Absolute and Relative Risks of Previous Pregnancy Loss and Subsequent Preterm Birth

Thesis

Submitted for Partial Fulfillment of Master Degree in Obstetrics and Gynaecology

By

Khaled Ali El-Metwaly

M.B.B.Ch Resident of Obstetrics and Gynaecology

Dammiata Public Hospital

Mansoura University

1999

Supervised by

Dr./ Sherif Mohammed El-Ghetany

Professor of Obstetrics and Gynaecology

Faculty of Medicine – Ain Shams University

Dr./ Khaled Saiid Moussa

Assistant Professor of Obstetrics and Gynaecology

Faculty of Medicine – Ain Shams University

Dr./ Noha Hamed Rabei

Lecturer of Obstetrics and Gynaecology

Faculty of Medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

2008

المخاطر المطلقة والنسبية لفقدان حمل سابق وحدوث ولادة مبكرة تالية

رسالـــــــة

توطئة للحصول على درجة الماجستير فى أمراض النساء والولادة

مقدمة من

طبيب/ خالد على المتولى

بكالوريوس الطب والجراحة

طبيب مقيم النساء والولادة بمستشفى دمياط العام

تحت إشراف

أ.د/ شريف محمد الغيطانى

أستاذ أمراض النساء والولادة

كلية الطب – جامعة عين شمس

أ.د/ خالد سعيد موسى

أستاذ مساعد أمراض النساء والولادة

كلية الطب – جامعة عين شمس

د/ نهى حامد ربيع

مدرس أمراض النساء والولادة

كلية الطب – جامعة عين شمس

كلية الطب

جامعة عين شمس

2008

Introduction

Preterm birth is the strongest cause of neonatal morbidity and mortality; furthermore , the sequel of preterm birth, for those infants who survive, often cause life long disabilities. Long physical and mental impairment is surely one of the greatest tragedies that can beset a person ,his or her family, society, and even the economics of the world (Cunningham et al.,1993)

Preterm labor and delivery, before 37 weeks of gestation, is the major cause of prenatal morbidity and mortality in the developed countries and is the single most important complication of pregnancy in absence of congenital anomalies (Creasy,1993).

Morrison et al.,1993 reported that 50% of women who have false labor pain eventually deliver preterm . The differentiation between false and true labor is very difficult because the only absolute differentiating factor is in the true one , the contractions that lead to irreversible progressive cervical changes and delivery.

Differentiating true from false labor is very important as preterm delivery remain one of the major causes of neonatal morbidity and mortality (Morrison et al., 1996) . There is increasing evidence that preterm delivery is preceded by significant changes in the biologic activity of chorionic and decidual cells (Lockwood et al., 1993) .

Abortion is the interruption or termination of pregnancy before medico legal viability (20 weeks). There are many factors that may act at the same time, these causes may be fetal causes, abnormalities of the placenta or membranes, maternal and or paternal causes (Ventura et al., 2000).

Review of Literature

Epidemiology of Preterm Labor:

Definition:

Preterm delivery is defined as the birth of an infant at less than 37 weeks of gestations. Preterm labor is usually defined as regular uterine contractions accompanied by cervical changes occurring at less than 37 weeks of gestations.(Tucker et al., 1991)

Preterm labor is also defined as the onset of labor in patients with intact membranes before 37 weeks of gestations.(Villar et al .,1994).

The world health organization(WHO) recommended that the preterm delivery is the occurrence of 2 or more uterine contractions within 10 minutes together with cervical effacement and or dilatation before 37 weeks of gestation (Arias, 1993).Any infant was born with birth weight less than 2500 gm is defined as low birth weight (Anderson,1997),but this is modified now to describe very low birth weight (less than 1500 gm) and extremely low birth weight (less than 1000 gm).(Cunningham et al .,2001)

Incidence :

To quantify the incidence of the preterm labor is a very difficult process as most studies do not discriminate between spontaneous and induced preterm labor (Vause and Johonson ,2000).There are

approximately 13 million infants are born prematurely each year world wide (Viller et al .,1994).

The incidence of preterm labor , however, varies from 5-10 % of all birth in developed countries (Rush et al.,1987).

The incidence has not declined in spite of obstetric and neonatal advances (Bottoms, 1999).

As it correlates greatly with the socioeconomic levels of the population, it increases much in the developing countries . According to Egyptian ministry of health statistics, the incidence of prematurity in Egypt reached up to 15.8% in the year of 1985 (Agustsson and Patel ,1987).

Pathophysiology of Preterm Labor

The pathogenesis of spontaneous preterm labor is not completely clear as it may be as early activation of the normal labor process idiopathically or results from a pathologic mechanism (Goldenberg , 2002). So it is most probably represents a syndrome rather than diagnosis (Errol et al., 1999).

There are four pathways can lead to preterm labor and delivery:-

1-Inflammation.

2-Decidual hemorrhage

3-Uterine over distention

4-Premature activation of the normal physiologic initiators of labor (ACOG,1999)

1- Inflammation:-

This is the most probable pathway and it is mostly involves premature decidual activation, this activation occur in the context of an occult upper genital tract infection (Goldenberg,2002).

Infection of the decidua , fetal membranes , and amniotic fluid is associated with preterm delivery (Goldenberg et al.,2000). And there is evidence that chorioamnionitis is more common in preterm deliveries than in term deliveries (Guzick and Winn,1985)

When infection is present, the levels of the products of the lipooxygenase and cyclooxygenase pathways are increased (Romero et al.,1991). and also the levels of cytokines are elevated in the infected amniotic fluid .

If the intrauterine environment become hostile to the fetus , the fetoplacental unit will trigger preterm labor (Romero et al ., 1989)

Cytokines and eicosanoides seems to be synergistic to each other in stimulating normal parturition cascade, and this lead to preterm labor (Errol et al.,1999).

2- Decidual Hemorrhage:-

In abruption placenta , thrombin may be the physiologic mechanism of preterm labor as thrombin is a very potent ecbolic as evidenced recently by many studies. (Elovitz et al.,1999).

3- Uterine Over Distention:-

In twins pregnancy or polyhydramnios ,uterine distention initiate expression of contraction associated proteins (CAPs) in the myometrium which include these coding for gap junction proteins, oxytocin receptors and prostaglandin synthetase. (Korita et al.,2002).

Also there is early activation of the placental-fetal endocrine cascade which lead to early increase in the maternal corticotrophin releasing hormone (CRH) and estrogen which can enhance the expression of myometrial CAPs genes.(Warren et al.,1990).

4-Premature activation of the normal physiologic initiators of labor:-

Birth process is divided into four phases: phase 0,1,2 and 3 this is made in recognition of the major uterine accommodations that characterize each phase and to define the morphological and functional transitions that must be made to progress in an orderly and timely manner from one phase to the next (Casey and McDonald, 1988a).

Phase 0:-

Is the time of smooth muscle relaxation and cervical rigidity, this is maintained through the action of various putative inhibitors on the uterus as:- progesterone, prostacycline, relaxin , nitric oxide, parathyroid hormone-related peptide, corticotrophin-releasing hormone, human placental lactogen, calcitonin gene related peptide, adrenomedullin, and vaso-active intestinal peptide. This phase is normally maintained from before implantation until late in gestation, the uterus is unresponsive to the natural stimuli (Casey and McDonald,1988b).

Phase 1:-

Or phase of activation which is the interval of uterine preparation for labor, this is clinically identified by distinctive signs during the last days of pregnancy by: ripening of the cervix, increasing the frequency

of uterine contractions and the development of the lower uterine segment . (Casey and McDonald,1988a).

Activation occurs in response to utrotropins, including estrogens and is characterized by increased expression of a series of contraction associated proteins , activation of certain ion channels, and an increase in connexin 43 which is a key component of gap junctions between adjacent myometrial cells leading to electrical synchrony within the myometrium and allow effective coordination of contractions (Garfield et al.,1988).

Phase 2 :-

Is the period of active labor or stimulation phase where the uterus can be stimulated to contract by the actions of uterotonins such as oxytocin and the stimulatory prostaglandin E2 and F2 alpha.(Casey and McDonald, 1988a; Errol et al.,1999).

Phase 3 :-

During this phase , involution of the uterus after delivery occurs and is mediated primarily by oxytocin (Errol et al.,1999).

The initiation of parturition is the transition from uterine phase 0 to phase 1 of parturition. This is the time late in pregnancy when uterine quiescence is suspended, enabling the recovery of the contractile competency of the uterus, preparatory to labor (Casey and McDonald,1988c).

Mechanism of birth:-

Birth results from activation and then stimulation of the myometrium. Activation occurs either through mechanical stretch of the myometrium or by endocrine stimuli. It was found that cortisol contributes to increased prostaglandin production in the fetal tissue through increase the type 2 prostaglandin-H2 synthase-2*(PG HS-2)* and decrease the 15-OH prostaglandin dehydrogenase.(Challis etal.,2000).

Cortisol increases expression of prostaglandin dehydrogenase in the chorion by reversing the stimulatory effects of progesterone and also may represents “progesterone withdrawal”. Also cortisol increase expression of placental corticotrophin- releasing hormone.(Liggins ,1981)

Other agents as proinflammatory cytokines increase *(PG HS-2)*and decrease prostaglandin dehydrogenase.(Ito et al.,1986).

Oxytocin which is produced locally within the uterus is thought to be involved in the labor process.(Herper et al.,2003).

Etiology and Risk Factors of Preterm Labor

A wide spectrum of causes have been implicated in preterm labor so it is likely to be multifactorial and not all preterm deliveries are the results of the same causes (Carlini et al., 2002).

1-Age :-

Women younger than 20 years carry a higher risk of preterm delivery not only for the first pregnancy but also for the second or third. Women older than 35 years also carry a higher risks. (Goldenberg et al., 2003).

2-Race:-

Black women carry nearly a double risk of preterm delivery compared to white women; it is 7% in dark women compared to 3.4% in white women. (Siega et al.,2001).

3- Occupational Factors :-

Women performing heavy manual work have higher incidence of preterm delivery compared to women enjoying sedentary life. (Henriksen et al.,1995).

4- Socioeconomic Status :-

Females with less education and lower socioeconomic status have a higher risk of preterm delivery.(Goldenberg,2002).

5- Body Built:-

Females with low body weight less than 50.8 kg are three times liable for preterm labor than those weighted more than 57.3 kg . Also females with body index less than 19.8 kg/m2 are at higher risk of preterm delivery (Wen et al., 1990).

Females shorter than 62 inches are more liable to preterm labor (Muller et al.,1989).

It was found that both poor and excessive weight gain during pregnancy is associated with increased preterm birth (Wen et al., 1990).

6- Marital Status :-

The incidence is higher in single females and those with illegal pregnancy (Muller et al.,1989).

7- Smoking :-

Women who smoke have about 20- 30 % increase in preterm birth compared to non smokers (Shiono et al.,1986).

Smoking increases the secretion of the enzyme platelet activating factor and acetyl hydrolase 20 which are a proinflammatory mediators

found in the amniotic fluid of women with preterm labor and preterm rupture of membranes and these stimulate production of prostaglandin E2 in the fetal membranes and cause contraction in the myometrial tissue. (Nina et al., 1998).

8- Number of Deliveries :-

Risks of preterm deliveries are more in primigravidae women (Orr et al., 2000).

9- Coitus during Pregnancy :-

This is doughty ; as some studies suggesting that incidence of orgasm after 30 weeks of pregnancy was significantly higher in women delivering preterm (George et al., 1999).

Another study found no evidence that coitus in the late pregnancy increases the risk of preterm delivery between 29 and 36 weeks (Amy et al., 2001).

10- Psychological and Emotional Stress :-

There is direct association between psychological stress in the 30 th week of pregnancy and labor before 37 weeks of pregnancy (Hedegaard et al., 1993).

11-Previous Preterm Delivery:-

One of the most significant risk factors is occurrence of spontaneous previous preterm delivery , the risk of recurrence in those women ranges from (17- 40%) and appears to depends on the number of prior preterm deliveries (Goldenberg,2002).

12- Multiple Gestations:-

About 50% of twins and nearly all higher multiple gestations end before 37 weeks of gestations .The average length of gestation for twins is 36 weeks, for triplets is 33 weeks, and for quadruplets is 31 weeks, while in singletons the average length of gestation is 39 weeks (Cunningham et al., 2005).

13- Previous Induced Abortion :-

There is a considerable increase of the preterm delivery rate after termination of pregnancy especially if the cervix is dilated more than 12 mm ,it reaches 13% after one termination and up to 20 % after three terminations (Siega et al., 2001).

14- Threatened Abortions :-

There is a high incidence of low birth weight , low gestational age and preterm delivery as a complication of early vaginal bleeding during pregnancy (Funderburk et al., 1980).