrence of stress 6 months before delivery, or during the $2^{nd}$ and $3^{rd}$ trimester, is associated with an increased number of pregnancy complication.

**Hemoglobin**

The study showed that the highest risk was found among women who had hemoglobin <10g%. with odds ratio and 95% confidential interval of 1.75 (1.07-2.86) which was statistically significant. This finding is in accordance with the study of Kaltredir DF(62) if haemoglobin and hematocrit dropped to less than 9 gm% and 31% respectively, preterm delivery and low birth weight infants accurred. Mothers with haemoglobin less than 7 gm% tended to be at risk of preterm delivery (Relative risk = 4.2).

Haemoglobin and hematocrit levels decrease during pregnancy because the fetus will act as a parasite, depleting the mother of iron. If, however, at any point in the pregnancy the haemoglobin falls below 11 gm% or the hematocrit below 33%, the diagnosis is anemia.

**Mean weight gain**

The study showed that the lowest risk of preterm delivery was found among pregnant women of mean weight gain <0.5 kg per week. The highest risk was found among pregnant women of mean weight gain 2 or more and the odds ratio with 95% confidential interval of 3.81 (2.09-6.96) which was statistically significant.

Maternal pre-pregnancy weight and weight gain, which refers to maternal nutritional status during pregnancy, associated positively with preterm delivery. Several anatomic, physiological and biochemical changes occur during a normal pregnancy. The purpose of these changes is to create an internal environment which is conductive to the healthy development of the fetus and to prepare the mother for labor, birth, and lactation. These changes in physiology form the basic for the nutrient requirements of the pregnant woman. Fetal health is significantly influenced by the efficiency of nutrient transport by the placenta. The rapid growth of the fetus increases the need for all nutrients.The mother’s weight gain and the week of delivery were compared, a positive correlation appeared.

Berkowitz GS(72)found that the odds ratio for inadequate weight gain” adjusted for pregnancy duration was 4.28 (95% confidence interval 2.3, 8.0) .

The average weight increase is estimated to be approximately 12 kg, of which about 3.5 kg (29%) represent the weight of the fetus at term; the uterus, amniotic fluid, and placenta account for about 2 kg and the breast for 1 kg. One and one-half kg are due to fluid retention and 4 kg. due to fat deposit. For practical purposes, it has been said that during the $2^{nd}$ and $3^{rd}$ trimesters of pregnancy a woman should put on 0.4 kg/wk(68).

Hediger ML(69)found that a low weekly rate of gain (less than 0.23 kg) after 20 weeds' gestation was associated with preterm birth.

Abrams B(70)studied the relationship between maternal weight gain and preterm delivery in 2163 women between 1978-1986. Categories of rate of weight gain were define as follows :

1. Low rate of gain = less than 0.27 kg/week
2. Average rate of gain = 0.27 – 0.52 kg/week
3. High rate of gain = more than 0.52 kg/week.

It was found that 37.3% of the preterm mothers gained less than 0.27 kg/week, compared with only 24.2% of the term group ($p<0.002$) Women with a low rate of gain were more than twice as likely to experience a preterm delivery as those with a high gain (higher than 0.52 kg/week); the odds ratio was 2.54 (95% confidence interval 1.49, 4.88). The mean weekly weight gain of preterm mothers ($0.33 \pm 0.19$ kg/week) was significantly ($p = 0.002$) lower than that of full – term mothers ($0.39 \pm 0.17$ kg/week). This difference in weight gain appeared e after 20 week' gestation .

# CHAPTER VI
# CONCLUSION AND RECOMMENDATION

## Conclusion

Preterm delivery is an important maternity and child health problem in the developing countries. Preterm birth accounts for up to 75 to 80% of all neonatal morbidity and mortality ( 1) Preterm infants have many problems in short-term and long-term life. In addition, Preterm birth leads devastating effects on emotion of parents, finance of families, and responsibility of society if the children are neglected. Therefore, preterm birth is an unwanted birth outcome. The incidence of preterm birth varies throughout the world (2). In the United States, preterm birth represents 8-10% of all births (3). In Thailand, the number of preterm delivery for the overall country is not available because infant birth weight is reported without the gestationl age. However, some institutions report statistics of preterm delivery. There are, for example, King Chulalongkorn Memoial Hospital, with a rate of preterm delivery of approximately 9.4% (4). Maharaj Nakorn Chiangmai Hospital, with a rate of singleton pregnancy with preterm delivery of 12 % and Siriraj Hospital, having a rate of singleton pregnancy with preterm delivery of 6.85% (9)

The first part of this study is historical cohort study with the objective to determine the incidence of preterm delivery among mulliparous women at Ramathibodi hospital during 1 January – 30 December 2005. The second part is case – control study with the objective to determine risk factors of preterm delivery. During the study period, there were 2,542 pregnant women who came to register for the first time. For those who loss to follow up attempt to contact was done by mail or telephone. Overall, 68.6 % of women who registered, had known outcomes of pregnancy (59.9% delivery, 8.7% abortion). Descriptive statistics were percentage, mean and standard deviation. Analytical statistics including odds ratio with 95% confidence intervals, chi – square test, and logistic regression analysis were used to

determine risk and association between factors and preterm delivery. SPSS$^{+}$ PC program was used for statistical analysis.

The results of the study showed that the incidence of preterm delivery was 12.48%.Most of the occurred at gestational ages of 34-36 weeks(7.16%). About 1-2% occurred at gestational ages of less than 28 wks(2.23%), 28-30wks(1.12%) and 31-33wks(1.97%). The case control study included 190 cases of preterm delivery and 190 cases of control. The controls were selected from pregnant women who came to register on the same day just after the cases and delivered at term. From univariate analysis, the significantly associated factors were maternal height≤155 cms, civil servant, mean weight gain≥1kg/wk, hemoglobin<10g% and medical complication before and deliveries pregnancy. However from multiple logistic regression analysis only premature rupture of membrane and maternal height were factors while were significantly associated preterm delivery.

In conclusion, incidence of preterm delivery at Ramathibodi hospital is comparable to other studies. Risk factors of preterm delivery are found to be difficult to be changed or intervened. However these finding could be applied to screen pregnant women, to advise them and prepare services to prevent and care of preterm delivery.

**Recommendation For Application**

1. The result of this study showed that that risk factors were preterm premature rupture of membrane and guideline for management is vaginal and cervical swab.

2. The result of this study showed that risk factors were maternal height would be used to screening, advice high risk pregnant women and every intervention to prevention complication of preterm delivery.

3. The result of this study should be encouraging growth in adolescent.

**Recommendation For Further Research**

1. Prospective study incidence and risk factor of preterm delivery.

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# APPENDIX

# แบบบันทึกข้อมูล

การศึกษาปัจจัยที่มีผลต่อการคลอดก่อนกำหนดในมารดาตั้งครรภ์ที่คลอดในโรงพยาบาลรามาธิบดี พ.ศ. 2548 – 2549

**ตอนที่ 1ข้อมูลทั่วไป**

1. ชื่อ-นามสกุล .....
2. อายุมารดา ..... ปี
3. HN แม่ ..... ลูก .....
4. LMP …….. EDC……คลอดวันที่ ..... เดือน.....พ.ศ.....
   อายุครรภ์เมื่อคลอด.....สัปดาห์
5. อาชีพมารดา
   1. แม่บ้าน
   2. รับจ้าง
   3. ค้าขาย
   4. รับราชการ รัฐวิสาหกิจ
   5. เกษตรกรรม
   6. อื่น ๆ ระบุ.....
   9. ไม่ได้บันทึกข้อมูลไว้
6. การศึกษา
   1. ไม่ได้รับการศึกษา
   2. ประถมศึกษา
   3. มัธยมศึกษา
   5. อนุปริญญา, ปวส. , ปวช.
   6. ปริญญาตรีขึ้นไป
   9. ไม่ได้บันทึกข้อมูลไว้
7. ส่วนสูง ..... ซม.

**ตอนที่ 2 ประวัติการคลอดในอดีต**

8. ลำดับที่การตั้งครรภ์ (G) .....
9. ลำดับที่การคลอด(P) …….....
10. บุตรคนสุดท้ายอายุ .....ปี หรือหลังแท้ง .....ปี
11. จำนวนการแท้งบุตร ..... ครั้ง
12. จำนวนการคลอดก่อนกำหนดหรือคลอดบุตรน้ำหนัก < 2500 กรัม ..... ครั้ง
13. จำนวนการสูญเสียทารกเมื่อคลอด(ทารกปริกำเนิด) ..... ครั้ง

**ตอนที่ 3 ประวัติการคลอดครรภ์ปัจจุบัน**

14. น้ำหนักในการฝากครรภ์ครั้งแรก .....กก. อายุครรภ์ ..... เดือน
15. น้ำหนักก่อนคลอด .....กก. อายุครรภ์ ..... เดือน
16. น้ำหนักเพิ่มระหว่างการตั้งครรภ์เฉลี่ย .....กก. / เดือน
17. ระดับฮีโมโกลบินเมื่อมาฝากครรภ์ครั้งแรก .....gm %
18. ระดับฮีโมโกลบินครั้งที่สอง .....gm % 9 ไม่ได้เจาะจง
19. ระดับฮีโมโกลบินเฉลี่ย .....gm %

**ตอนที่ 4 ภาวะแทรกซ้อนระหว่างการตั้งครรภ์**

20. ความดันโลหิตสูงกว่า 140 / 90 mmHg

    1.มี 2. ไม่มี 9 ไม่ได้บันทึกข้อมูลไว้

21. ถุงน้ำคร่ำแตกก่อนกำหนด (PROM)

    1.มี 2.ไม่มี 9 ไม่ได้บันทึกข้อมูลไว้

22. มีเลือดออกระหว่างตั้งครรภ์

    1.มี 2.ไม่มี 9 ไม่ได้บันทึกข้อมูลไว้

23. ประเภทการตั้งครรภ์

    1.ครรภ์แฝด 2.ครรภ์เดี่ยว 9.ไม่ได้บันทึกข้อมูลไว้

24. การเจ็บป่วยของมารดาขณะตั้งครรภ์

| | ไม่มี | มี | ไม่ได้บันทึกไว้ |
|---|---|---|---|
| 24.1. หัดเยอรมัน | 0 | 1 | 9 |
| 24.2.เบาหวาน | 0 | 1 | 9 |
| 24.3.ความดันโลหิตสูง | 0 | 1 | 9 |
| 24.4.โรคหัวใจ | 0 | 1 | 9 |
| 24.5.โรคไต | 0 | 1 | 9 |
| 24.6โรคปอด | 0 | 1 | 9 |
| 24.7.โรคตับ | 0 | 1 | 9 |
| 24.8.อื่นๆ | 0 | 1 | 9 |

25. ทารกน้ำหนัก .....Gums

**คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล**
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# เอกสารรับรองโดยคณะกรรมการจริยธรรมการวิจัยในคน
# คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี
# มหาวิทยาลัยมหิดล

**เลขที่ ๒๕๔๕/๔๓๘**

| | |
|---|---|
| **ชื่อโครงการ** | อุบัติการณ์และปัจจัยเสี่ยงของการคลอดก่อนกำหนดที่โรงพยาบาลรามาธิบดี |
| **เลขที่โครงการ/รหัส** | ID ๑๒-๔๕-๑๗ ย |
| **ชื่อหัวหน้าโครงการ** | ผู้ช่วยศาสตราจารย์นายแพทย์สัญญา ภัทราชัย |
| **ที่ทำงาน** | ภาควิชาสูติศาสตร์-นรีเวชวิทยา<br>คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี<br>มหาวิทยาลัยมหิดล |

***ขอรับรองว่าโครงการดังกล่าวข้างต้นได้ผ่านการพิจารณาเห็นชอบโดยสอดคล้องกับแนวปฏิญญา เฮลซิงกิ จากคณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี***

**ลงนาม** _____

**กรรมการและเลขานุการจริยธรรมการวิจัยในคน** (รองศาสตราจารย์ แพทย์หญิงดวงฤดี วัฒนศิริชัยกุล)

**ลงนาม** _____

**ประธานกรรมการจริยธรรมการวิจัยในคน** (ศาสตราจารย์ นายแพทย์บุญส่ง องค์พิพัฒนกุล)

**วันที่รับรอง** ๑๕ ธันวาคม ๒๕๔๕

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# Documentary Proof of Ethical Clearance Committee on Human Rights Related to Researches Involving Human Subjects Faculty of Medicine, Ramathibodi Hospital, Mahidol University

**MURA2006/438**

| | |
|---|---|
| **Title of Project** | Incidence and Risk Factors of Preterm Delivery at Ramathibodi Hospital : 2005-2006 |
| **Protocol Number** | ID 12-49-17 |
| **Principal Investigator** | Asst. Prof. Sanya Patrachat, M.D. |
| **Official Address** | Department of Obstetrics and Gynecology<br>Faculty of Medicine, Ramathibodi Hospital<br>Mahidol University |

***The aforementioned project has been reviewed and approved by Committee on Human Rights Related to Researches Involving Human Subjects, based on the Declaration of Helsinki.***

| | |
|---|---|
| **Signature of Secretary Committee on Human Rights Related to Researches Involving Human Subjects** | .....<br>Assoc. Prof. Duangrurdee Wattanasirichaigoon, M.D. |
| **Signature of Chairman Committee on Human Rights Related to Researches Involving Human Subjects** | .....<br>Prof. Boonsong Ongphiphadhanakul, M.D. |
| **Date of Approval** | December 15, 2006 |

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ที่ จวค ๑๗๒๕/๒๕๔๕ คณะกรรมการจริยธรรมการวิจัยในคน

วันที่ ๒๖ ธันวาคม ๒๕๔๕

เรื่อง แจ้งผลการพิจารณาของคณะกรรมการจริยธรรมการวิจัยในคน

เรียน ผู้ช่วยศาสตราจารย์นายแพทย์สัญญา ภัทราชัย

อ้างถึงโครงการวิจัยเรื่อง อุบัติการณ์และปัจจัยเสี่ยงของการคลอดก่อนกำหนดที่โรงพยาบาลรามาธิบดี

หมายเลขโครงการวิจัย ID ๑๒-๔๕-๑๗ ข

ในนามของคณะกรรมการจริยธรรมการวิจัยในคน ผมขอแสดงความยินดีที่โครงการวิจัยดังกล่าวข้างต้นของท่านได้ผ่านความเห็นชอบจากคณะกรรมการฯแล้ว

เพื่อให้สอดคล้องกับระเบียบปฏิบัติคณะแพทยศาสตร์โรงพยาบาลรามาธิบดี ว่าด้วยการศึกษาวิจัยและการทดลองในมนุษย์ พ.ศ. ๒๕๔๔ คณะกรรมการฯ ขอให้ท่านถือปฏิบัติโดยเป็นไปตามข้อแนะนำดังต่อไปนี้

๑. การดำเนินการวิจัยจะต้องเป็นไปตามโครงร่างวิจัยล่าสุดที่ผ่านการพิจารณาจากคณะกรรมการจริยธรรมการวิจัยในคนแล้ว
๒. การดำเนินการวิจัยจะต้องไม่เบี่ยงเบนไปจากโครงร่างวิจัยหรือมีการเปลี่ยนโครงร่างการวิจัยก่อนที่การแก้ไขเพิ่มเติมโครงร่างวิจัยนั้นจะได้รับการอนุมัติและเห็นชอบจากคณะกรรมการจริยธรรมการวิจัยในคนก่อน ยกเว้นในกรณีจำเป็นที่จะต้องกระทำไปก่อนเพื่อขจัดอันตรายเฉพาะหน้าที่เกิดขึ้นกับผู้ยินยอมตนให้ทำวิจัย
๓. ในกรณีที่มีการเปลี่ยนแปลงชื่อโครงการจากชื่อเดิมที่เสนอไว้ ต่อคณะกรรมการฯ ต้องแจ้งชื่อมายังคณะกรรมการฯ เพื่อออกหนังสือรับรองให้เสมอ
๔. ผู้ยินยอมตนให้ทำวิจัยจะต้องได้รับเอกสารชี้แจงข้อมูล/คำแนะนำแก่ผู้ยินยอมตนให้ทำวิจัย (Patient/Participant Information Sheet) และลงนามในหนังสือยินยอมโดยได้รับการบอกกล่าวและเต็มใจ (Informed Consent Form) ก่อนเริ่มดำเนินการวิจัย
๕. ในเอกสารชี้แจงข้อมูล/คำแนะนำแก่ผู้ยินยอมตนให้ทำวิจัย (Patient's Information Sheet) จะต้องพิมพ์ข้อความดังต่อไปนี้ไว้ด้วยทุกครั้ง

" ถ้าท่านมีข้อข้องใจหรือมีความกังวลใจเกี่ยวกับวิธีดำเนินการวิจัยของโครงการวิจัยนี้ ท่านสามารถติดต่อได้ที่ ประธานกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์โรงพยาบาลรามาธิบดีหน่วยจริยธรรมการวิจัยในคนชั้น ๓ สำนักงานวิจัยคณะฯ อาคารวิจัยและสวัสดิการ โทรศัพท์ ๐๒-๒๐๑ ๑๕๔๔ ในเวลาราชการ "

๖. ความลับของผู้ยินยอมตนให้ทำวิจัย จะต้องถูกปกปิดไว้ตลอดเวลา ยกเว้นถ้าเป็นคำสั่งตามกฎหมาย

สุดท้ายนี้ ขอให้โครงการวิจัยของท่านประสบผลสำเร็จตามความมุ่งหมายอันจะนำมาซึ่งความเจริญก้าวหน้าทางวิชาการ และเพื่อประโยชน์ของมนุษยชาติสืบต่อไป

ขอแสดงความนับถือ

(ศาสตราจารย์บุญส่ง องค์พิพัฒนกุล)
ประธานกรรมการจริยธรรมการวิจัยในคน

# BIOGRAPHY

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