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RECURRENCE OF PULMONARY TUBERCULOSIS ASSOCIATED WITH COMORBIDITIES - CURRENT INTERDISCIPLINARY PROBLEM

Elena TUDOR[1], MD, PhD, associate professor, member-cor. ASMM,
Constantin IAVORSCHI[1,2], dr. hab. in med., professor, acad. AȘMM,
Albina BRUMARU[1], MD, PhD, associate professor,
Stela KULCIȚKAIA[2], MD, PhD, associate professor,
Lidia RÎVNEAC[1], MD, PhD, associate professor,
Valentina BOLOTNICOVA[1], MD, PhD, associate professor,
Andrei CORLOTEANU[1], doctorand,
Ecaterina AXENTII[1], phthisiopneumologist,
Anna MOSCOVCIUC[1], **MD, PhD,** associate professor,
Svetlana MATVYEYEVA[3], **MD, PhD,** associate professor,
Olga SHEVCHENKO[3], **DM,** professor,
Irina PÎRLOG[1], scientific researcher,
Corina ROTARU-LUNGU[1], scientific researcher,
Zinaida CIOBANU[1], scientific researcher

[1]IMSP Institute of Phthisiopulmonology "Chiril Draganiuc", Chisinau, Republic of Moldova
[2]Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
[3]Kharkiv National Medical University, Kharkiv, Ukraine

e-mail: eltudor@yandex.ru

Summary.

Introduction. The recurrence of pulmonary tuberculosis remains a significant public health problem in many countries of the world, despite the remarkable progress in the treatment and rehabilitation of patients with new cases of tuberculosis. It is demonstrated that the high incidence of recurrence of pulmonary tuberculosis is conditioned by the influence of some factors combination. Currently, the comorbidities, which impose the risk of disease recurrence directly or indirectly, are of a major importance. Thus, it is important to study the clinical and epidemiological characteristics of pulmonary tuberculosis recurrence associated with the comorbidities.

Materials and methods. There were studied 715 patients with pulmonary tuberculosis recurrence, including 503 patients with comorbidities, as well as statistical reporting data for the Right Bank region of the Dniester River and ATU (Autonomous Territorial Unit) of Gagauzia, Republic of Moldova during 2019-2021.

Results. The obtained results demonstrate that in phthisiopulmonology the presence of comorbidities constitutes a significant and important medico-social problem. In the structure of relapses associated with comorbidities, it was noted the predominance of extensive infiltrative processes, high frequency of cases with destruction in the lung tissue and bacillary cases. The need to review and improve the general antituberculosis measures accepted both in the work of phthisiopneumologists and primary care specialists is argued in order to improve the prognosis of TB treatment associated with comorbidities.

Conclusion. The recurrence of pulmonary tuberculosis associated with comorbidities requires an integrated multidisciplinary approach.

Keywords: pulmonary tuberculosis, relapse, rehabilitation, comorbidity, multidisciplinary approach, medical care.

Rezumat. Recidiva tuberculozei pulmonare asociată cu comorbidități - problemă interdisciplinară actuală

Introducere. Recidiva tuberculozei pulmonare rămâne o problemă semnificativă de sănătate publică în multe țări ale lumii, în ciuda progresului remarcabil în tratamentul și reabilitarea pacienților cu caz nou de tuberculoză. Este demonstrat, că incidența înaltă a recidivei TB pulmonare este condiționată de influența unor combinații de factori. În prezent, comorbiditățile, care impun riscul de recidivă a bolii direct sau indirect, sunt de o importanță majoră. Astfel, este important de a studia particularitățile clinica și epidemiologice a recidivei tuberculozei pulmonare asociate cu comorbidități.

Materiale și metode. S-a studiat 715 de cazuri cu recidivă a tuberculozei (TB) pulmonare, inclusiv 503 pacienți cu comorbidități, precum și datele de raportare statistică pentru regiunea malului drept al râului Nistru și UTA Găgăuzia Republica Moldova pentru perioada anilor 2019-2021.

Rezultate. Rezultale obținute demonstrează, că în ftiziopulmonologie prezența comorbidităților constituie o problemă medico-socială semnificativa și importantă. În structura recidivelor asociate cu comorbidități, s-a remarcat predominarea proceselor infiltrative extinse, frecvență înaltă a cazurilor cu distrucție în țesutul pulmonar și a cazurilor bacilifere.

Este argumentată necesitatea revizuirii și ameliorării măsurilor antituberculoase generale acceptate atât în activitatea ftiziopneumologilor, cât și a specialiștilor din asistența medicală primară pentru a ameliora prognosticul tratamentului TB asociate cu comorbidități.

Concluzie. Recidiva tuberculozei pulmonare asociată cu comorbidități necesită o abordare multidisciplinară integrată.

Cuvinte cheie: tuberculoză pulmonară, recidivă, reabilitare, comorbiditate, abordare multidisciplinară, îngrijiri medicale.

Резюме. Рецидив туберкулеза легких на фоне сопутствующей патологии – актуальная междисциплинарная проблема.

Введение. Рецидив туберкулеза легких остается значимой проблемой общественного здравоохранения во многих странах мира, несмотря на значительный прогресс в лечении и реабилитации больных с новыми случаями туберкулеза. Показано, что высокая частота рецидивов туберкулеза легких обусловлена влиянием некоторой совокупности факторов. В настоящее время большое значение приобретают сопутствующие заболевания, которые прямо или косвенно создают риск рецидива заболевания. Таким образом, актуально изучение клинико-эпидемиологической характеристики рецидива туберкулеза легких на фоне сопутствующей патологии.

Материалы и методы. Изучено 715 случаев рецидива туберкулеза легких (ТБ), в том числе 503 больных с сопутствующими заболеваниями, а также данные статистической отчетности по региону Правобережья Днестра и АТО Гагаузия Республики Молдова за период 2019-2021 гг. .

Полученные результаты. Полученные результаты свидетельствуют о том, что во фтизиопульмонологии наличие коморбидности представляет собой значимую и важную медико-социальную проблему. В структуре рецидивов, связанных с сопутствующей патологией, отмечено преобладание обширных инфильтративных процессов, высокая частота случаев с деструкцией в легочной ткани и бациллярных случаев. Аргументируется необходимость пересмотра и совершенствования общих противотуберкулезных мероприятий, принятых как в работе фтизиопульмонологов, так и специалистов первичного звена с целью улучшения прогноза лечения туберкулеза, связанного с сопутствующими заболеваниями.

Заключение. Рецидив туберкулеза легких на фоне сопутствующих заболеваний требует комплексного мультидисциплинарного подхода.

Ключевые слова: туберкулез легких, рецидив, реабилитация, коморбидность, мультидисциплинарный подход, медицинская помощь

Introduction.

The triggering phenomenon and the extent of the pulmonary tuberculosis spread (TB) relapses are the basic indicators that characterize the intensity of the epidemiological situation in tuberculosis. According to literature data [1, 2], the recurrence of pulmonary TB remains a significant public health problem in many countries of the world, despite the remarkable progress in the treatment and rehabilitation of patients diagnosed with TB new cases. It is demonstrated that the high incidence of pulmonary TB recurrence is conditioned by the influence of a combination of factors, among which the most expressive triggering mechanisms in the development of the reactivation of the tuberculosis process have been established [3] Currently, the comorbidities, which impose the risk of the disease recurrence, directly or indirectly, are of major importance. Since the 1990s, the public health system has been dominated by the problem of relapses of pulmonary tuberculosis in association with socially diseases, such as HIV infection, diabetes, alcoholism, chronic obstructive pulmonary disease (COPD), bronchial asthma [AB] and others. [4, 5, 6, 7]. In addition, in everyday life the population faces a multitude of factors that weaken the body's defensive mechanisms and lead to the development of pathologies. The complex interaction of environmental and genetic factors, people's way of life, chronic infections have generated the problem of mixed pathology. When one or more concurrent diseases are associated with pulmonary tuberculosis - new case or TB recurrence, there is a summation of clinical signs with the phenomena of mutual aggravation [8]. The comorbidity changes the strategy of detection and diagnosis, treatment and monitoring of patients [9]. The mutually aggravating relationship of pulmonary tuberculosis relapses with chronic comorbidities contributes to the interdisciplinary integration of specialists [10, 7]. At the same time, some aspects of this problem require research. The objective difficulties in the clinical, radiological, laboratory diagnosis of pulmonary TB relapses associated with comorbidities and the particularities of the manifestations depending on the age, gender, social status of the patients lead to the need to study the particularities of the evolution of pulmonary TB relapse in association with the comorbidities. The outbreak of the COVID-19 infection pandemic requires the study of pulmonary TB recurrence in the context of the comorbidity and interdisciplinary interaction in their management [11, 12].

The purpose of the research is to study the clinical and epidemiological peculiarities of pulmonary tuberculosis recurrence associated with comorbidities.

Material and methods. The subject of the retrospective-prospective study presented the cases of relapse of pulmonary tuberculosis associated with the comorbidities registered in the region of the right bank of the Dniester River and the Gagauzia Autonomous Territorial Unit (UTA) of the Republic of Moldova for the period of 2019-2021. The study included 715 adult patients (age≥18 years) with relapsed pulmonary TB, including 503 (70.3%) patients with comorbidities, including SARS-CoV-2 coronavirus infection. Patients with cases of retreatment and therapeutic failure were excluded from the study. It was used the clinical-epidemiological analysis method. Statistical processing and comparison of the obtained data was performed using the Student's t-test. The statistical validity of the obtained data was considered if $p<0.05$. The indicators characterizing the qualitative criteria are indicated by absolute number and relative value in percentage (%).

Results.

There were registered 305 (42.7%) cases with one concurrent disease and 198 (27.6%) patients with two or more diseases. The variability of the spectrum of concomitant pathology and frequency is as follows: HIV infection – 11.2%, chronic alcoholism - 11.2%, mental illness – 7.8%, liver diseases, including viral hepatitis B, C – 7, 5%, chronic obstructive pulmonary disease – 2.8%, diabetes – 2.5%, drug addiction – 2.1%, diseases of the gastrointestinal tract – 1.4%, COVID-19 - 1.6%, neoplasms of the lungs – 0.7%.

The main characteristics of cases with recurrent of pulmonary tuberculosis are shown in Table 1.

The data presented in the table demonstrate that the absolute number of patients with relapses during this period decreased from 430 in 2019 to 285 in 2020 (by 33.7%) and the passive detection still prevailed. At the same time, it can be noted the decrease in the incidence of pulmonary TB from 14.11 per

Table 1.

Characteristics of the patients with recurrent pulmonary tuberculosis.

Parameters and indicators	Years and frequency				
	2019 (n=430)		2020 (n=285)		P value
	abs.	%	abs.	%	
1. Gender:					
men	338	78,6	240	84,2	0,06
woman	92	21,4	45	15,8	
2. Age, years:					
18-34	83	19,3	40	14,0	0,189
35-64	299	69,5	211	74,0	
65+	48	11,2	34	11,9	
3. The clinical form of tuberculosis:					
nodular	2	0,5	2	0,7	
infiltrative	394	91,7	251	88,1	0,392
disseminated	14	3,2	16	5,6	
caseous	-	-	1	0,4	
fibrocavitary	20	4,6	15	5,3	
4. The presence of pulmonary destruction	143	33,3	171	60,0	0,001
5. The presence of bacillary forms	151	35,1	222	77,9	0,001
6. Comorbidity	163	37,9	142	49,8	0,002
7. The way of detection:					
prophylactic examination	157	36,5	125	43,9	0,005
addressing accusations to the IMMP	273	63,5	160	56,1	
8. Structure of lethality					
Total number of deaths, including:	76	17,7	65	22,8	0,092
deceaseds of advanced TB and complications	47	10,9	37	13,0	0,005
deceaseds of other causes	29	6,7	28	9,8	
9. Mortality rate per 100 thousand population	1,6		1,3		

100 thousand population in 2019 to 11.90 per 100 thousand registered population in 2020. This moment can be conditioned by several factors, including the COVID-19 infection pandemic with the related anti-epidemic and organizational measures, in particular, the regime with strict restrictions, led to interruptions in the process of active and timely detection of both new cases and relapses of pulmonary tuberculosis. This causes the worsening of the structure of the clinical forms of pulmonary TB and the phases of the tuberculosis process. In the foreground there were the extensive pulmonary processes, expressed in the form of infiltrative, disseminated and fibro-cavitation TB. Most significantly, this was expressed by an increase in the volume of destruction (bilateral process) and the proportion (%) of lung tissue destruction and mycobacterial emission. During the pandemic of the COVID-19 infection, the years 2019-2020, there were 8 patients with relapse of pulmonary TB in association with COVID-19, of which, 3 patients with a severe form and 5 with a moderate form of the evolution of the COVID-19 infection. There was noted no notable clinical and radiological progression of the tuberculous process.

The analysis of mortality, which is one of the most important and informative indicators characterizing the severity of the epidemiological situation and the level of organization, detection, diagnosis and treatment, in the cases with recurrence of pulmonary TB is on the increasing, from 17.7 % in the year 2019 to 22.8% in the year 2020, of which die from advanced TB and complications 10.9% in the year 2019 and 13.0% in 2020.

Discussions.

The obtained results confirm the previously published data regarding an increased risk of developing pulmonary TB recurrences and unfavorable outcomes among elderly patients with chronic comorbid pathology and the predominance of male patients [1]. Moreover, there were noted significant respiratory disorders in cases of tuberculosis associated with chronic obstructive pulmonary disease, which were observed regardless of age and gender, demonstrating that pulmonary tuberculosis creates conditions for the development, aggravation of concomitant pathologies of the respiratory system.

Through the synthesis of the relationship between the pathogenetic mechanisms, the clinical and epidemiological indicators of pulmonary tuberculosis and the parameters of associated diseases, it was found that the comorbid pathology in some cases presents the background of the reactivation of the tuberculous process, contributes to difficulties in establishing the diagnosis, an unfavorable outcome of treatment of the pulmonary TB relapse, and to an severe evolution worsening the prognosis of the patient's life. The tuberculosis infection was frequently one of the main triggers of COPD exacerbations and severe evolution. In the cases of diabetes associated with pulmonary tuberculosis, in the vast majority (up to 85%), diabetes was a pre-existing disease, on the background of which, at different stages of evolution, tuberculosis and its recurrences developed. The highest risk of association of pulmonary tuberculosis was observed in patients with prolonged decompensation of diabetes, regardless of type [6, 13].

The evolution of the polymorphous clinical picture in patients with pulmonary TB associated with comorbidities not only makes the detection and diagnosis difficult, but also complicates the treatment regimen. In addition, the comorbidities worsen patients' psycho-emotional state, which affected treatment adherence, compliance, and ultimately the therapeutic success.

In the context of the aforementioned, it is also worth noting that a number of medical and biological factors, among which MBT resistance to anti-tuberculosis drugs, have an impediment in successfully solving the problem of pulmonary TB relapses associated with comorbidities, which leads to a negative impact on patients' attitude towards the disease and on the treatment adherence.

Currently, taking into account the goals of the World Health Organization strategy to control of tuberculosis and the data reflecting the results of TB surveillance and monitoring, the increase in the number of comorbidities associated with pulmonary TB and the emergence of a new coronavirus infection indicate the need to optimize the collaboration of phthisiopneumologists and family doctors with infectious disease specialists, psychiatrists, endocrinologists, gastrologists, cardiologists, etc. It is important to emphasize that in the current epidemiological situation of TB, it is necessary to improve not only early detection methods, modernization of diagnosis and treatment of pulmonary TB relapses in patients with comorbidities, but also a wider use of rehabilitation methods, being a complement to therapy medicines. According to the definition of the Board of Directors of the American Thoracic Society and the Executive Committee of the European Respiratory Society „Pulmonary rehabilitation accompanies the essential care of the patient, which includes education, changes in the patient's lifestyle, improves the physical and mental health of patients with chronic respiratory diseases

and promotes long-term health improvement. The pulmonary rehabilitation program includes an assessment of the patient's condition, physical training, patient education, nutritional adjustment and psychological support" [10, 14]. Patient rehabilitation measures after the active phase of the disease play a significant role, which must be carried out taking into account the clinical form of TB, the nature of comorbidities, individual characteristics of the body, lifestyle and other aspects. All this underlines the extreme importance of the integration of specialists and a patient-centered approach in the management of patients, as they open new directions for the development of public health.

Conclusions

According to the obtained data, we conclude that comorbidity plays an important role in the development and evolution of pulmonary TB relapses. Understanding their complex interconnection requires a multidisciplinary approach, which will contribute to the improvement of the management of recurrence of pulmonary tuberculosis associated with comorbidities.

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