Cytotoxin associated gene A positive strain of Helicobacter Pylori in Preterm labor

Thesis

Submitted for Partial Fulfillments of Master Degree in Obstetrics and Gynecology

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العلاقة بين العدوى بالسم الخلوى المرتبط بجين (cag-A)Aللبكتيريا الحلزونية والولادة المبكرة

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Lamiaa Said Mohammed

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List of Abbreviations

ACOG : American College of obstetricians and Gnecologists

Cag. A:Cytotoxin associated gene protein

PROM :Premature rupture of membrane

PTB : Preterm birth

SPTL :Spontanious Preterm labor

Vac. A: Vaculatingcytotoxin A

HP :Helicobacter pylori

NSAID :Non-steroidal anti-inflammatory drug

MALT : Mucosa-associated lymphoid-tissue

GERD : Gastro-esophageal reflux disease

ITP : Idiopathic thrombocytopenic purpura

PCR :Polymerase chain reaction

COPD :Chronic obstructive pulmonary disease

C-UBT :Carbon Urea Breath Test

ELISA :Enzyme-linked immunosorbent assay

CAP : Contraction associated proteins

IVF : Invitro fertilization

IL4,10 :Interleukin-4,10

ACG :American College of Gastroenterology

CRH :Corticotropin releasing hormone

MMP:Matrix metalloprteinase

GA :Gestational age

LMP :Last menstrual period

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Protocol of Thesis

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Introduction

Preterm labor is defined as the presence of uterine contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix prior to term gestation. Occurring at 20-37 weeks' gestation, preterm labor precedes almost half of preterm births and is the leading cause of neonatal mortality in the United States**(McLaren et al.,2015).**

Preterm birth is one of the major health hazards of humans, being the greatest cause after congenital anomalies of neonatal morbidity and mortality. Although there are many conditions that lead to preterm delivery. Spontaneous preterm labor in pregnancies with intact fetal membranes represents the largest cause of preterm delivery accounting for about half of preterm births **(Cunningham et al., 2005).**

In about half the cases, the cause of preterm delivery is not known. However, accumulating evidence suggests that subclinical intrauterine infection with unknown etiology may be responsible for the majority of cases **(Romeroet al., 2002).**

Approximately 12 percent of babies in the United States are born preterm; 80 percent of these are due to preterm labor that occurs on its own or after preterm premature rupture of the fetal membranes (or "broken bag of waters"). The remaining 20 percent are planned early deliveries that are done for maternal or

fetal problems that prevent the woman from being able to safely continue with her pregnancy**(Goldenberg et al.,2008).**

Not all women who have preterm labor will deliver their baby early estimates are that between 30 and 50 percent of women who develop preterm labor will go on to deliver their infant at term. If preterm labor leads to an early delivery, the premature newborn is at risk for problems related to incomplete development of its organ systems. These problems include difficulty with breathing, staying warm, feeding, as well as injury to the eyes, intestines, and nervous system**(Chang et al.,2013).**

Preterm birth is a major cause of newborn complications and death. Regular prenatal care can help to identify some, but not all, women at risk for preterm labor. Should preterm labor occur, measures can be taken to delay delivery and decrease the risk of newborn complications **(Iams et al.,2011).**

It is difficult to predict who will develop preterm labor. Certain obstetrical conditions and other factors are known to increase a woman's risk. However, most preterm births occur in women who have no known risk factors ,the strongest risk factor for preterm birth is a previous preterm birth although most women who have had a preterm birth will have a term pregnancy in the future. As an example, one study found that only 22 percent of women with a previous preterm delivery had a preterm delivery with their next pregnancy.

Other factors that may increase a woman's risk include:

- Being pregnant with twins, triplets, or more.
- A history of cervical surgery (eg, conization or cone biopsy) for abnormal Pap smears, if the amount of the cervix removed is large.
- Abnormalities of the uterus.
- Uterine bleeding, especially in the second or third trimester.
- Use of certain illicit drugs, such as cocaine.
- Cigarette smoking.
- Some infections.
- Low prepregnancy weight and low weight gain during pregnancy.
- Excessive amniotic fluid.
- Moderate to severe anemia early in the pregnancy.
- A short interval (less than 12 to 18 months) between pregnancies(deliveries).
- Abdominal surgery during pregnancy**(van Baaren et al.,2014).**

Black women appear to have double the incidence of preterm labor and delivery when compared to white women. The risk of preterm delivery is also higher in women under 18 to 20 years of age. Older maternal age alone (over 35 to 40) is not associated with an increased risk of preterm labor. However, older women are more likely to have other conditions (such as hypertension and diabetes) that can cause complications requiring

preterm delivery(**Crowther et al.,2014).**

H.pylori has been recognized to play a role in diseases of the gastrointestinal tract. It has been hypothesized that H. pylori may increase the risk of pre term labor . **(Irene Sandven et al., 2009).**

Helicobacter (H.) is a Gram-negative bacterium responsible for the large majority of cases of chronic gastritis, peptic ulcers, and mucosal-associated lymphoid tissue (MALT) lymphoma .The pathogenicity of H. pylori infection depends on the inflammatory response to chronic infection, which is thought to be determined by many factors, including the strain-specific factors, the host's immune response, and environmental factors . Cytotoxin-associated gene A (CagA) is the marker for the Cag pathogenicityisland of H. pylori which has a well-characterised virulence determinant. The Cag pathogenicity island of H. pylori possesses 32 genes that encode a type four secretion system, and is associated with higher levels of inflammatory mediators and a more severe clinical outcome, compared to a CagA- negative strain.

In Egypt, the prevalence rates of H. pylori infection and its related diseases are almost similar to those reported from other countries in the Middle East, Europe and the United States **(Notoet al.,2012).**

H.pylori is thought to spread between persons through the feco-oral or oral-oral route. Contaminated water is a possible

environmental reservoir (**Rodriguez et al.,2005).**

study conducted on 286 pregnant Japanese women analysed the possible correlation between anti- H.pylori antibodies in vaginal samples and preterm labour, but the authors concluded that H. pylori probably plays no clinically significant role in the pathogenesis of preterm birth **(Kurotsuchi et al., 2008).**