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INTEGRAL CHARACTERISTICS OF THE FORECAST OF DEVELOPMENT OF A CONGENITAL CLEFT LIP AND PALATE IN THE CONTEXTOF THE RISK FACTORS OF DIFFERENT NATURE

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ABSTRACT

Background: It is known that in the Russian Federation 4.5% of children have various congenital malformations and anomalies. The most common congenital malformations of the development include congenital clefts of the upper lip and palate. (CCULaP). The frequency of birth of children with this defect is up to 38% of all developmental defects in children. CCULaP refers to the most common and severe malformations of the maxillofacial area (MA). According to the World Health Organization(WHO), the frequency of birth of patients with crevices in the world is 0.6-1.6 per 1000 newborns. In the group of congenital malformations of human development CCULaP account for between 12 and 30%. **Objective:** To construct linear mathematical models for the development of congenital clefts of the upper lip and palate, taking into account risk factors of various nature. **Methods:** The object of the study was 216 children and their mothers. 186 of these children were with congenital malformations of the maxillofacial region from birth to 14 years. 30 healthy children together with their mothers formed the control comparison group. The material was processed using one-dimensional and multi-dimensional statistics using the STATISTICA 10.0 software package. **Result:** The obtained results formed the basis of the software program "Prediction of development of congenital crevices of the upper lip and palate in pregnant women, taking into account various risk factors" (CCULaP), which made it possible to automate the calculation process. The software product "CCULaP" is implemented in the algorithmic language Visual Basic 6.0. **Conclusion:** As a result of the study, models and decisive prediction rules for congenital clefts of the upper lip and palate were obtained, as well as the software for predicting the development of congenital clefts of the upper lip and palate of the fetus taking into account various risk factors of different nature (CCULaP) were developed.

KEYWORDS: congenital cleft, lip, palate, mathematics, method, dentistry, prediction, pathology, process.

INTRODUCTION

It is known that in the Russian Federation 4.5% of children have various congenital malformations and anomalies. The most common congenital malformations of the development include congenital clefts of the upper lip and palate. (CCULaP). The frequency of birth of children with this defect is up to 38% of all developmental defects in children.[1, 2]

CCULaP refers to the most common and severe malformations of the maxillofacial area (MA). According to the World Health Organization(WHO), the frequency of birth of patients with crevices in the world is 0.6-1.6 per 1000 newborns. In the group of congenital malformations of human development CCULaP account for between 12 and 30%.[3, 4]

It should be noted that the congenital clefts of the upper lip and palate in the world is not only a medical, but also a social problem. Over the past two decades, there has been a 2-fold increase in the frequency of birth of children with this pathology. In the structure of infant mortality in perinatal and early childhood congenital defects occupy a significant place. And congenital orofascial malformations are among the five most common intrauterine malformations. This pathology is multi-factorial, various exogenous and endogenous factors are involved in its emergence and development: hereditary, environmental, infectious diseases, drugs, or the combined effect of several factors. Nowadays, the tasks of determining the degree of impact of these factors, their role in the development of congenital clefts of the upper lip and palate are relevant.[7,9]

Research objective

To construct linear mathematical models for the development of congenital clefts of the upper lip and palate, taking into account risk factors of various nature.

The aim of the study

The construction of linear mathematical forecast models (IMF) of the development of AHIS taking into account risk factors of various nature.

MATERIALS RESEARCH METHODS

The object of the study was 216 children and their mothers. 186 of these children were with congenital malformations of the maxillofacial region from birth to 14 years. 30 healthy children together with their mothers formed the control comparison group. The subject of the study is venous blood and serum for the quantitative determination of the main indicators of the immune system to study the clinical and immunological efficacy of immune-corrective drugs in children and their mothers.

The material was processed using one-dimensional and multi-dimensional statistics using the STATISTICA 10.0 software package. The task was to build mathematical models (MMDP) of the developmental prognosis of congenital clefts of the upper lip and palate, which are able to predict with great accuracy the development of pathology in the fetus based on the medical data of the maternal organism. The construction of mathematical models of the forecast was carried out using the method of least squares, because of the least squares method - the estimates have the lowest possible variance in the class of all linear unbiased estimates and are, accordingly, the best for unknown parameters.[5, 6]

RESULTS AND DISCUSSION

In order to obtain an effective model, the least squares method imposes on a number of assumptions on the original sample.

1) The assumption of a zero average. When examining a process, we cannot cover all the parameters that have an influence on it, and include, as a rule, the most significant parameters into consideration. This hypothesis requires that the cumulative effect of excluded variables on the process being studied is mutually compensated and reduced to zero.

2) The assumption of the constancy of the conditional variance and the absence of autocorrelation. Here it is required that the experiment be carried out with stable environmental parameters, and that the influence of the parameters excluded from consideration does not multiply when combined.

3) The assumption of the absence of simultaneity. This hypothesis requires that the indicators we are considering do not have functional dependencies with those excluded. Fulfillment of this requirement allows all random perturbations of the resulting model to be attributed to the influence of excluded factors, and then all the properties of the estimates will be determined by the quality of the original variation series.

4) Assumption of rank. This assumption requires that between the parameters studied there should be no functional connections, that is, the existence of a linear relationship between them is excluded.

In fact, all these requirements are aimed at ensuring that the original data sample is homogeneous.

In order to obtain an effective model, the least squares method requires that the original data sample is homogeneous.

Mathematical models were built in the form of linear functions. When building on the coefficients of the model, conditions of their effectiveness were imposed not lower than the level of $p < 0.05$ by the Student's criterionThe threshold values of the decision rules were determined from the condition of the best compliance with the original clinical material. As a result, prediction models for congenital clefts of the upper lip and palate and decisive prediction rules of the following type were obtained:

For environmental factors

Isx (E) = 1,2607 – 0,0136X(4) + 0,009X(15) – 0,003X(21) – 0,0119X(22) +
+ 0,0115X(23) + 0,0057X(25) – 0,0091X(26) + 0,0026X(29) – 0,0197X(30)

decision rule has the form

$$\text{If } Isx(E)\begin{cases} < 0{,}45 & - \text{ there is CCULaP} \\ > 0{,}53 & - \text{ there is CCULaP} \\ \text{otherwise} & - \text{ may develop CCULaP} \end{cases}$$

For infectious factors

Isx (Inf) = 0,0002X(3) – 0,0066X(4) – 0,0005X(7) + 0,0224X(11) +
+ 0,0067X(13) - 0,0003X(19) – 0,0018X(20) + 0,0061X(26) + 0,0054X(27)

decision rule has the form

$$\text{If } Isx(Inf)\begin{cases} < 0{,}35 & - \text{ there is no CCULaP} \\ > 0{,}50 & - \text{ there is CCULaP} \\ \text{otherwise} & - \text{ may develop CCULaP} \end{cases}$$

For hereditary factors

Isx (Gen) = - 0,0886X(4) + 0,0036X(5) – 0,0017X(7) + 0,1368X(8) -
- 0,0048X(9) + 0,6195X(10) – 0,0179X(13) - 0,0008X(16) + 0,0207X(27)

decision rule has the form

$$\text{If } Isx(Gen)\begin{cases} < 0{,}28 & - \text{ there is no CCULaP} \\ > 0{,}45 & - \text{ there is CCULaP} \\ \text{otherwise} & - \text{ may develop CCULaP} \end{cases}$$

For medicinal factors

Isx (Terapi) = 2,023 - 0,0001X(1) - 0,0292X(2) + 0,0008X(14) + 0,0005X(16) -0,0011X(19) - 0,0026X(20) – 0,0035X(21) + 0,0206X(23) - 0,0094X(25) +0,0146X(26)

decision rule has the form

$$\text{If } Isx(Terapi) \begin{cases} < 0{,}50 & - \text{there is no CCULaP} \\ > 0{,}57 & - \text{there is CCULaP} \\ \text{otherwise} & - \text{may develop CCULaP} \end{cases}$$

for combined case

Isx (Tero) = 0,0307X(2) + 0,0009X(3) - 0,0015X(5) - 0,002X(9) - - 0,0857X(11) + 0,0028X(12) + 0,0267X(13) + 0,0225X(15) - 0,001X(16) - - 0,0008X(19) + 0,0047X(29)

decision rule has the form

$$\text{If } Isx(Terapi) \begin{cases} < 0{,}30 & - \text{there is no CCULaP} \\ > 0{,}75 & - \text{there is CCULaP} \\ \text{otherwise} & - \text{may develop CCULaP} \end{cases}$$

Where

X(1) -	Leukocyte	X(11) -	CD16,%	X(22) -	Fag.,%
X(2) -	Lymphocyte%	X(12) -	CD16,abc	X(23) -	C3,
X(3) -	Lymph.abs	X(13) -	CD20,%	X(25) -	SIK
X(4) -	CD3, %	X(14) -	CD20,abc	X(26) -	IL-1β
X(5) -	CD3,abc	X(15) -	CD25, %	X(27) -	TNFα
X(7) -	CD4,abc	X(16) -	CD25,abc	X(29) -	IL-6
X(8) -	CD8,%	X(19) -	IgG	X(30) -	IL-4
X(9) -	CD8,abc	X(20) -	IgA		
X(10) -	CD4/CD8	X(21) -	IgM		

The obtained results formed the basis of the software program "Prediction of development of congenital crevices of the upper lip and palate in pregnant women, taking into account various risk factors" (CCULaP), which made it possible to automate the calculation process. The software product "CCULaP" is implemented in the algorithmic language Visual Basic 6.0.

CONCLUSION

As a result of the study, models and decisive prediction rules for congenital clefts of the upper lip and palate were obtained, as well as the software for predicting the development of congenital clefts of the upper lip and palate of the fetus taking into account various risk factors of different nature (CCULaP) were developed.

SUMMARY

The work is devoted to the construction of linear mathematical models of prognosis of congenital cleft lip and palate in the context of risk factors of different nature: environmental, infectious, hereditary, medicinal, combined. The method of least squares is used in the construction of the integral characteristic. With the aim of achieving effective assessments in the construction, the coefficients of the model superimposed condition of their effectiveness is not below the level of $p<0.05$ according to student's criterion.

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