POSTTERM PREGNANCY CAUSES AND RISK

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1.1 Background

Maternal and infant health may be acted as a benchmark that can be used to assess population growth in a country. Therefore, an accurate measurement is used to determine it. In general, the maternal mortality rate and infant mortality rate are the best and easiest method to determine the country’s ability to assess an organize health services, especially in the obstetric fields. According to the Survei Demografi dan Kesehatan Indonesia (SKDI) 2012, the maternal mortality rate / AKI (associated with pregnancy, labor, and postpartum pregnancy) is 359 per 100,000 live birth, while infant mortality rate / AKA is 32 per 100,000 live birth.¹

Pregnancy may lead to a death with many factor and one of the cause is long gestation period. So, it’s very important to monitor the normal period pregnancy which is 40 weeks in average or may be vary from 37-42 weeks.² This is also use to detect her baby’s condition such as baby’s position before birth and any abnormality. Sometimes, the pregnancy will occur more than 42 weeks which is called postterm pregnancy.

Postterm pregnancy or prolonged pregnancy is defined as pregnancy that has extended to or beyond 42 weeks of gestation (294 days), or estimated date of delivery (EDD) + 14 days.² This anomaly is associated with an increased risk of fetal and neonatal mortality and morbidity, as well as an increased maternal morbidity.²³ Postterm pregnancy along with antepartum stillbirth (gestation period less than 37 weeks) is a major public health that contribute to perinatal mortality than either deaths from complications of prematurity or the sudden death infant death syndrome.² This case is preventable by doing induction of labor (IOL) at term, however both clinicians and patients are concerned about the risk including uterine hyper-stimulation, failed induction, and an increase rate of Caesarean section. Postterm pregnancy is also highly associated with an increased costs related to antenatal fetal monitoring and can be a source of significant anxiety for the pregnant woman.²
The incidence of postterm pregnancy is about 7% of all pregnancies in general, while in Indonesia is about 22%. The prevalence itself may varies depending on population characteristics (such as the prevalence of obesity) and local management practice. One of the predisposition factor for postterm pregnancy is the mother itself. Because only a small number of mother who really know the exact date of her first menstrual period. This is also lead to an incomplete data to diagnose patient with postterm pregnancy.

The symptoms beside the prolonged date of giving birth is the baby’s condition. If the mother didn’t know the exact date of her menstrual period, the baby’s appearance may be the key to diagnose postterm pregnancy. Some of the symptoms are creases on the baby’s palm and soles of their feet, a lot of hair, and discoloration of the skin.

The writers are interested in this subject because, as shown above about the incidence in Indonesia about the case for postterm pregnancy is quite high and many cases aren’t reported (so, it might be higher than the data shows above). Therefore, the writers want to present an information that can be used to a better assessment of postterm pregnancy, from how to diagnose to treat the patient with this case.


CHAPTER II
CONTENT

2.1 Etiology

Etiology of postterm pregnancy is usually unknown. Several risk factors have strong relation include primiparity, previous postterm pregnancy, male fetus, obesity, hormonal factors and genetic predisposition. There is no clear explanation about how obesity affects pregnancy and timing of delivery. But from several studies found that obese women have a high incidence of postterm pregnancy. It may cause by adipose tissue is hormonally active and the hormonal changes are altered the labour of obese women.²

Genetic factors may be also involved in postterm pregnancy. Women who born from postterm pregnancy are at higher risk of it. Also twin studies also support a genetic predisposition. Rates of prolonged pregnancy are increased in women whose twin sister has had a previous postterm pregnancy. This association is greater in monozygotic than in dizygotic twins.²

Hormonal factors also effect the incidence of postterm pregnancy include progesterone and corticotrophin releasing hormone (CRH). When labour there is alteration of progesterone hormone which leads to smooth muscle contraction to initiate labour.⁶ In the presence of lower CRH secretion, the cascade of events that induces labour and signals the end of pregnancy is not activated, and therefore pregnancy will continue.⁷

2.2 Pathogenesis

The pathogenesis of postterm pregnancy is not clearly understood. Some risk factors above such as primiparity, previous postterm pregnancy, male fetus, hormonal factors, and genetic predisposition were identified with some possible explanation, however, the pathogenesis of this condition is not yet clear.² To know the postterm pregnancy pathogenesis, it is essential to shed some lights on the pathophysiology of parturition and try to understand why these mechanism fail to be triggered in postterm pregnancies. The mechanisms of parturition include interactions between hormonal, mechanical, and inflammatory processes,
in which placenta, mother, and fetus each play a vital role. Synthesis of CRH by the placenta has been related to the length of gestation.\(^8\) The CRH increases exponentially as pregnancy advances and peaks at the time of labor. In women who deliver postterm, the exponential rise is slower than those delivering at term.\(^7\) This data suggests that postterm delivery is due to a change in the biological mechanism regulating the length of gestation. It is also possible that inherited predisposition due to polymorphism in the genes on the physiological pathway linking CRH to birth has a role in postterm pregnancy.\(^2\) The maternal phenotype may change the response of maternal tissues to the usual hormonal signals to birth as may occur in the obese woman.

Research conducted by Smith and colleagues (2009) revealed that CRH can directly stimulate fetal adrenal production of dehydroepiandrosterone sulfate (DHEAs), the precursor for placental oestriol synthesis.\(^9\) The rising oestriol driven by CRH increases the end of gestation more rapidly. Concurrently the rise in maternal progesterone concentration during pregnancy slows at the end of pregnancy or even falls. This may be due to CRH inhibit the placental progesterone synthesis.\(^10\) Therefore, physiologically, the pro-pregnancy effect of progesterone (promoting relaxation) will decline and the pro-labor effect of oestriol (promoting contraction) will increase at the end of pregnancy. But in postterm pregnancy, the rise of CRH concentration is slower and these condition causes duration of pregnancy longer than it is should be.\(^7\)

### 2.3 Diagnosis

As we know, postterm pregnancy is associated with an increased risk of fetal and neonatal mortality and morbidity, as well as an increased in maternal morbidity\(^2\), that it needs to be prevented as possible as it could. If this condition is occurring already, then the doctor should directly diagnose postterm pregnancy after doing some examinations to make sure the diagnosis.

There are several steps to diagnose pregnant women with postterm pregnancy, including:
2.3.1 Anamnesis

a. Sacred Seven

- Symptom and Chronology
  Usually postterm pregnancy women come to the doctor complaining about prolonging pregnancy time (more than 9 months or more than 42 weeks old pregnancy) and/or decreasing or weakening baby’s movement.

- Onset
  The onset of prolonging pregnancy time varies started from 43 weeks or more, by determining pregnancy dating the doctor can conclude whether the pregnancy is preterm, full term, late term, or postterm. Last menstrual period has traditionally been used to calculate the expected date of delivery (EDD) which steps are LMP date + 7, month – 3, year + 1 (for a routine 28 days of menstrual cycle), but many inaccuracies exist because of menstrual cycle irregularity, recent use of hormonal contraception, or because of bleeding in early pregnancy.²

- Location
  Mostly there are no symptom occurring in any specific location because the patient basically only complaining about late delivery date.

- Quality
  Sometimes if the mother ever experienced gravidae, she will acknowledge that the baby’s movement is weakening.

- Quantity
  Due to an increase of baby size and also a decrease of baby’s space of movement and insufficiency of oxygen for the baby’s age inside the amniotic sac, the baby tends to be inactive so that the quantity of baby’s movement will be decrease.

- Predisposing or triggering factors

- Other Symptoms
Rarely the mother complains about decreasing body weight or waist circumference although the baby is getting bigger inside the mother’s uterus.

b. Basic Four
   - Family History
     It is important to know the delivery history of the parents, grandparents, siblings, and others family members that related to the baby (whether the delivery is normal or instrumental, premature, etc.)
   - Environmental and Social History
     Environmental factors can affect both of the baby’s and mother’s nutritional support and other physiological supports that are important to both.
   - Previous and Current Medical History
     It is need to be known whether the mother is having any condition that could be a complicating factor for the delivery.
   - Medication History
     It is need to be known whether the mother is using any medication that related to the current condition and whether the mother is having any allergic to a certain medication so that the doctor should avoid to use the medication.

2.3.2 History of Antenatal Examination
   a. Pregnancy test
     If the patient done the immunological test after 2 weeks delaying of menstruation, it is assumed that the gestational age is entering the 6th weeks.
   b. Baby’s Movement
     Baby’s movement or quickening mostly felt by the age of 18-20th weeks of pregnancy (week 18th in primigravidae and week 16th in multigravidae). To know the delivery time, we can use the formula quickening + 22 weeks in primigravidae and quickening + 24 weeks in multigravidae.
c. Fetal Heart Beat

Fetal heart beat can be heard by using Laennec stethoscope started from the 18-20th weeks of pregnancy and also can be heard by using Doppler at the age of 10-12th weeks of pregnancy.

The pregnancy can be assumed as postterm pregnancy if we found 3 or more of the following criteria:

- More than 36 weeks after a positively proven pregnancy test
- More than 32 weeks after the fetal heart beat can be heard by using Doppler
- More than 24 weeks after the first quickening
- More than 22 weeks after the fetal heart beat can be heard by using Laennec stethoscope

2.3.3 Measuring The Height of Fundus Uteri

After the age of 20th weeks of pregnancy, the height of fundus uteri can be used to determine the certain pregnancy dating.

2.3.4 Ultrasonography

Routine ultrasound examination for pregnancy dating demonstrated a reduction in the rate of false positive diagnosis and thereby the overall rate of postterm pregnancy from 10-15% to approximately 2-5%. A Cochrane systematic review in 2000 found a similar reduction in the overall rates of induction of labour for postterm pregnancy among women who underwent sonographic gestational age assessment before 24 weeks of gestation. When using ultrasound for dating it is necessary to understand the margin of error reported at various times during gestation. The variation by ultrasonography generally is ± 7 days up to 20 weeks of gestation, ± 14 days between 20 and 30 weeks of gestation, and ± 21 days beyond 30 weeks of gestation. A calculated gestational age by ultrasound must be therefore considered as an estimate and must take into account the range of possibilities. If the estimated gestational age by a patient’s last menstrual period differs from the ultrasound estimate by more than these accepted variations, the ultrasound estimate of gestational age should be used instead of the patient’s menstrual cycle estimate.
2.3.5 Laboratory Test

a. Amniotic Fluid Tromboplastin Activity (ATCA)
   ATCA will increase following an increase of the gestational age. If the ATCA given is between 42-46 second, it can be assumed that the pregnancy is a postterm one.

b. Amniotic Fluid Sitology
   With the nile blue sulphate staining, we can see the adipocyte cell in the amniotic fluid which can determine the gestational age. If the amniotic fluid contains 50% or more adipocyte cells, so that the gestational age is 39 weeks or more.

c. Lesitin/spingomielin Level
   If the ratio of lesitin and spingomielin level in amniotic fluid is equal, the gestational age is assumed to be 22-28th weeks, if the gestational age is an even number then the ratio will be 2:1. Although this method cannot decide whether the patient is having a postterm pregnancy or not, but it remains useful for determining whether the baby is full term to be deliver or not.5

2.4 Prevention and Treatment

Although some form of intervention is considered to be indicated for prolonged pregnancies, the types and timing of interventions are not unanimous. The decision centers on whether labor induction is warranted or if expectant management with fetal surveillance is best. In a survey, reported that 73 percent of members of the American College of Obstetricians and Gynecologists routinely induced women at 41 weeks. Most of the remainder performed twice weekly fetal testing until 42 weeks.11

2.4.1 Pregnancy Dating

Accurate pregnancy dating is crucial to the diagnosis and management of postterm pregnancy. Last menstrual period has traditionally been used to calculate the expected date of delivery (EDD). But many inaccuracies could exist because of cycle irregularity, recent use of hormonal contraception or because of bleeding early in pregnancy. Routine ultrasound examination for pregnancy dating
demonstrated a reduction in the rate of false positive diagnosis and thereby the overall rate of postterm pregnancy from 10-15% to approximately 2-5%, and thereby minimized unnecessary intervention.¹

A calculated gestational age by ultrasound must be therefore considered as an estimate and must take into account the range of possibilities. If the estimated gestational age by a patient’s last menstrual period differs from the ultrasound estimate by more than these accepted variations, the ultrasound estimate of gestational age should be used instead of the patient’s menstrual cycle estimate.¹

2.4.2 Antepartum Fetal Surveillance

There are no randomized controlled trials (RCTs) that demonstrate that antepartum fetal surveillance decreases perinatal morbidity or perinatal mortality in late-term and postterm pregnancies. Most retrospective studies of antepartum fetal surveillance in pregnancies that extended beyond the estimated date of delivery initiated testing between 41 weeks and 42 weeks of gestation.¹²

Although antepartum fetal surveillance may be indicated for pregnancies at or beyond 41 0/7 weeks of gestation, there are insufficient data to define the optimal type or frequency of testing.¹ There are several options for fetal surveillance, (1) counting fetal movements during a 2-hour period each day, (2) nonstress testing three times weekly, and (3) amniotic fluid volume assessment two to three times weekly with pockets < 3 cm considered abnormal.¹¹

Ultrasound assessment of amniotic fluid volume appears to be important. Delivery should be considered if there is evidence of fetal compromise or oligohydramnios. Umbilical artery Doppler velocimetry has no proven benefit in monitoring the postterm fetus and is not recommended for this indication.¹ It also seems that testing, using nonstress testing (CTG) and AF volume assessment, constitutes an acceptable standard by many clinicians.¹

2.4.3 Induction of Labor (IOL)

The most decisive way to prevent postterm pregnancy is induction of labor prior to 42 weeks’ gestation. However, since complications increase during 40 and 41 weeks' gestation and both clinicians and patients are concerned about the risks of induction of labor, it is perceivably better for women to go into spontaneous labor at 39 weeks of gestation on their own
Induction of labour is indicated when the benefits of delivery outweigh the risks associated with induction. The main concern around induction of labour in postterm low risk pregnancies is related to uterine overstimulation, fetal distress, failure of induction and increase in caesarean section rates. There are also risks associated with induction in particular groups of patients with specific risk factors such as risk of uterine rupture in women with previous caesarean section. Induction of labour is more likely to succeed when the cervix is favourable. Several techniques have been evaluated to assess cervical favourability and to predict the likelihood of success in women undergoing labour induction. These include digital cervical examination (Bishop score), ultrasound assessment of cervical length and more recently biochemical markers (oestriol/oestradiol ratio).²

A favourable cervix is defined as a cervix with Bishop score of ≥ 6 and where determination unfavorable cervix by a Bishop score < 6.¹¹ Digital cervical assessment has been shown to be superior to transvaginal ultrasound assessment of cervical length at term to predict the time interval from IOL to deliver. However, digital cervical assessment remains subjective and could lack reproducibility.¹

Oestrogens have been demonstrated to be important hormones involved in the regulation of several functions during pregnancy. Oestriol (E3), oestradiol (E2), and the oestriol/oestradiol ratio in particular play an important role in the control of parturition by creating a specific oestrogenic environment at the onset of labour. Oestrogens were therefore, studied on the basis that they may contribute to a better assessment of women with postterm pregnancy that are at risk of unsuccessful induction, such as women with an unfavourable cervix.¹ It was found that maternal serum E3/E2 ratio is significantly higher in women responding to IOL.¹

A. Unfavorable Cervix

As many as 80% of women who reach 42 weeks gestation have an unfavourable cervix (Bishop Score < 6).¹¹ Using cervical ripening prior to induction in these cases appears to have some advantage in terms of outcome regardless of parity or method of induction. Pre-induction cervical ripening has resulted in fewer failed inductions, reduced fetal and maternal morbidity, reduced
medical cost, and possibly a reduced rate of caesarean delivery in the general obstetric population.\(^1\) A number of investigators have evaluated prostaglandin E2 (PGE2) for induction in women with an unfavorable cervix and prolonged pregnancies. Previously study concluded that PGE2 gel could be used safely in postterm pregnancies. In another study, mifepristone was reported to increase uterine activity without uterotonic agents in women beyond 41 weeks.\(^{11}\)

B. Postterm Women with Previous Caesarean Section

A successful vaginal birth after cesarean delivery is associated with decreased maternal and neonatal morbidity. A trial of labor after cesarean delivery (TOLAC) is a reasonable option in the management of uncomplicated postterm pregnancies. A large observational study showed no increase in the risk of uterine rupture associated with TOLAC attempted at or beyond the estimated date of delivery. For women who desire TOLAC and who have not had a prior vaginal delivery, awaiting spontaneous labor, as opposed to undergoing labor induction, most likely avoids further additional increased risk of uterine rupture. Thus, TOLAC remains an option for women with postterm pregnancies who have not had a prior vaginal delivery, but these women should be counseled regarding their individual risks such as failure of TOLAC and of uterine rupture.\(^{12}\)

2.5 Complication

There are several complications that may be induced through postterm pregnancy, some of which include fetal, neonatal and maternal complications which have always been underestimated. These complications consist of fetal and neonatal mortality rates, along with fetal morbidity which includes passage of meconium, meconium aspiration syndrome, macrosomia and dysmaturity.\(^2\)

According to previous studies, perinatal mortality rate is twice as high at 42 weeks of gestation and it can even reach a 4-fold increase at 43 weeks or a 5-7-fold increase at 44 weeks. This means that postterm pregnancy, which is stated to be the condition in which a pregnancy reaches 42 weeks (294 days)\(^{13}\), may be associated with this complication. As for the etiology of this condition, utero-
placental insufficiency, meconium aspiration and intrauterine infection are believed to be the underlying causes.  

Meconium aspiration syndrome, one of the most common manifestations of fetal morbidity in postterm pregnancy, refers to some respiratory compromise such as tachypnea, cyanosis, and reduced pulmonary compliance occurring in newborn infants due to the exposure of meconium (the first feces of a newborn infant) in the uterus. A study states that the incidence of this syndrome has shown a significant reduction between 1990 and 1998 due to a reduction in postterm pregnancy rates, not because of conventional interventions. This proves that postterm pregnancy plays a big role in causing meconium aspiration syndrome.

Fetal macrosomia, or an estimated fetal weight of $\geq 4.5$ kg, is also believed to be associated with postterm pregnancy, because postterm infants are usually larger than those born on term. This may cause prolonged labour, cephalo-pelvic disproportion and shoulder dystocia – a condition where the anterior shoulder of the infant cannot pass below the pubic symphisis of the mother during delivery. This will then lead to a risk of orthopaedic injury as well as neurological injury.

Dysmaturity syndrome, which is defined to be infants who have characteristics similar to chronic intrauterine growth restriction from utero-placental insufficiency, is also a fetal morbidity that can be a complication of postterm pregnancy. The infant usually has thin wrinkled peeling skin, a thin body, long hair and nails, oligohydramnios (amniotic fluid deficiency), and frequent passage of meconium. Though this may cause a risk of complications such as hypoglycemia, seizures, and respiratory insufficiency, there is still no clear data on its affect to an infant’s neurologic sequelae that may cause a shift in the child’s intelligence.

All of these complications aside, postterm pregnancy does not represent a threshold below which risks are uniformly distributed. This is due to the fact that many complications that have been mentioned above can still even happen after 38 weeks of gestation. Some of the fetal risks such as presence of meconium, increased risk of neonatal acidemia, and even stillbirth have been described as being greater at 41 weeks of gestation and even at 40 weeks of gestation as compared with 39 weeks’ gestation. In addition to stillbirth being increased prior
to 42 weeks of gestation, one study found that the risk of neonatal mortality also increases beyond 41 weeks of gestation. Thus, 42 weeks does not represent a threshold below which risk is uniformly distributed. Indeed, neonatal morbidity (including meconium aspiration syndrome, birth injury, and neonatal acidemia) appears to be the lowest at around 38 weeks and increase in a continuous fashion thereafter.\textsuperscript{15}

### 2.6 Prognosis

Postterm born children are more than twice as likely as term born children to have clinical ADHD. Postterm birth increased the risk of neonatal encephalopathy and death during the first year of life, but the long-term effect are not clear yet. A recent study found that 13\% of children born postterm had a neurological or developmental disorder at the age of 5 years. This can be explained by some possibility: First, prolonged labour, cephalopelvic disproportion and shoulder dystocia are increased in postterm children. A perinatal lack of oxygen has been associated with behavioural problems. Second, a non-optimal postterm placenta offers fewer nutrients and less oxygen than a full term fetus requires. The lack of nutrients and oxygen may predispose to abnormal fetal development and this may lead to abnormal emotional and behavioural development.

Disturbance of ‘placental clock’, which controls the length of pregnancy, is involved. A marker of this clock is the placental secretion of corticotrophin-releasing hormone (CRH), which is lower in women who deliver postterm than in women delivering at term. CRH is the principal regulator of the maternal and fetal hypothalamic–pituitary–adrenal (HPA) axis. It has been suggested that placental endocrine malfunctioning or maternal stress at critical times during fetal development may influence the fetal HPA axis, leading to neuroendocrine abnormalities that could increase the child’s vulnerability to emotional and behavioural problems later in life. Last, the cause for postterm could also be the cause for having behavioural problems, for example neurodevelopmental factors related to behavioural problems could be involved in the complex process of birth.\textsuperscript{16}
Maternal risks for mother with postterm pregnancy are also greater than mother with term pregnancy\textsuperscript{17}. The complications varied with gestational age. There are increasing risk of labor dystocia (9-12\% vs 2-7\%), severe perineal injury (3\textsuperscript{rd} and 4\textsuperscript{th} degree perineal lacerations) related to macrosomia (3.3\% vs 2.6\%), and twice the risk of cesarean delivery (14\% vs 7\%)\textsuperscript{2}. Other maternal morbidity such as chorioamnionitis and endomyometritis all increase progressively after 39-40 weeks of gestation, while postpartum hemorrhage increased at 41 weeks of gestation\textsuperscript{16,18}. 
CHAPTER III
CONCLUSION

3.1 Conclusion

Postterm pregnancy is defined as pregnancy that has extended to or beyond
42 weeks of gestation (294 days), or estimated date of delivery (EDD) + 14 days.
The Etiopathogenesis of postterm pregnancy is usually unknown. Several risk
factors have strong relation include primiparity, previous postterm pregnancy,
male fetus, obesity, hormonal factors and genetic predisposition. There are several
steps to diagnose pregnant women with postterm pregnancy, including anamnesis
using sacred seven and basic four, history of antenatal examination, measuring the
height of fundus uteri, using ultrasonography, and some laboratory examination
will help to diagnose postterm pregnancy. Before we do the intervention, there are
some thing that must be considered that is crucial to the diagnosis and
management of postterm pregnancy such as pregnancy date, and antenatal fetal
surveillance. The most decisive way to prevent postterm pregnancy is induction of
labor prior to 42 weeks’ gestation. Induction of labour is indicated when the
benefits of delivery outweighs the risks associated with induction. The main
concern around induction of labour in postterm low risk pregnancies is related to
uterine overstimulation, cervix condition, fetal distress, failure of induction and
increase in caesarean section rates. There are several complications that may be
induced through postterm pregnancy, some of which include fetal, neonatal and
maternal complications. All of these complications aside, postterm pregnancy
does not represent a threshold below which risks are uniformly distributed. Risks
for mother and postterm born children with postterm pregnancy are also greater
than the one with term pregnancy.
REFERENCE


