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ADVANCED MODELLING STRATEGIES IN PRETERM LABOUR RISK

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Key words: regression models, premature labour, risk factors.

Summary

We performed a case control study to evaluate risk factors for preterm labour in 1200 women. 600 women who delivered prematurely and randomly selected group of 600 women who gave birth at term were questioned using a standardised questionnaire. Simple data analysis, multiple regression analysis, including logit and probit regression models and multiple stepwise regression were performed to identify independent risk factor of preterm labour. Based on this analysis and in respect of these independent factors an equation was suggested which allows to evaluate mathematically risk for preterm labour and can be used in gynaecologists' practice.

Introduction

All over the world, preterm labour is one of the most significant issues in relation with the protection of maternal-child health. Over the recent 30 years, no field of medicine has achieved such amazing results as have been achieved in the treatment of this pathology: survival rate is 15% for newborns weighting 501-750 g and 50 percent for 751-1000 g [6]. However, obstetricians and gynaecologists prefer birth of a healthy, full-term, viable baby to expensive treatment of pregnancy complications. That is why the research of risk factors for preterm labour and institution of preventive measures is among the obstetrical priorities.

According to the WHO, preterm labour is defined as the delivery between 22 weeks' gestation (birth weight ≥ 500 g) and 37 weeks' gestation (259 days since the first day of the last menstrual period) [23]. According to the data from different sources, the incidence of preterm births varies from 5 to 15 percent of all pregnancies [3–5, 13, 19]. In Lithuania, this pathology accounts for 6 – 8 percent of all births, and the percentage of premature births delivered at the Department of Obstetrics and Gynaecology of Lithuania University of Health Sciences makes from 8 to 10 percent of all births delivered there in [10]. Premature labour is the most common complication in the third trimester of pregnancy. The birth of a premature infant is a clinical crisis, since the preterm labour poses serious risk for both the mother and foetus.

The literature sources present studies of different factors from psychosocial to genetic [8, 14–18, 20, 21], however we did not manage to find the study presenting an explicit technique for the evaluation of the entirety of factors a pregnant woman is exposed to and the level of preterm labour risks caused by such factors. Therefore, in addition to our goal to study and evaluate a wide spectrum of factors for preterm labour we also aimed to develop the technique enabling to predict preterm labour, which could be used by the physicians practising obstetrics and gynaecology in their daily work.

The aim of this paper is to define the most important independent factors for preterm labour and to evaluate mathematically risk for preterm labour based on simple data analysis, multiple regression analysis, including logit and probit regression models and multiple stepwise regression.

Study methods

A case control study, i.e., a comparative study in women with preterm and full-term labour, was performed at the Department of Obstetrics and Gynaecology of Lithuania University of Health Sciences. All women who delivered during the period of 18 months at the department from 22nd through 37th weeks of gestation (n=600) were included into the study.

The control group consisted of women who gave birth at term (n=600) at Department of Obstetrics and Gynaecology of Lithuania University of Health Sciences over the same period of time. Women were randomly assigned to the control group using the birth register list. During the period under investigation, 4121 women gave birth at term at the Department of Obstetrics and Gynaecology of Lithuania University of Health Sciences. Women in the control group (n=600) accounted for 14.5 percent of the above mentioned number of labours. Every sixth women who

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gave birth at term was randomly interviewed. Such a sample properly represents the study population and prevents the study results from possible systemic errors. 100 percent of the respondents consented to take part in the study.

The percentage of urban residents in both groups was rather similar amounting to 326 (54.33 percent) in the target group and 417 (69.50 percent) in the control group. However the number of small town and rural residents was statistically significant higher in the target group amounting to 45.67 percent (n = 274) as compared to 30.50 percent (n = 183) in the control group.

Parturient women were questioned within three days after delivery using a standardised questionnaire, and the source records were analysed. The questionnaire contained 186 questions covering a full range of factors such as harmful habits, working conditions, lifestyle choices, obstetric and gynaecologic history, general medical history, history of past diseases and family history, exposure to stress (resistance and predisposition to stress in the target and control groups were evaluated using the test method developed by Kindler H.C. and Ginsburg M.C. [7]), etc.

Statistical analysis. Software packages Statistica 5.0, EPI-Info and MS Excel were used for the analysis of the study findings. The relationship between the impact of the

		Impact X	
		Present	Not present
Preterm labour	Present	a	b
	Not present	c	d

Fig. 1. Odds ratio diagram

$$\text{Odds ratio} = \frac{a}{b} : \frac{c}{d}.$$

risk factor and the condition under investigation (preterm labour) was estimated by odds ratio OR. The odds ratio OR is defined as the ratio of the odds of preterm labour to the odds of full-term labour (see Fig. 1).

The $\frac{a}{b}$ event indicates the odds in respect of persons with the condition under investigation (preterm parturients) and the $\frac{c}{d}$ event indicates the odds in respect of persons without the condition under investigation (full-term parturients). The OR value exceeding 1.0 shows the relation between the impact of the factor and the condition under investigation (preterm labour).

The confidence interval CI of the odds ratio was estimated at the confidence level of 0.95 (95 percent) and evaluated using the beta coefficient [1]. The CI depends on the sample volume and confidence level.

For the evaluation of continuous values the following statistical characteristics were used: mean ($\bar{x}$), average square error ($s_{\bar{x}}$), confidence interval for the mean (CI), standard deviation (SD). Relative frequencies were used to evaluate the likelihoods of discrete values [1].

The hypothesis of equality of means and probabilities was tested using the Student (t) test. The relation between the discrete values and labour (full-term and preterm) was estimated using the χ^2 test. In case of low number (incidence) of cases the exact Fisher test was used instead of χ^2 test.

The contingency coefficient was estimated according to Pearson. The probability (p) value of less than 0.05 (5 percent) was chosen for all analyses performed. χ^2 test was used to determine independent risk factors. Software package Epi-Info was used to perform the non-linear Logit, Probit regression and multiple linear stepwise regression in respect of independent risk factors for preterm labour. Determination coefficient was used to express the probability of the multiple stepwise regression. Percentage accuracy was used to express the probability of the non-linear Logit and Probit regression.

Simple data analysis. Data obtained during the interview and data collected from the source documents were grouped as follows:

1. Medical factors.
2. Biological factors.
3. Anthropometric factors.
4. Psychosocial factors.
5. Work character and working conditions of women during pregnancy.
6. Lifestyle choices of pregnant women.
7. Harmful habits during pregnancy.
8. Course of labour, complications and perinatal outcomes.

In each of the groups listed, main potential factors for preterm labour were studied. The confidence intervals of the odds ratio, main statistical characteristics were estimated, hypothesis of equality of means and probabilities was tested, etc. A detailed simple analysis was performed.

See factors for preterm labour (determined according to the OR, CI, p) presented in Table 1 in the order of reduction of the OR.

After the analysis of all potential factors for preterm labour was performed, independent factors for preterm labour were determined using the χ^2 test of independence:

1. Primary and lower education of the woman.
2. Unstable marital status (unmarried, divorced, living in a common-law marriage, widow).

Table 1. Factors for preterm labour

No.	Factor	OR
1	2	3
1.	Events of threatening preterm labour during pregnancy	59.26
2.	Essential hypertension of the gravida	34.80
3.	Myomas in the uterus	34.80
4.	History of preterm labour	31.55
5.	Smoking during pregnancy (≥ 5 cigarettes per day)	19.21
6.	History of ≥ 2 spontaneous abortions	18.49
7.	Anomalies of genital organs	16.82
8.	Primary and lower education	15.03
9.	Trichomoniasis	14.71
10.	Unsatisfactory living conditions	13.96
11.	Syphilis	12.44
12.	Diabetes mellitus	11.17
13.	Work in the power industry	9.74
14.	Economic problems (in terms of satisfaction of food needs)	8.14
15.	Previous history of low birth weight	7.56
16.	Low (0-5 kg) pregnancy weight gain	7.18
17.	≥ 2 induced abortions	7.16
18.	Previous history of Caesarean section	7.14
19.	Surgical intervention during pregnancy	7.06
20.	Work in the metal industry	6.85
21.	Renal and urinary tract anomalies of the gravida	6.80
22.	Number of child-births: ≥ 4 child-births	6.19
23.	Constant feeling of fear during pregnancy	5.84
24.	Operation of the cervix (other than during pregnancy)	5.66
25.	Unstable marital status (unmarried, divorced, living in a common-law marriage, widow)	5.62
26.	Previous history of infertility	5.60
27.	Gravida's work under intensive noise up to 12 hours per day	5.14
28.	Heredity from the maternal side	4.98
29.	Work related with going on business trips (≥ 1 time per month)	4.95
30.	Physical activity of the gravida (long walking ≥ 5 km per day)	4.70
31.	Compensated cardiac and cardiovascular disorder of the gravida	4.57
32.	Lifting of heavy things (≥ 10 kg)	4.47
33.	Anaemia in pregnancy (with Hb 91-100 g/L)	4.24
34.	Shift work during pregnancy	4.19
35.	Intensive house chores	4.19
36.	Gravida's exposure to dust at work	4.13
37.	Vaginal infection in the first half of pregnancy	4.04
38.	Bacterial vaginosis	4.02
39.	Bad psychological climate at home	3.83
40.	Bad antenatal care (failure to attend maternity centre)	3.82
41.	Short stature of the gravida (≤ 151-160 cm)	3.81
42.	Sexual activity during pregnancy (≥ 2 times per week)	3.78
43.	Vaginal infection in the second half of pregnancy	3.73
44.	Psycho-emotional shock during the 22-28 weeks' gestation	3.65
45.	Gravida's predisposition to stress	3.56
46.	Shift work of the gravida	3.06
47.	Periodontal disease during pregnancy	2.92
48.	Feeling of anxiety during pregnancy	2.86
49.	Harmful work conditions of the male partner during the conception	2.36
50.	Unplanned pregnancy	2.32
51.	Standing at work during pregnancy for long hours (10-12 hours per day)	2.06
52.	Daily use of public transport during pregnancy	2.06
53.	Obesity (I°, II°, III°)	2.05
54.	Viral infection during pregnancy	1.78
55.	Colpitis mycotica	1.72
56.	Age (≤ 17 and ≥ 30 years)	1.49
57.	Exposure to chemical substances during pregnancy	1.39
58.	Moderate and heavy use of alcohol during pregnancy	1.16

3. Gravida's work under intensive noise up to 12 hours per day.

4. Shift work of the gravida (in the morning, day and night shifts).

5. Standing at work of the gravida for long hours (10-12 hours per day).

6. Physical activity of the gravida: long walking (≥ 5 km per day).

7. Age of the gravida ≤ 17 and ≥ 30 years.

8. Psycho-emotional shock during the 22-28 weeks' gestation.

9. Constant feeling of fear during pregnancy.

10. Low weight gain (0-5 kg) during pregnancy.

11. Number of child-births: ≥ 4 child-births.

12. Previous history of ≥ 2 induced abortions.

13. Previous history of infertility.

14. Previous history of preterm labour.

15. History of ≥ 2 spontaneous abortions.

16. Previous history of Caesarean section.

17. Previous history of low birth weight.

18. Essential hypertension of the gravida.

19. Renal and urinary tract anomalies of the gravida.

20. Myomas in the uterus.

21. Anomalies of genital organs.

22. Vaginal infection in the first half of pregnancy.

23. Vaginal infection in the second half of pregnancy.

24. Gravida's predisposition to stress.

Multiple regression analysis of the factors for preterm labour. Logit and Probit regression analysis.

Having performed the non-linear Probit regression of the factors mentioned with the accuracy of 77.00 and 89.67 percent in respect of the target and control group respectively, and the non-linear Logit regression with the accuracy of 80 and 87.33 percent in respect of the target and control group respectively, regression coefficients and the respective factors were presented in Table 2.

The accuracy of predictions obtained using the Probit and Logit regression models will be evaluated on the basis of the residual errors, i.e., we will see if the observed values differ a lot from that obtained using the regression function for the prediction. The accuracy of the Probit and Logit regression models is demonstrated by the residual dispersion diagrams and residual histograms presented in Fig. 2, 3, 4 and 5.

Multiple stepwise regression

In addition, independent factors for preterm labour were determined using the multiple forward stepwise regression principle ($R^2 = 0.66781$). See these factors in Table 3 listed according to the intensity of their impact.

Here: a_0 is a free member.

It is obvious that women with unfavourable obstetrical history, i.e., women with a previous history of low birth weight, very young (£ 17 years) or older than 30 years women, women exposed to emotional shock during the 22-28 weeks' gestation and women working in a standing position for long hours, are at the highest risk for preterm labour.

The accuracy of the multiple forward stepwise regression model is demonstrated by the residual dispersion diagrams and residual histograms in Fig. 6 and 7.

Results obtained. Based on the Logit, Probit regression and multiple linear stepwise regression performed in respect of the above mentioned independent factors for preterm labour, as well as consideration and evaluations of the process under investigation the following equation can be suggested as the one most exactly describing the preterm labour:

$$y = a_0 + a_1x_1 + a_2x_2 + ... + a_nx_n \qquad (1)$$

a_i where y is the outcome of the pregnancy, i.e., full-term or preterm labour;

Table 2. Factors for preterm labour obtained using the Probit and Logit regression model

No.	Factor	Regression coefficient	
		Probit	Logit
1.	Primary and lower education of the woman	0.849481	1.970998
2.	Unstable marital status	0.517956	1.191620
3.	Gravida's work under intensive noise up to 12 hours per day	0.508707	1.232475
4.	Shift work of the gravida (in the morning, day and night shifts)	0.387801	0.860792
5.	Standing at work of the gravida for long hours (10-12 hours per day)	0.111082	0.3200349
6.	Physical activity of the gravida (long walking ≥ 5 km per day)	0.496291	1.062350
7.	Age of the gravida (≤ 17 and ≥ 30 years)	0.385925	0.528281
8.	Psycho-emotional shock during the 22-28 week of gestation	0.127143	0.501681
9.	Constant feeling of fear during pregnancy	0.337921	0.993013
10.	Low weight gain (0-5 kg) during pregnancy	1.029995	1.940561
11.	Number of child-births ≥ 4 child-births	0.740852	1.453421
12.	≥ 2 induced abortions	0.4322517	0.628463
13.	Previous history of infertility	1.445883	2.172687
14.	Previous history of preterm labour	1.166543	3.001996
15.	Previous history of ≥ 2 spontaneous abortions	0.921540	2.637318
16.	Previous history of Caesarean section	1.822835	2.503682
17.	Previous history of low birth weight	0.133975	1.074835
18.	Essential hypertension of the gravida	0.906696	2.444888
19.	Renal and urinary tract anomalies of the gravida	0.819269	1.772965
20.	Myomas in the uterus	0.697031	1.677806
21.	Anomalies of genital organs	1.302262	3.091380
22.	Vaginal infection in the first half of pregnancy	0.565709	1.049293
23.	Vaginal infection in the second half of pregnancy	0.464122	0.871401
24.	Gravida's predisposition to stress	0.415171	1.007802

Table 3. Factors for preterm labour according to the data of multiple forward stepwise regression

No.	Factor	Multiple forward stepwise regression coefficient (a_i)
1.	Previous history of preterm labour	0.146085
2.	Vaginal infection in the second half of pregnancy	0.218932
3.	Constant feeling of fear during pregnancy	0.129418
4.	Unstable marital status	0.143143
5.	Vaginal infection in the first half of pregnancy	0.118504
6.	Low weight gain (0-5 kg) during pregnancy	0.206745
7.	Gravida's predisposition to stress	0.135032
8.	Physical activity of the gravida (long walking ≥ 5 km per day)	0.130960
9.	Shift work of the gravida	0.117372
10.	Primary and lower education	0.183750
11.	Age (≤ 17 and ≥ 30 years)	0.935540
12.	Previous history of Caesarean section	0.289387
13.	Previous history of infertility	0.283129
14.	Previous history of ≥ 2 spontaneous abortions.	0.221461
15.	≥ 2 induced abortions	0.134290
16.	Renal and urinary tract anomalies of the gravida	0.135125
17.	Gravida's work under intensive noise up to 12 hours per day	0.148258
18.	Psycho-emotional shock during the 22-28 week of gestation	0.733060
19.	Anomalies of genital organs	0.170086
20.	Myomas in the uterus	0.141053
21.	Essential hypertension of the gravida	0.115478
22.	Standing work of the gravida for long hours (10-12 hours per day)	0.484110
23.	Previous history of low birth weight	0.921850
24.	Number of child-births (≥ 4 child-births)	0.056361
		$a_0 = 0.093749$

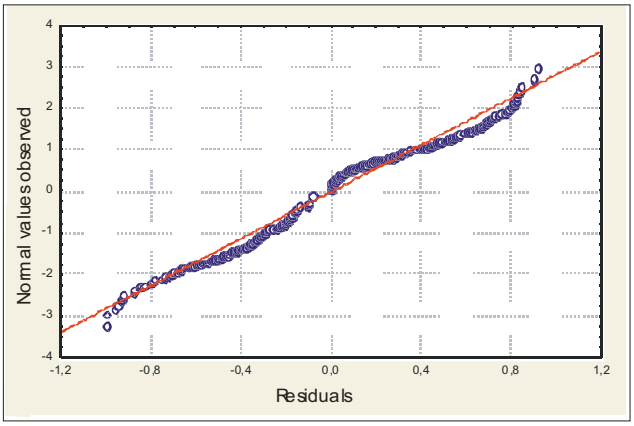

Fig. 2. Residual dispersion diagram according to the Probit regression model.

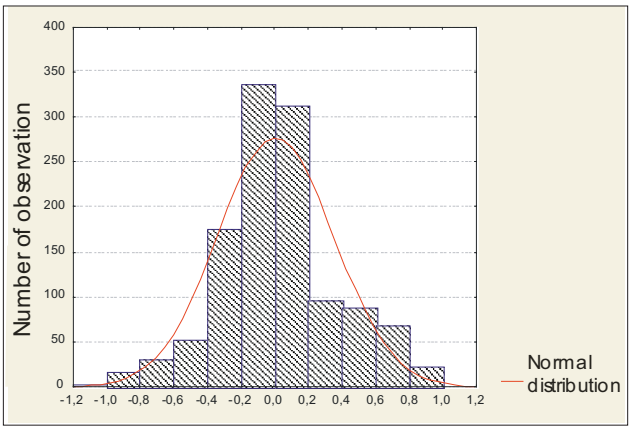

Fig. 3. Histogram of residuals according to the Probit regression model.

a_0 is a multiple stepwise regression coefficient ($0 \le i \le n$, n is a number of factors) presented in Table 3. x_i is an i^{th} acting factor (see Table 3), $x_i = 1$ when the factor is observed and $x_i = 0$ when there is no acting factor. In our study, 0 and 1 were used as programming codes.

a_0 is a free member. In our case $a_0 = 0.093749$.

Where $y \to 1$ the preterm labour is predicted; where $y \to 0$ the full-term labour is predicted.

Discussion

Though preterm labour is an obstetrical pathology, which is known and studied for a long time, the literature sources still present conflicting data about the impact of different factors on the level of preterm labour risk. Not all of the authors manage to prove the significance of

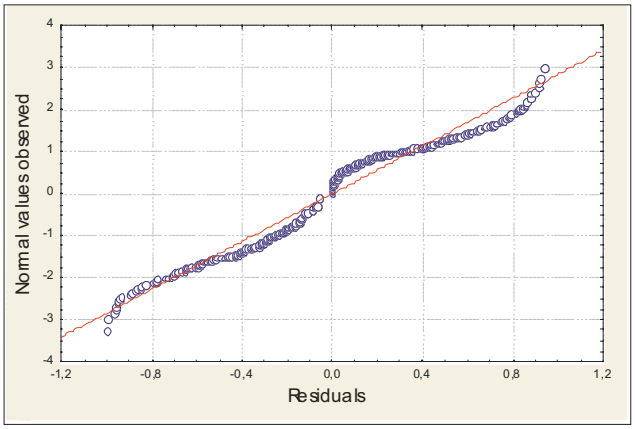

Fig. 4. Residual dispersion diagram according to the Logit regression model.

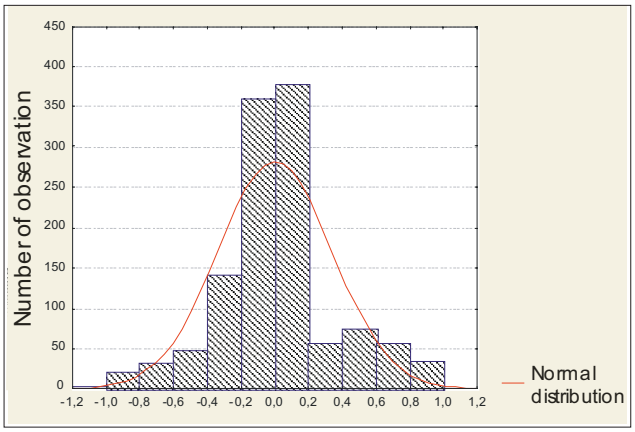

Fig. 5. Histogram of residuals according to the Logit regression model.

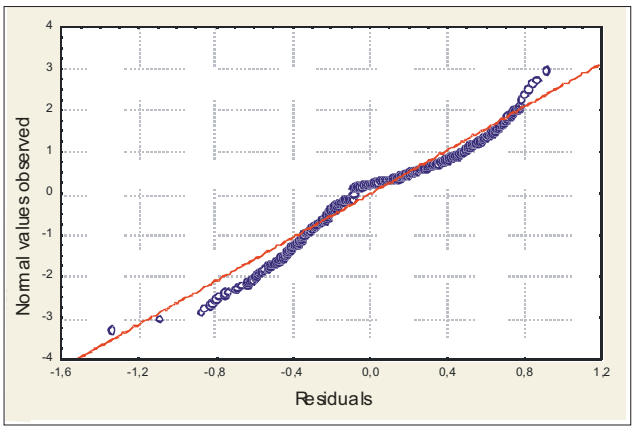

Fig. 6. Residual dispersion diagram according to the multiple forward stepwise regression model.

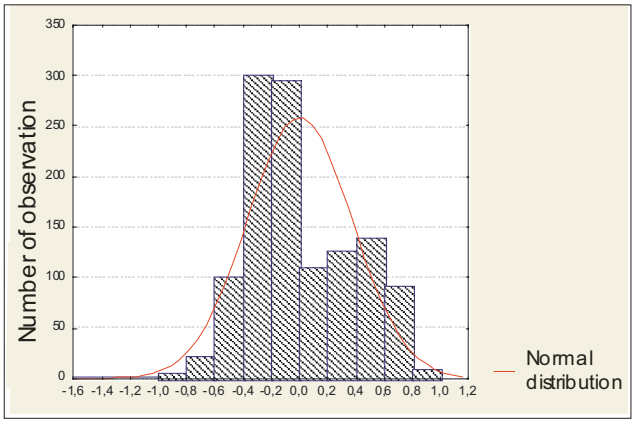

Fig. 7. Histogram of residuals according to the multiple forward stepwise regression model.

such simple biological, medical and social factors as age, infection of genital tract, smoking [2, 9, 11, 12, 22]. Naturally, the results are influenced by the character of the study, number of study subjects, economical, cultural and healthcare specificities of the countries in which the studies take place [3, 5, 19]. Therefore the study performed by us is primarily valuable as the largest one analysing the issue of preterm labour in our country on the basis of contemporary epidemiologic and statistical methods.

The other important aspect of this study is an integrated approach to the entirety of factors women are exposed to expressed with the help of statistical methods adapted for the solution of a specific problem. In the literature sources, the attempts to develop systems for the prediction of preterm labour can be found, however they failed to be put in practice due to complexity or failure to include sufficient number of factors [4, 6, 14, 17]. Having studied the impact of independent factors on preterm labour we present the equation, which rather exactly describes the preterm labour risk and can be easily applied by the physicians in their practice. Based on the determined risk factors and having mathematically evaluated the danger posed by them to the pregnant woman in respect of preterm labour the physician can pay more attention to the pregnant women exposed to higher risk. Not all of the risk factors can be prevented, however a considerable number of preventive measures are available such as changing of working conditions, quitting harmful habits, psychologist's advice in respect of the psycho-emotional stress experienced, etc.

Conclusion

Analysis of the data collected during the study shows that the mathematical methods can be successfully applied in the medicine. The result obtained – an equation for the prediction of preterm labour – should help to improve the care of pregnant women and prevent at least a part of preterm labours.

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RIZIKOS FAKTORIŲ ĮTAKA GIMDYMO LAIKUI

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Raktažodžiai: regresijos modeliai, priešlaikinis gimdymas, rizikos faktoriai.

Santrauka

Įvadas. Įvairių literatūros šaltinių duomenimis, priešlaikinių gimdymų dažnis varijuoja apie 5-15 proc. visų nėštumų. Lietuvoje ši patologija sudaro 6 – 8 proc., o Lietuvos sveikatos mokslų universiteto Akušerijos-ginekologijos klinikoje priešlaikinių gimdymų būna nuo 8 iki 10 proc. Tai dažniausia trečio nėštumo trimestro komplikacija. Nesubrendusio naujagimio gimimas yra klinikinė krizė, nes naujagimio ir motinos gyvybei bei sveikatai nuolat gresia pavojus. Todėl priešlaikinis gimdymas sudaro didelę riziką motinai ir vaisiui.

Metodai. Atlikta atvejų kontrolės studija – palyginamoji prieš laiką gimdžiusių moterų ir laiku gimdžiusių moterų studija. Tirtos visos prieš laiką pagimdžiusios moterys nuo 22-os iki 36-os nėštumo savaitės pabaigos (n = 600). Kontrolinę grupę sudarė laiku gimdžiusios moterys (n = 600). Tyrėjų sudarytu standartizuotu klausimynu (jame yra 186 klausimai) per tris dienas po gimdymo apklaustos gimdyvės ir atlikta jų pirminių dokumentų analizė. Tyrimo rezultatų analizė atlikta programų paketais Statistica 5.0, EPI-Info ir MS Excel. Ryšys tarp rizikos veiksnio poveikio ir tiriamosios būklės (priešlaikinio gimdymo) vertintas poveikio šansų santykiu.

Rezultatai. Atlikus regresinę duomenų analizę: Logit, Probit bei daugiamatę žingsninę regresijas, nustatyta, kad didžiausią įtaką priešlaikiniam gimdymui turėjo šie rizikos faktoriai - nepalanki anamnezė, nėštumo eigos ypatybės, moters ligos, moters amžius, polinkis į stresą, psichosocialiniai veiksniai.

Išvada. Tyrimo metu surinktų duomenų analizė rodo, kad matematiniai metodai gali būti sėkmingai taikomi medicinoje. Užrašyta priešlaikinio gimdymo prognozavimo lygtis – gali padėti gerinti nėščiųjų priežiūrą ir mažinti priešlaikinių gimdymų skaičių.

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