

PROGNOSIS OF RESISTANT TUBERCULOSIS COURSE AMONG CHILDREN AND TEENAGERS

¹ Bekembayeva G.S., ² Tashpulatova F.K.

¹ NJSC "Medical University Astana", Republic of Kazakhstan

² Tashkent Pediatric Medical Institute, 100125 Uzbekistan Tashkent, Bogishamol 223

✓ Resume

The simulation mathematical model serves not only for mathematical calculations, but also for formation of system ideas of epidemic process of a tuberculosis infection. By means of the specified model, there is an opportunity to estimate efficiency of the differentiated antitubercular actions concerning groups of the increased risk, their influence on an epidemiological situation.

Key words: tuberculosis, epidemiology, children, model, risk of group

ПРОГНОЗ РАЗВИТИЯ РЕЗИСТЕНТНОГО ТУБЕРКУЛЕЗА СРЕДИ ДЕТЕЙ И ПОДРОСТКОВ

¹ Бекембаева Г.С., ² Ташпулатова Ф.К.

¹ НАО «Медицинский университет Астана», Республика Казахстан.

² Ташкентский Педиатрический Медицинский Институт

✓ Резюме

Имитационная математическая модель служит не только для математических расчетов, но и для формирования системных представлений об эпидемическом процессе туберкулезной инфекции. С помощью указанной модели, есть возможность оценить эффективность дифференцированных противотуберкулезных мероприятий в отношении групп повышенного риска, их влияние на эпидемиологическую ситуацию.

Ключевые слова: туберкулез, эпидемиология, дети, модель, риск группы.

БОЛАЛАР ВА ЎСМИРЛАР ОРАСИДА ДОРИЛАРГА ТУРҒУН СИЛ РИВОЖЛАНИШИ ПРОГНОЗИ

¹ Бекембаева Г.С., ² Тошпўлатова Ф.К.

¹ МАЖ(НАО) «Астана Тиббиёт университети», Қозоғистон Республикаси

² Тошкент педиатрия тиббиёт институти

✓ Резюме

Имитацион математик модель нафақат математик ҳисоблар қилиш учун, балки сил инфекциясининг эпидемиологик жараёни ҳақида тизимли тушунча ҳосил қилишга хизмат қилади. Ушбу модель ёрдамида хавф гуруҳлари орасида силга қарши дифференциалашган чора- тадбираларнинг самарасини ва уларнинг эпидемиологик ҳолатга таъсирини баҳолаш имконияти мавжуд.

Калит сўзлар: сил, эпидемиология, болалар, модель, хавф гуруҳлари.

Relevance

The Republic transition to market relations, having entailed going far social transformations, put most countries population in extraordinary

conditions. Nowadays in CIS-republics the results of social and epidemiological experiment of TB-infection growth were observed on a country scale,

when the management priorities and evaluation of phthisiological service were changed [1,2]. The more significance acquired economical and mathematical ways of management. The task of control epidemiological process, planning and timely carry out anti-epidemiological measures, determination tasks regularity of anti-tuberculosis service cannot be solved without operative prognosis of epidemiological situation on tuberculosis [3]. In this connection it is actual to carry out short-term prognosis of epidemiological tuberculosis indices among children and teenagers in the Republic. The prediction of epidemiological process was based on detection and study its course regularities [4,5]. For deep study process regularities it was necessary to use systemic analysis of one tool mathematical simulation [6].

The simulation as a variety mathematical model served not only for mathematical calculations, but for formation systemic imaginations on epidemic process of tuberculosis infection. With the help of given model the possibility to evaluate efficacy of differentiated anti-tuberculosis measures on increased risk groups and their influence on epidemiological situation occurred.

The data of 1918 showed positive tendency stabilization of children morbidity situation in Kazakhstan. It was marked the decrease of index from 13,3 per 100000 population in 2017, and, in 2018 it was 11,8 per 100.000 population. The teenagers morbidity was 47,9 per 100.000 population in 2017, but in 2018 it was 46 per 100.000 population in 2018. It was considered that decrease was caused by general tendencies of epidemiological situation on tuberculosis in the Republic but not real reduce of infection reservoir among children. The trouble was the fact of annual safety and increase specific weight of destructive pulmonary tuberculosis among the primary revealed children, and, it was 11,4%. But at the same time from the generalized TB-forms 4 children died which was 0,08 per 100.000 population. And in 2018 the morbidity was 0,3 in children per 100.000 population. One of the causes was non-qualitative formation of tuberculosis risk groups in PMSC (prediction medical sanitary care) net.

Study dynamics tendencies of epidemiological situation and prediction construction indices for the next years became priority direction of anti-tuberculosis institutions in resistant tuberculosis prevalence period. It is obvious that the prediction being maintained on hypothesis with keeping existed tendencies in conditions of non-stable economic position and social conditions influencing essentially on tuberculosis process development cannot be long-term.

Last decade the main danger of tuberculosis endemy development became the increased number of sick people with tuberculosis and being affected with mycobacterium tuberculosis resistant to anti-

tuberculosis drugs including children and teenagers. The rate of primary multi-resistant tuberculosis was in 1,5 times higher among the teenagers than in children, and, occurrence of secondary multi-resistant tuberculosis was on the same level. The treatment efficacy of such patients mainly depended on possibility of timely and objective control of its behavior. In connection with it the search of new ways of determination for evaluation clinical situation and detection reveal factors characteristic for the patients with risk development drug-resistant tuberculosis will promote timely change of therapeutic tactics and treatment correction.

The aim of study was creation mathematical model of prediction for drug-resistance and determination factors, making the most influence on morbidity with drug-resistant forms of tuberculosis among children and teenagers.

Material and methods

Methods of study were the correlation and factor analyses, method of main components, imitation simulation in the research. For prediction epidemic process of given study the work out of equalization with use method of binary logistical regression was carried out. The study with method of main components was also performed where the interrelation structure of some indices in dynamics of correlation analysis was carried out. At prediction of timely series epidemiological indices the support was on supposition that the main factors and tendencies of last period, which determined the course of tuberculosis process, had definite inertness and were preserved for prediction period, and together with, they wouldn't change in connection with last indices and do it a little.

For elucidation occurrence causes and tuberculosis development among children and teenagers with primary revealed pulmonary tuberculosis and drug-resistant forms of TB the special map for the primary revealed patients with drug-resistant tuberculosis of respiratory organs, was worked out. The map reflected the next factors: patient's age, social status, clinical form of TB, data of bacterial diagnosis, TDS tuberculin diagnosis, presence of BCG scar, living and domestic conditions, number of family members, social well-being of family, presence of associated diseases, contact with tuberculosis patient, carry out chemical prophylaxis, terms of conversion abacillation and closing decomposition cavity.

Results and discussion

There were two groups of patients: 105 people with TB MRS (the first main group) 72 children and teenagers with the primary revealed tuberculosis of respiratory organs; (the second control group) they got treatment in ATD clinic at department of pulmonary tuberculosis for children and teenagers.

For prediction of drug resistance TB the various

social and medical factors making influence on its development were researched. After preliminary study and further processing them 14 features were selected (X_{1-14}): sex, age, material and living conditions, place of location, method of reveal, complaints at admission, presence of contact with tuberculosis person, size of BCG scar, data of tuberculin diagnosis, clinical form of tuberculosis, clinical general blood analysis, prevalence of process, associated diseases, complications of tuberculosis process. Then the researching features were processed on computer with binary logistical regression complex programs.

At study interrelation DR (drug resistance) with different clinical and social factors the next data were taken. By the feature «sex» in selection with primary revealed respiratory tuberculosis were prevailed 55,6% boys, the girls were 44,4%. Among children and teenagers with drug resistant tuberculosis, on the contrary, prevailed 61,9% girls, 38,1% boys were sick. The contingent mainly consisted of teenagers from 15 to 17 years old and they were 67,2%; from 12 to 14 years old were 22,6%; from 7 to 11 years were 6,8%; children of junior age group from 1 to 6 years were only 3,3% cases. Among sick persons prevailing city residents were 68,4% cases above country people 31,6%. The children and teenagers of both groups were mainly (62,5 % and 53,3%) during prophylactic examination. The social and living conditions of children and teenagers in both groups were unsatisfactory in 55,6% and 62,9% cases accordingly. It is necessary to mark that in cases of reveal the drug resistant tuberculosis the unfavorable factors were marked in many percentages of cases, but the true differences between groups were not taken ($p > 0,05$).

The analysis of post-vaccine BCG scars showed that at patients with drug resistant tuberculosis the rate of post-vaccine scars with size under 2 mm was true higher (10,5%), than at the patients with the first revealed tuberculosis (1,4) ($p < 0,01$). The results of tuberculin diagnosis at children and teenagers of both groups the true differences were not revealed (81,3% и 81,7% accordingly).

The feature “clinical tuberculosis form” was divided into seven categories according to modern clinical classification. From the clinical forms of tuberculosis in both examining groups the most often the infiltrate pulmonary tuberculosis occurred (56,9% and 84,8%) cases accordingly. Then by disease rate the primary tuberculosis complex (12,5% and 9,5%), exudative pleurisy (18,1% and 1,9%) were diagnosed. The pulmonary focal tuberculosis (5,6% and 1,0), disseminated pulmonary tuberculosis (2,8% и 1,0%) were less revealed, and, almost with the same frequency the tuberculosis of intra-thoracic lymphatic nodes (per 1,4% and 1,9% accordingly) was diagnosed, and, least of all were tuberculosis of peripheral lymphatic nodes (2,8%) at patients with primary diagnosed tuberculosis.

From seven clinical forms of tuberculosis the statistically meaning difference ($p < 0,01$) between patients of the first and second groups was marked at reveal exudative pleurisy of tuberculosis etiology. Moreover, the exudative pleurisy was in ten times more diagnosed in the drug resistant tuberculosis patients than in persons with tuberculosis of lymphatic nodes (LN).

The cavities of decomposition at primary revealed patients were in 61,4%, and in patients with drug resistancy it was 67,3%, and, there was no revealed true difference between groups ($p > 0,05$).

At analysis feature “bacteriodischarge” it was marked the true ($p < 0,01$) predominance of massive bacteriodischarge in patients with MDR (multi drug resistance). In the first group of examined patients the bacteriochargers were 8 (5,7 %), but in the second group the bacteriochargers were 82 (86,1%) people. By the method of bacteriological seeding in patients with primary revealed tuberculosis the MBT (mycobacterial tuberculosis) was sown only in 19 (13,7%) patients, and, in patients of the second group it was in 100% cases. Moreover, at the first revealed patients the process was characterized by benign and limited course, but the presence of massive bacteriodischarge supposed the possibility of development his drug resistant tuberculosis.

At clearing up tuberculosis contact at primary revealed children and teenagers in comparison with drug resistant tuberculosis patients there were true differences at contact with the family dead person (0% and 33,3% accordingly), with focus of TB MDR (multi drug resistance) (14% и 12,4% accordingly). Among the first revealed patients the contact in family with tuberculosis person without drug resistance occurred true more (30,6%), than in patients with drug resistant tuberculosis (6,7%) ($p < 0,05$).

The dynamics of stopping bacteriodischarge was the most demonstrative in the first group of patients, where it was at all 8 sick persons under 4 months of treatment (at 6 patients it was at the first two months of treatment, at 2 patients it was at the first third and fourth months). In the second group of patients the conversion of sputum was for the first 4 months 70 (85,4%) patients. These data were in accordance with S.S. Okulovskaya's studies who proved that phenomenon of drug resistancy in 56% was accompanied with increase growth intensity and bacteriodischarge massivity.

The prevalence study pathological changes in other organs revealed predominance of toxic changes in kidneys (1,4 and 34,4%) and in liver (9,4 and 21,0%) in patients with drug resistant forms of tuberculosis.

The bronchial damage rate had not small important fact in patients with DR (drug resistancy) (62,9% at patients with MDR against 33,3% in the first revealed persons), the differences in indices became high true ($p < 0,01$). The more often occurring

bronchus pathology as bronchial tuberculosis in patients with DR tuberculosis was diagnosed in 28,6% cases, the while it was not practically occurred in the first revealed patients.

The complications of tuberculosis process as pulmonary bleedings, exudative pleurisy, atelectasis, bronchus damages, cardiopulmonary and breathing insufficiency more true occurred in patients with drug resistant tuberculosis than in primary revealed patients (47,7% and 14,1% accordingly) ($p < 0,05$).

At clinical and general blood analysis the true differences on number of blood lymphocytes and hemoglobine: at the first revealed patients the lymphopenia took place in 19,4% cases, hypochromic anemia was 73,6%, but when the lymphopenia in patients with DR tuberculosis occurred in 57,1%, and anemia was 100% relatively ($p < 0,05$).

Thus, the risk factors were presence of contact with sick bacteriodischager, complications of tuberculosis process, changes in general blood analysis as as lymphopenia and hypochromic anemia, massive bacterioidischages, presence of accompanied kidney and liver pathologies.

We draw a conclusion on measure detection index named after Kox & Shell and Nadelcerkes. As at linear regression they also showed that part dispersion which can be explained with help of logistic regression. The part of dispersion explained by logistic regression in our case was 45,2%.

Control significance of coefficient differences from the zero was carried out by A.Wald's statistics that presented relative square according coefficient to it's standard error.

With the help of suggested mathematical model the new possibilities of prediction drug-resistant tuberculosis development, which were more characteristic for such patients, were revealed. The prediction of DR-tuberculosis allows to start timely adequate therapy.

Thus, the clinical structure, presence tuberculosis contact, BCG-scars, associated pathology, complications of specific process, changes in clinical general analysis and bacterioidischage in 105 patients with drug resistant tuberculosis were examined. For evaluation significance of clinical laboratory and social risk factors the diagnostic table with 14 features was worked out. For evaluation true category differences at comparisons in various groups the methods of binary logistic regression and criterion X^2 (for three parameters), for the the recognition method was chosen the analysis by A.Wald, where the detection measure was determined by Kox & Shell.

According to the model it is a patient with complicated course of tuberculosis process, massive bacterioidischage, absence of conversion sputum smear at the first months of treatment, torpid clinical laboratory dynamics of process. At secondary study of patient's sputum the "low" level of BAC in a month of treatment with ATM was revealed. The

great significance has presence of tuberculosis contact with MDR patient or family tuberculosis focus. At blood analysis study the lymphopenia and hypochromic anemia, and, at bronchoscopy the presence of specific bronchus damage can be observed. The use of suggested methods allow to make prediction of GR development at early terms of examination and to manage adequate treatment.

The study revealed new possibilities of prediction DR-tuberculosis at children and teenagers connecting with clinical laboratory and social factors which were very essential as they allowed more fully to predict the disease course and to make influence on adequate therapy. On the base of factors study the mathematical model was created, which allows with 89,8% to determine the character of disease course.

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