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Cluster analysis as a method of mathematical interpretation of immunological parameters in health workers

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Abstract. The monitoring of metabolic and immunological processes in individuals exposed to occupational risk factors, is one of the components of a preventive approach to improving the health levels in working population. However, the diagnostic value of laboratory indexes appears varying. Aim It is therefore necessary to identify the most optimal set of indexes that can be used as biomarkers. Methods The achievements of modern mathematics can substantially extend our potential to explore the occupational and work-related diseases in medical workers. Results As a method, cluster analysis can be used for substantiating the criteria for estimating occupational hazards, as well as for developing a risk assessment concept when analyzing latent forms of chronic diseases in health workers. Conclusions The study has produced a number of conclusions validating the dependence between the risk of chronic diseases in medical workers they exposure to harmful occupational factors. In our study, comprehensive estimations covered not only the qualitative data relating to status and professional activity of health workers, but also such important quantitative data as immunological indexes that reflect the level of immune defence in medical workers. Such an approach gives the opportunity to expose, in a timely manner, additional diagnostic signs and to enhance the efficiency of therapeutheic measures for health workers.

1. Introduction

The increase in morbidity has been observed in the Russian Federation over the past decade among health workers. In terms of prevalence of chronic diseases (diseases of the circulatory, respiratory, digestive, musculoskeletal, nervous and genitourinary systems), medical workers rank the fifth, outscoring workers in such hazardous industries as chemical [4, 7].

Among the physical factors that affect health levels in medical workers is medical equipment and devices [1, 8, 11, 12, 13, 14, 15]. The high diseases incidence among medical workers can be attributed to the negative impact of physically worn and obsolete medical equipment, alongside with other harmful occupational factors (chemical, biological, and psycho-emotional). The degree of deterioration of medical equipment is as high as 70%–75% in most regions of the Russian Federation [9].

The situation is aggravated by climatic, geographical, and environmental contexts of the area where medical workers are based (European North of Russia), which are a potential cause of the increased level of their morbidity in combination with harmful occupational factors [2, 10].
Despite the traditionally high coverage of employees exposed to harmful occupational factors by periodic medical examinations, the picture of initially diagnosed somatic pathologies is grave, with severe, pronounced forms of chronic diseases prevailing. The on-site preventive medical examinations seem to fail to perform their main function of detecting, at an early stage, the signs of chronic diseases, which is of great importance both for health preservation and identification of the most appropriate preventive treatment method [5].

The monitoring of metabolic and immunological processes in individuals exposed to harmful occupational factors is one of the components of a preventive approach to improving the health levels in working population [6].

Since the diagnostic value of laboratory parameters varies, it is necessary to choose the most optimal informative indicators that can be used as biomarkers [3].

2. Methods
The morbidity rate among 3013 doctors and nurses – the employees of a typical health care institution in Arkhangelsk Region – was studied on the basis of data obtained through annual periodic preventive medical examinations and this survey. The related immunological studies were conducted at the Institute of Environmental Physiology.

3. Results
The analysis has shown that the most representative categories of chronic diseases in the studied group of medical workers are the diseases of:
- digestive system (t = 1);
- circulatory system (t = 2);
- urogenital system (t = 3);
- respiratory (t = 4);
- neoplasms (t = 5);
- other (t = 0).

The tool to determine the likelihood of developing a certain disease is offered by Multiple Logit Model in SPSS (Statistical Package for the Social Science). Please see Table 1 for the parameters of logistic regression.

| Diagnosis | Variables       | B    | Wald  | Degree of freedom | Exp(B) |
|-----------|-----------------|------|-------|-------------------|--------|
| Diseases of circulatory system | absolute term   | -1,457 | 4,281 | 1                  | -      |
|                      | department/unit | 0,936 | 5,546 | 1                  | 2,551  |
|                      | position        | -19,833 | 4,000 | 1                  | 0,000  |
|                      | sex             | -0,728 | 4,142 | 1                  | 0,483  |
|                      | number of diseases | 0,936 | 7,317 | 1                 | 2,549  |
|                      | work experience | 0,015 | 5,109 | 1                  | 1,015  |
|                      | leukocytes      | -0,138 | 5,008 | 1                  | 0,871  |

The values in column Exp (B) indicate how many times the chances of developing the diseases change when the corresponding value of the variable changes by one. The indicators that have the greatest impact on the value of Yt are given in Table. 2.


Table 2: The most important indicators affecting the likelihood of developing the disease (Yt).

| T | Disease                              | Indicators, in descending order of influence                                      |
|---|--------------------------------------|-----------------------------------------------------------------------------------|
| 1 | Diseases of the digestive system     | monocytes, CD3+, neutrophilic leukocytes, CD71+, CD95+                            |
| 2 | Diseases of the circulatory system   | monocytes, CD8+, department/unit, number of diseases                              |
| 3 | Diseases of the genitourinary system | CD3+, CD8+                                                                         |
| 4 | Diseases of the respiratory system   | CD95+, position, Department, leukocytes                                          |
| 5 | Neoplasms                            | neutrophil leukocytes, monocytes, CD71+, CD8+, phagocytic number, sex             |

Thus, knowing the set of parameters characterizing a particular employee, it is possible to determine the probability of occurrence in them of the disease in question.

The properties of the model allow one to compare not only the percentage of the disease probability in one particular employee, but also the rate of their occurrence in different employees. In particular, it is possible to compare the probability of disease (Yt), using the same set of parameters, but assuming that one employee is a doctor ( ) and the other is in the category of "average medical personnel" and for him.

The factors affecting the resulting variable Y are diverse (some of them are measured in nominal scale, while other variables are quantitative). The analysis of the data array containing information about the employees of the medical and diagnostic unit at a health care institution can also be carried out by way of dividing the objects under observation into clusters. The number of clusters is taken equaling 8, and the assumption is made that observations fall into clusters according to the diseases listed in Table 3.

Table 3: Disease categories used in the processing of data in SPSS.

| Value of indicator | Presence of diseases                                      |
|--------------------|----------------------------------------------------------|
| 1                  | digestive system                                        |
| 2                  | circulatory system                                       |
| 3                  | urogenital system                                        |
| 4                  | respiratory                                              |
| 5                  | endocrine system                                         |
| 6                  | musculoskeletal system and connective tissue             |
| 7                  | other cases                                              |
| 8                  | neoplasms                                                |
| 9                  | disease not specified                                    |

The measure of the distance between objects is the Euclidean distance. This distance can be found by using the formula for i-th and j-th observations (i, j = 1, 2,..., 96):

\[ d_{ij} = \sqrt{\sum_{k=1}^{m} (x_{ik} - x_{jk})^2}, \]  \( \text{(1)} \)

where k is the variable number, k = 1,..., m (22 values correspond to the factors in tables 1, 2 and the value of the resultant trait Y);

and - values of the k - th factor in the i-th and j-th observations, respectively.

For example, we find the distance to the centers of the clusters identified for a specific employee with a set of factor values (X1, ..., X22) using the formula (1). We get eight values. In particular, distances are obtained for an employee who is not in the control group (i = 97):  = 246,52;  = 232,71;  = 1838,96;  = 1194,50.
The distance is the smallest. We believe that this particular employee belongs to the fourth cluster and may be exposed to respiratory diseases.

Thus, the smallest of the distances to the cluster centers determines to which cluster this particular employee belongs and what measures need to be taken to improve the values of the indicators that, according to the General characteristics of the cluster, can lead to the most common diseases in them.

We have found that the informative diagnostic signs or precursors of chronic diseases for differential diagnosis are: CD3+, CD71+ and CD95+ (diseases of digestive system); CD8+ (diseases of circulatory system); CD3+, CD8+ (diseases of genitourinary system); CD95+ (diseases of respiratory system); and CD8+, CD71+ (tumors). We refer to the detected changes as "immunological symptoms" corresponding to a certain group of chronic diseases. The total percentage of correctly received answers equaled 98%.

4. Conclusions

The risk of chronic diseases in health workers depends on the impact of occupational factors. The proposed method of mathematical interpretation of immunological parameters of blood allowed identifying a set of immunological symptoms as predictors of chronic diseases. The detection of immunological symptom in a medical worker during preventive examinations should be considered as a predisposition or a possible presence of a chronic somatic disease with subsequent development of a complex of diagnostic and therapeutic measures.

The study relied a comprehensive assessment of not only qualitative data that relates to the occupational status of workers, but also important quantitative data – immunological indicators that reflect the level of immune protection in health workers.

The proposed concept of the use of immunological biomarkers for early diagnostics of latent forms of chronic diseases during preventive examinations, has shown its effectiveness for the medical support of health workers in the course of their work, and is being successfully implemented by health care institutions in Arkhangelsk Region.

Attention should be paid to improving working conditions and eliminating occupational risk factors; the use of laboratory diagnostics of latent forms of chronic diseases; timely, quality diagnostics and treatment of work-related pathology with focus on prevention.

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