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# 한국여성에서 조산 발생위험인자로서의 자궁경부길이 및 phosphorylated insulin-like growth factor binding protein-1와 GSTM1의 유전자다형성에 관한 연구

이화여자대학교 의학전문대학원 산부인과학교실[1], 예방의학과교실[2], 소아과학교실[3], 이화글로벌센터 의학연구소[4]

이경아[1] · 김영주[1,4] · 박혜숙[2,4] · 박은애[3,4] · 하은희[2,4]

# Cervical Length, Phosphorylated Insulin-Like Growth Factor Binding Protein-1, and Genetic Polymorphism of Gstm1: Risk Factors for Preterm Delivery in Korean Low-Risk Women

Kyung A Lee, M.D., Ph.D.[1], Young-Ju Kim, M.D., Ph.D.[1,4], Hyesook Park, M.D., Ph.D.[2,4], Eun Ae Park, M.D., Ph.D.[3,4], Eun-Hee Ha, M.D., Ph.D.[2,4]

*Departments of [1]Obstetrics and Gynecology, [2]Preventive Medicine, [3]Pediatrics, Ewha Womans University School of Medicine, [4]Medical Research Institute, Ewha Global Challenge Center, Ewha Womans University, Seoul, Korea*

**Objectives:** To evaluate the efficacy of cervical length, phosphorylated insulin-like growth factor binding protein-1 (phIGFBP-1), and genetic polymorphisms of *glutathione S-transferase mu1* (GSTM1) as risk factors of preterm delivery in Korean low-risk women.

**Methods:** Cervical length was measured using transvaginal sonography at 22-28 weeks of gestation in 301 singleton pregnancies and a rapid test was performed to detect phIGFBP-1 in cervical secretions at 24-30 weeks of gestation. The *GSTM1* gene polymorphism using DNA samples from pregnant women were detected by polymerase chain reaction. We used the $\chi^2$ test, Student's t-test, and multiple logistic regression analysis for our investigations.

**Results:** Cervical length in preterm delivery was shorter than that of term delivery ($P$<0.0001). The rate of a positive phIGFBP-1 test in preterm delivery was higher than that of term delivery ($P$<0.0001). Using Receiver operating characteristics curves, optimal cut-off length for preterm delivery (before 37 weeks) was 3.05 cm. The sensitivity, specificity, positive predictive value, and negative predictive value for cervical length were 66%, 89%, 77%, and 83%, respectively. Also, the sensitivity, specificity, positive predictive value, and negative predictive value for all factors for the positive group including phIGFBP, cervical length, and *GSTM1*-null type were 75%, 100%, 100%, and 93%, respectively. The risk of preterm delivery in patients having below 3.05 cm of cervical length was higher than in controls (odds ratio [OR]=12.9; $P$<0.0001). In addition, the risk of preterm delivery in patients having a positive test for phIGFBP-1 was higher than in controls (OR=77.1; $P$<0.0001).

**Conclusion:** Cervical length, phIGFBP-1 test, and the null type of the *GSTM1* gene are useful as risk factors of preterm delivery in Korean low-risk women.

**Key words:** Cervical length, Glutathione S-transferase M1, Phosphorylated insulin-like growth factor binding protein-1, Preterm delivery, Risk factor

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주관책임자 : 김영주
E-mail : kkyj@ewha.ac.kr

Preterm birth, defined as delivery before the completion of 37 weeks of gestation, is the major cause of perinatal mortality and morbidity in the world and its incidence has increased over the past 20 years. The prevalence of preterm birth in Korea is estimated to occur in approximately 5-6% of births in Korea and this prevalence is now rapidly increasing due to increased age and twin pregnancies.[1]

Risk factors for preterm birth can be categorized into several groups that include demographic information and obstetric history, genetic factors, biophysical factors (such as contraction and cervical length), and biologic markers (such as fetal fibronectin and phosphorylated insulin-like growth factor binding protein-1).[1-4]

A short cervix is a risk factor for preterm birth, and screening for cervical length in the mid-second trimester has been evaluated in high-risk pregnancies and as a population screening.[5,6] Various studies show quite controversial conclusions about the relevance of clinical examination as a screening method because there are many false positives and false negatives.[5,6]

Recent studies have shown that the phosphorylated insulin-like growth factor-binding protein-1 (phIGFBP-1), a protein secreted by decidual cells, which leaks into cervical secretions when fetal membranes detach from the deciduas before the onset of labor and phIGFBP-1 measurement, is very useful in the prediction of preterm delivery in asymptomatic patients with prior preterm delivery.[7,8]

Because of familial and recurrent characteristics of preterm delivery, many researchers have focused on genetic susceptibility for preterm delivery.[2,9] Oxidative stress-related genes which involve the metabolic detoxification process were reported to be associated with preterm delivery.[9] Especially, the glutathione S-transferase mu 1 (GSTM1), which is major phase II enzyme for the metabolic detoxification process, is a good candidate gene for preterm delivery.[9] However, there is still no report that evaluates the efficacy of identifying risk factors of preterm delivery in the Korean population.

The aim of this study was to evaluate the efficacy of cervical length, phIGFBP-1, and the genetic polymorphism of *GSTM1* as risk factors of preterm delivery in Korean low-risk women.

## MATERIALS AND METHODS

### Population and Data Collection

This study involved a case-control study performed between December 2005 and November 2006 in Ewha Womans University Hospital, which was approved by the Institutional Review Board. Trained interviewers managed participants, who signed the consent forms before enrollment, to record general information about clinical data. Patients who had vaginal bleeding, cervical dilatation of $\geq$3 cm, multiple pregnancies, a clinical history of cervical incompetence, a history of preterm birth, any spontaneous pregnancy low at <20 weeks' gestation, congenital anomaly, spontaneous premature rupture of the membrane, abruption placenta, placenta previa, intrauterine growth retardation, or preeclampsia were not included in the study. We determined gestational age in accordance with the onset of the last menstrual period or the first ultrasonographic estimation in case that the last menstrual period was unreliable. Preterm delivery was defined as delivery before 37 weeks of gestation.

Cervical length was measured using transvaginal sonography at 22-28 weeks of gestation. Those who consented were asked to empty their bladders and were placed in the dorsal lithotomy position. The ultrasound probe was inserted into the vagina and placed at the anterior fornix, and cervical length was measured as previously described.[10]

A rapid strip test (Actim Partus Test; Medix Biochemica, Kauniainen, Finland) was performed to detect phIGFBP-1 in cervical secretions from 24 to 30 weeks of gestation. At sampling, all patients had intact membranes and no vaginal bleeding. The cervical sample for assay of phIGFBP-1 was taken with a cotton-tipped swab during speculum examination of the cervix and extracted with specimen extraction solution. The lower end of the swab was inserted into the external cervical orifice and left in place for 10 seconds. Then the swab was placed in 0.5 mL of a sample buffer solution-containing test tube, where it was left for 15-20 seconds to allow the front liquid to enter the diagnostic area. The

dipstick was removed and placed on a surface in the horizontal position. A positive result appeared in 5 min as two blue lines on the dipstick, and a negative result as a single blue line. Positive results were corresponded with a sample extract that contained 10 μg/L or more of phIGFBP-1.

When the enrolled pregnant women were admitted for delivery, 5 cc of whole blood were collected from the antecubital vein of each patient. Whole blood was sampled from an indwelling cannula into heparinized tubes and sterile ethylenediamine tetraacetic acid-containing vacutainer tubes.

After delivery, we collected the clinical data from the charts. We included 301 subjects who gave birth to a singleton infant and had a gestation between 24 and 42 weeks. Finally, 161 women with a preterm delivery and 140 normal controls with a term delivery were enrolled in the present study.

## Genotyping Analysis

We extracted genomic DNA from whole blood using an QIAmp blood kit (Qiagen, Hilden, Germany). The *GSTM1* deletion polymorphism was detected by polymerase chain reaction (PCR) reaction, which was performed in a total volume of 50 μL in the presence of 10 mM Tris-HCI, pH 8.3; 50 mM KCI; 0.2 mM of each dNTP; 2.0 mM $MgCl_2$; 1.25 units Taq DNA polymerase (Takara Shuzo Co., Shiga, Japan); 20 pmol of each primer; and 100 ng of genomic DNA as a template, as done by Chen *et al.* (1997).[11]

**Table 1.** Clinical characteristics in preterm and control groups

| | N (%) | | *P*-value[a] |
|---|---|---|---|
| | Preterm | Control | |
| Maternal age (years) | 30.7±4.7 | 31.9±4.2 | 0.02* |
| Maternal education (years) | | | <0.0001† |
| ≤ 12 | 69 (47.6) | 24 (18.2) | |
| > 12 | 76 (52.4) | 108 (81.8) | |
| Maternal BMI at delivery (kg/m$^2$) | | | 0.005† |
| <25 | 78 (49.7) | 55 (39.9) | |
| 25-30 | 52 (32.9) | 70 (50.7) | |
| ≥30 | 28 (17.7) | 13 (9.4) | |
| Parity | | | 0.07† |
| 0 | 80 (49.7) | 63 (45.0) | |
| 1 | 54 (33.5) | 63 (45.0) | |
| ≥2 | 27 (16.8) | 14 (10.0) | |
| Infant sex | | | 0.62† |
| Male | 92 (57.1) | 76 (54.3) | |
| Female | 69 (42.9) | 64 (45.7) | |
| Infant birth weight (gm) | 2,152±587 | 3,339±404 | <0.0001* |
| Gestational age (weeks) | 33.5±2.5 | 38.9±1.2 | <0.0001* |
| Total | 161 (53.5) | 140 (46.5) | |

Values are expressed as mean±SD or number (%), as appropriate.
BMI: body mass index.
**P*-value as obtained by student *t*-test. †*P*-value as obtained by $\chi^2$ test.

The primer for *GSTM1* was employed to amplify a 215 base pair (bp) fragment. We considered the absence of the 215 bp fragment in both alleles as the *GSTM1*-null genotype and the presence of the 215 bp fragment in one or both alleles as the *GSTM1*-positive genotype.

### Statistical Analysis

We evaluated the relationships of maternal education, body mass index (BMI) at delivery, parity, infant's sex, phIGFBP-1 and GSTM1 with preterm delivery using the $\chi^2$ test. We tested differences of averaged maternal age, infant's birth weight, gestational age and cervical length between subjects with preterm and term delivery using the Student's t-test. Receiver operator curve (ROC) analyses were done to verify the optimal cut-off scores satisfying both sensitivity and specificity for preterm delivery. The area under the ROC curves (AUC), standard errors (SE), and the 95% confidence interval were estimated to evaluate the diagnostic accuracy of cervical length for preterm delivery. If the AUC ($0.5 \leq$ AUC $\leq 1$) is close to 1, then it has greater accuracy. We performed logistic regression analyses, after adjusting for maternal education, BMI at delivery, parity and infant's sex, to investigate the impact of the cervical length and genetic factors as a risk for preterm delivery. All statistical analyses were done using Statistical Analysis Software 9.1 and Statistical Package for the Social Sciences 10.0. A *P* value of $<0.05$ was considered statistically significant.

## RESULTS

Table 1 shows clinical characteristics in preterm and control groups. The group with preterm delivery was younger than the control group ($P=0.02$). There were significant differences in maternal education ($P<0.0001$), maternal body mass index at delivery ($P=0.005$), infant birth weight ($P<0.0001$), and gestational age ($P<0.0001$), respectively. There was no significant difference in parity and infant sex ($P>0.05$) (Table 1).

The incidence of cervical length, phIGFBP-1, and genetic polymorphism of *GSTM1* is presented in Table 2. Cervical length in preterm delivery was shorter than that of term delivery ($P<0.0001$). The rate of positive phIGFBP-1 test in preterm delivery was higher than that of term delivery ($P<0.0001$). However, there was a marginally significant difference for genetic polymorphisms of *GSTM1* between two groups ($P=0.06$) (Table 2).

Table 3 shows ROC curve analysis of cervical length for preterm delivery. We tried to perform ROC curve analysis of cervical length for the risk of preterm delivery. ROC curve analysis of

**Table 2.** Incidence of cervical length, phIGFBP-1, and genetic polymorphism of *GSTM1* in preterm and control groups

| | N (%) | | *P*-value |
|---|---|---|---|
| | Preterm (N=161) | Control (N=140) | |
| Cervical length (cm) | 2.6±1.1 | 3.7±0.7 | <0.0001* |
| phIGFBP-1 | | | <0.0001† |
| Positive | 43 (28.5) | 1 (0.9) | |
| Negative | 108 (71.5) | 116 (99.2) | |
| GSTM1 | | | 0.06† |
| Null | 92 (62.2) | 61 (50.8) | |
| Positive | 56 (37.8) | 59 (49.2) | |

Values are expressed as mean±SD or number (%), as appropriate.
phIGFBP-1: phosphorylated insulin-like growth factor binding protein-1, GSTM1: glutathione-S-transferase M1.
**P*-value as obtained by student t-test. †*P*-value as obtained by $\chi^2$ test.

cervical length showed that 3.05 cm of cervical length was the best cut-off point for predicting preterm birth. When cervical length was <3.05 cm, sensitivity was 65% and specificity was 89%. In addition, positive predictive value (PPV) was 77% and negative predictive value (NPV) was 83% (Table 3).

Predictive values of phIGFBP-1, cervical length, and *GSTM1* polymorphisms for preterm delivery are presented in Table 4. In all factor positive cases, the predictive values were 75% of sensitivity, 100% of specificity, 100% of PPV, and 93% of NPV. Among two factor-positive cases, the best predictors for preterm delivery were cervical length and null type of *GSTM1* gene polymorphism and the predictive values were 79% of sensitivity, 95% of specificity, 91% of PPV, and 88% of NPV. Among one factor- positive cases, the best predictor for preterm delivery was cervical length and the predictive values were 66% of sensitivity, 90% of specificity, 77% of PPV, and 83% of NPV (Table 4).

Table 5 shows the risk of preterm delivery according to cervical length, phIGFBP-1 and *GSTM1* polymorphism as determined using logistic regression analysis, after adjusting for infant sex, parity, maternal age, educational level, and BMI at delivery. The risk of preterm delivery in patients having below 3.05 cm of cervical length was higher than in controls (odds ratio [OR]=12.9; $P<0.0001$). Also, the risk of preterm delivery in patients having a positive test for phIGFBP-1 was higher than in controls (OR=77.1;

**Table 3.** Receiver operator curve (ROC) analysis of cervical length for preterm delivery

| Cervical length cut-off (cm) | AUC* | | | Sensitivity | Specificity | PPV* | NPV* |
|---|---|---|---|---|---|---|---|
| | AUC | SE | 95% CI | | | | |
| | 0.80 | 0.04 | 0.72-0.88 | | | | |
| <2.95 | | | | 0.60 | 0.91 | 0.79 | 0.81 |
| <3.05† | | | | 0.65 | 0.89 | 0.77 | 0.83 |
| <3.12 | | | | 0.67 | 0.84 | 0.69 | 0.83 |

SE: standard error, CI: confidence interval.
*AUC: area under the ROC curve, PPV: positive predictive value, NPV: negative predictive value. †Optimal cut-off length for preterm delivery by ROC analyses.

**Table 4.** Predictive values of phIGFBP-1, cervical length, and *GSTM1* polymorphism for preterm delivery

| phIGFBP-1 | Sensitivity | Specificity | PPV* | NPV* |
|---|---|---|---|---|
| Cervical length | | | | |
| GSTM1 null type | | | | |
| All-factor positive | 0.75 | 1.00 | 1.00 | 0.93 |
| Two-factor positive | | | | |
| phIGFBP-1 & Cervical length | 0.59 | 1.00 | 1.00 | 0.88 |
| phIGFBP-1 & GSTM1 null | 0.39 | 1.00 | 1.00 | 0.58 |
| Cervical length & GSTM1 null | 0.79 | 0.95 | 0.91 | 0.88 |
| One factor positive | | | | |
| phIGFBP-1 | 0.29 | 0.99 | 0.98 | 0.52 |
| Cervical length | 0.66 | 0.90 | 0.77 | 0.83 |
| GSTM1 null | 0.62 | 0.49 | 0.60 | 0.51 |

phIGFBP-1: phosphorylated insulin-like growth factor binding protein-1, GSTM1: glutathione-S-transferase M1.
*PPV: positive predictive value, NPV: negative predictive value.

**Table 5.** Risk of preterm birth according to cervical length, phIGFBP-1 and *GSTM1* polymorphism

| | N (%) | | OR* | 95% C.I. | *P*-value |
|---|---|---|---|---|---|
| | Preterm | Control | | | |
| Cervical length (cm) | | | | | |
| < 3.05 | 36 (65.5) | 11 (10.6) | 12.9 | 5.1-33.0 | <0.0001 |
| ≥ 3.05 | 19 (34.6) | 93 (89.4) | 1.00 | reference | |
| phIGFBP-1 | | | | | |
| Positive | 43 (28.5) | 1 (0.9) | 77.1 | 9.2-645.3 | <0.0001 |
| Negative | 108 (71.5) | 116 (99.2) | 1.00 | reference | |
| GSTM1 | | | | | |
| Null | 92 (62.2) | 61 (50.8) | 1.7 | 1.0-3.1 | 0.06 |
| Positive | 56 (37.8) | 59 (49.2) | 1.00 | reference | |

GSTM1: glutathione-S-transferase M1, OR: odds ratio, CI: confidence interval.
*Adjusted for infant's sex, parity, maternal age, educational level and body mass index at delivery.

*P*<0.0001). The risk of preterm delivery in patients having null type *GSTM1* gene polymorphism was higher than in controls (OR=1.7), although there was a marginally significant difference for GSTM1 polymorphism between the two groups (*P*=0.06) (Table 5).

## DISCUSSION

Although there were many risk factors for preterm delivery including demographic factors, obstetric history, genetic factors, a short cervical length by ultrasound, or biological markers,[1-4] there was no report that evaluated the efficacy for risk factors of preterm delivery in the Korean low-risk population. In this study, we found that cervical length, phIGFBP-1 test, and the null type of *GSTM1* are useful as risk factors for preterm delivery in our population.

There were several reports about the role of cervical length screening in low-risk populations.[12-15] The potential for cervical screening to identify the risk of preterm delivery from low-risk population is controversial. Our findings confirm those of previous studies showing that there is an inverse relation between the length of the cervix and the frequency of preterm delivery.[12-15] We attempted to perform ROC curve analysis of cervical length for the risk of preterm delivery. ROC curve analysis of cervical length showed that 3.05 cm of cervical length was the best cut-off point for predicting preterm delivery. In our study, a cervical length cut-off of 3.05 cm had a sensitivity of 65%, a specificity of 89%, a positive predictive value of 77%, and a negative predictive value of 83%. These predictive values showed higher sensitivity and higher positive predictive value than other studies.[12,16] According to Hassan *et al.*, a cervical length cut-off of 15 mm for early preterm delivery showed a sensitivity of 8.2%, a specificity of 99.7%, a positive predictive value of 47.6%, and a negative predictive value of 96.7%.[12] Although the predictive value of the cervical screening test to identify the risk of preterm delivery were very low in previous studies,[12,16] we can conclude that the cervical screening test is possible to use for the identification of risks of preterm delivery in Korean low-risk women because our study shows high sensitivity and positive predictive value.

This study also showed that the odds ratio for preterm delivery before 37 weeks was 12.9 and this result was similar with other reports.[13,15] To *et al.* screened 6,819 women prospectively at 22-24 weeks' gestation and the odds ratio for a short cervix was 24.9.[13] Also Hibbard *et al.* in a prospective study found that the relative risks for delivery before 35 weeks were 4.5, 7.5, and 7.8 for the

$10^{th}$, $5^{th}$, and $2.5^{th}$ percentiles, respectively.[15]

Insulin-like growth factor is a protein synthesized by the liver and is involved in the control of fetal growth and development. Its binding protein (IGFBP-1) is found in different isoforms and the highly phosphorylated isoform (phIGFBP-1), which is produced by the deciduas and is not present in the amniotic fluid, may be an indicator of tissue damage at the choriodecidual interface in pregnant women.[17] Our study showed that the rate of a positive phIGFBP-1 test in preterm delivery was higher than that of term delivery. Furthermore, the predictive values were 29% of sensitivity, 99% of specificity, 98% of positive predictive value, and 52% of negative predictive value. According to Paternoster *et al.*, the predictive values in an asymptomatic population were 22% of sensitivity, 92% of specificity, 12% of positive predictive value, and 96% of negative predictive value.[17] However, the predictive values in a symptomatic population were 69% of sensitivity, 91% of specificity, 50% of positive predictive value, and 96% of negative predictive value, such that they concluded that phIGFBP-1 seemed to be a valuable test in predicting preterm delivery in symptomatic patients.[17] Although our results showed low sensitivity, we can consider that the phIGFBP-1 test can be a valuable test in predicting preterm delivery in Korean low-risk populations because of high specificity, high positive predictive value, and high negative predictive value.

The use of phIGFBP-1 in the prediction of preterm delivery might be more advantageous than another biological marker, fetal fibronectin, because phIGFBP-1 is unaffected by urine and seminal plasma and has a lower cost.[17,18] However, maternal blood can interfere with both the fetal fibronectin and phIGFBP-1 assays and we excluded patients having vaginal bleeding from our study groups. The explanation between positive phIGFBP-1 test and preterm delivery would be explained by the fact that the patients having a positive phIGFBP-1 test may have tissue damage at the choriodecidual interface and the tissue damage may result in frequent infections. These infections may lead to uterine contractions, cervical changes, rupture of fetal membranes and finally preterm delivery.[19]

Preterm delivery is a complex trait that is determined by genetic factors and other environmental factors. Several papers have reported that oxidative stress-related genes are associated with a risk for preterm delivery.[20-22] In this study, we found that the risk of preterm delivery in patients having a null type *GSTM1* gene polymorphism was higher than in controls, although there was a marginally significant difference for *GSTM1* polymorphism between two groups. Also, among two factor-positive cases, the best predictors for preterm delivery were cervical length and null type *GSTM1* gene polymorphism and the predictive values were 79% of sensitivity, 95% of specificity, 91% of positive predictive value, and 88% of negative predictive value.

Enzymes belonging to the GST family are involved in the detoxification process of a wide range of environmental toxins and carcinogens. The GSTs are a supergene family of enzymes that are believed to exert a critical role in cellular protection against toxic foreign chemicals and oxidative stress.[23] Yamada *et al.* found that the gestational age at birth in women with the *GSTM1* null genotype was significantly lower than in women carrying *GSTM1*.[24] Also, Hong *et al.* showed that pregnant women who had the *GSTM1* null genotype produced babies with lower weights when exposed to environmental tobacco smoke.[25]

The biological mechanism between null type *GSTM1* gene polymorphisms and preterm delivery may be due to disturbance of cell regulation caused by DNA adducts and damage.[26,27] DNA damage may occur as a result of a lack of detoxification of metabolites by enzymes including GSTM1, which can result in DNA strand breakage, DNA protein cross links, DNA adducts, or sister chromatid exchanges.[26,27] According to Nukui *et al.*, women and/or newborns with the *GSTT1* null genotype who were exposed to cigarette smoke during pregnancy were at elevated risk for preterm delivery and they also considered that the ability to identify high-risk woman by genotyping has the potential for reducing the frequency of preterm births.[22]

We also found that in all factor-positive cases, the predictive values were 75% of sensitivity, 100% of specificity, 100% of positive predictive value, and 93% of negative predictive value in

Korean low-risk women. These markers can be very useful markers in preventing preterm delivery if pregnant women can be diagnosed by cervical length by ultrasonogram, phIGFBP-1 test using vaginal secretion, and *GSTM 1* genotyping by PCR.

This study has several strengths. First, it is the first study about the risk factors for preterm delivery in a Korean low-risk population using cervical length, phIGFBP-1 test, and *GSTM1* gene polymorphism. Secondly, we found that in all factor -positive cases, the predictive values were 75% of sensitivity, 100% of specificity, 100% of positive predictive value, and 93% of negative predictive value. Our results are highly predictive and we can use these factors as the risk factors for preterm delivery. However, our study has a limitation because of the small sample size and we could not verify the environmental factors which might affect the *GSTM1* gene polymorphism.

In conclusion, we confirmed that cervical length, phIGFBP-1 test, and the null type of *GSTM1* are useful as risk factors for preterm delivery in Korean low-risk women and these marker may be very useful for the detection of preterm delivery risk.

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## 「국문초록」

**목적:** 본 연구에서는 한국 여성 중 조산발생 저위험군에서 자궁경부길이 및 phosphorylated insulin-like growth factor binding protein-1 (phIGFBP-1)과 *glutathione S-transferase mu1 (GSTM1)*이 조산발생 위험과 관련이 있는지에 관해 알아보고자 하였다.

**연구방법:** 2005년 12월부터 2006년 11월까지 본원을 방문하여 산전진찰을 받고 생존아를 분만한 단태임신 301명을 연구대상으로 하였다. 임신 22주에서 28주 사이에 경질초음파 (transvaginal sonography)를 시행하고 임신 24주에서 30주 사이에 질분비물의 phIGFBP-1을 측정하였으며, *GSTM1* 다형성 분석을 위한 모체혈액을 이용한 유전자 검사를 시행한 경우를 포함시켰다. 다태임신과 태아의 주요 선천성기형이 있는 경우는 제외하였다. 통계적 분석으로는 Student *t*-test, $\chi^2$ test, 로지스틱 회귀분석 등을 이용하였다.

**결과:** 자궁경부길이는 조산군에서 만삭분만군에 비해 짧았다 ($P$<0.0001). 조산군의 phIGFBP-1 test 양성 빈도는 조산군에서 만삭분만군에 비해 높았다 ($P$<0.0001). 짧은 자궁경부길이 (<3.05 cm)는 3.05 cm 이상인 경우에 비해 조산의 위험을 유의하게 증가시켰고 ($P$<0.0001), phIGFBP-1 test 양성인 경우도 음성인 경우보다 조산의 위험을 증가시켰다 ($P$<0.0001). Receiver operating characteristics 곡선에서 자궁경부길이 결정점 3.05 cm는 조산 예측에 있어 민감도 66%, 특이도 89%, 양성예측도 77%와 음성예측도 83%를 보였다. 3.05 cm 미만의 자궁경부길이와 phIGFBP-1 양성인 경우 및 GSTM1의 null type인 경우를 모두 고려하였을 때 민감도, 특이도, 양성예측도 및 음성예측도는 각각 75%, 100%, 100%, 93%였다.

**결론:** 한국 여성 중 조산발생 저위험군에서 조산을 예측하는 데 자궁경부길이, phIGFBP-1 rapid test 및 *GSTM1* 유전자 분석은 유용하리라 생각된다.

**중심 단어:** 자궁경부길이, Glutathione S-transferase M1, Phosphorylated insulin-like growth factor binding protein-1, 조산, 위험인자