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FREQUENCY OF CLINICAL FORMS OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS, FIRST IDENTIFIED IN THE REPUBLIC OF AZERBAIJAN

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According to the World Health Organization about a quarter of the world population (1.7 billion), including about 70 million children and adolescents are infected with tuberculosis mycobacteria. Due to the fact that bacterial secretion among children and adolescents with tuberculosis is lower than that in adults, early detection, treatment and monitoring of dynamics are more difficult. The researches indicate that totally 7,839 primary tuberculosis patients were registered in the country in the last three years (2021–2023). 8.7 % (686 people) of the initially detected patients were children and adolescents. 70.4 % (483 people) and 29.6 % (203 people) of the registered children and adolescents had pulmonary and extrapulmonary tuberculosis. Out of them, 56.3 % (386 people) and 43.7 % (300 people) were men and women, respectively. 76.2 % (368 people) of the children and adolescents with pulmonary tuberculosis had infiltrative tuberculosis, 16.8 % (81 people) had focal tuberculosis, 1.2 % (6 people) had cavernous tuberculosis, 1.0 % (5 people) had fibro-cavernous tuberculosis, 1.9 % (9 people) had disseminated tuberculosis, and 2.9 % (14 people) had primary tuberculosis complex of the respiratory organs. During the research period, 203 people were diagnosed with extrapulmonary tuberculosis. 64 % (130 people) and 36 % of the patients were men and women, respectively. Out of the initially registered patients, 36 % (73 people) had tuberculosis pleurisy, 13.8 % (28 people) had tuberculosis of the central nervous system and meninges, 3.9 % (8 people) had tuberculosis of bones and joints, 3.4 % (7 people) had tuberculosis of the genitourinary tract, and 20.6 % (42 people) had peripheral lymph tuberculosis of the lymph nodes, and 4.9 % (10 people) had tuberculosis of the intestine, peritoneum and mesenteric lymph nodes. The high incidence rate of the severe clinical forms of tuberculosis such as cavernous, fibro-cavernous, central nervous system and meningeal tuberculosis among children and adolescents indicates the existence of deficiencies in early detection, as well as epidemiological tension.

Key words: latent tuberculosis, children and adolescents, primary tuberculosis, pulmonary tuberculosis.

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ЧАСТОТА КЛІНІЧНИХ ФОРМ ТУБЕРКУЛЬОЗУ У ДІТЕЙ І ПІДЛІТКІВ, ПЕРВИННО ДІАГНОСТОВАНИХ У РЕСПУБЛІЦІ АЗЕРБАЙДЖАН

За даними Всесвітньої організації охорони здоров'я (ВООЗ), близько чверті населення світу (1,7 мільярда осіб), включаючи близько 70 мільйонів дітей та підлітків, інфіковані туберкульозними мікобактеріями. Через нижчу бактеріальну екскрецію у дітей та підлітків з туберкульозом порівняно з дорослими, рання діагностика, лікування та моніторинг динаміки захворювання ускладнені. Дослідження показують, що за останні три роки (2021–2023) у країні було зареєстровано 7839 випадків первинного туберкульозу. 8,7 % (686 осіб) від числа вперше виявлених пацієнтів становили діти та підлітки. Серед зареєстрованих дітей та підлітків 70,4 % (483 особи) мали туберкульоз легень, а 29,6 % (203 особи) – позалегеневий туберкульоз. З них 56,3 % (386 осіб) були чоловіками, а 43,7 % (300 осіб) жінками. У 76,2 % (368 осіб) дітей і підлітків з туберкульозом легень був інфільтративний туберкульоз, 16,8 % (81 людина) осередковий туберкульоз, 1,2 % (6 осіб) кавернозний туберкульоз, 1,0 % (5 осіб) фіброзно-кавернозний туберкульоз туберкульоз та 2,9 % (14 осіб) первинний туберкульозний комплекс органів дихання. За період дослідження у 203 осіб було діагностовано позалегеневий туберкульоз. З них 64 % (130 осіб) пацієнтів були чоловіками та 36 % – жінками. Серед спочатку зареєстрованих пацієнтів у 36 % (73 особи) був туберкульозний плеврит, у 13,8 % (28 осіб) – туберкульоз ЦНС та мозкових оболонок, у 3,9 % (8 осіб) – туберкульоз кісток та суглобів, у 3,4 % (7 осіб) – туберкульоз сечостатевої системи, у туберкульоз сечостатевої системи периферичних лімфатичних вузлів, а у 4,9 % (10 осіб) – туберкульоз кишечника, очеревини та брижових лімфатичних вузлів. Висока частота тяжких клінічних форм туберкульозу, таких як кавернозний, фіброзно-кавернозний, ЦНС та менінгеальний туберкульоз, серед дітей та підлітків вказує на наявність недоліків у ранній діагностиці, а також на епідеміологічну напруженість.

Ключові слова: латентний туберкульоз, діти та підлітки, первинний туберкульоз, легеневий туберкульоз.

According to the World Health Organization (WHO), children accounted for approximately 4 % of newly diagnosed tuberculosis cases diagnosed in 2018–2022 [12]. In the WHO report for 2021, of the 10.6 million new cases of tuberculosis reported, 1.17 million are in children. The number of deaths from tuberculosis in 2021 was 1.59 million. Children aged 0 to 14 years accounted for 14 % of deaths [8, 13]. In most cases, tuberculosis in children was diagnosed after death [5, 8]. Approximately a quarter of the world's population (1.7 billion people), including about 70 million children and adolescents, are infected with Mycobacterium tuberculosis [8, 9]. At the same time, 50 million people worldwide are infected with

tuberculosis every year [7]. In economically developing countries, the number of people infected with tuberculosis is 100 people per 100,000 population [7, 15]. The mortality rate from tuberculosis in the structure of mortality from infectious diseases is up to 40 %. The lack of a systematic screening strategy for early detection of tuberculosis is the main reason that not all cases of the disease in children are detected at the initial stages [8, 14]. Increasing the effectiveness of tuberculosis prevention among children leads to a decrease in the incidence of tuberculosis and is one of the priority issues of pathobiology.

Without solving the problem of diagnosis and prevention of latent tuberculosis infection (LTBI), it

will not be possible to reduce the incidence of tuberculosis in all countries [8]. It is important to stimulate the development of new diagnostic tests with high predictive value for the diagnosis of LTBI throughout the world. Such tests can identify those who are highly likely to develop the disease among people infected with tuberculosis mycobacteria [8, 14].

Bacterial excretion among children and adolescents with tuberculosis is lower than in adults, as this indicator varies from 3.0 % at the age of 5–6 years and up to 25.8 % at the age of 15–17 years [1, 6]. In this regard, chemotherapy is often chosen empirically, and the possibilities of microbiological monitoring of treatment effectiveness are significantly limited. In most cases, X-ray diagnostic methods are the main examination tool for timely diagnosis of tuberculosis in children and adolescents, as well as for dynamic monitoring during treatment [4, 6, 11]. Epidemiological indicators of tuberculosis among children and adolescents reflect the general epidemiological situation with tuberculosis in the region [3, 10]. Despite the positive dynamics of tuberculosis statistics in our country, the incidence of severe clinical forms among children and adolescents remains high. In this regard, the study of the prevalence of clinical forms of tuberculosis among children and adolescents registered for the first time in the Republic of Azerbaijan is very relevant.

The purpose of the study was to establish the timely diagnosis of clinical forms of tuberculosis among children and adolescents registered in the Republic of Azerbaijan for the first time.

Materials and methods. Retrospective studies were conducted to determine the specific severity of

pulmonary tuberculosis and extrapulmonary forms of tuberculosis in children and adolescents, which were first identified by analyzing the "Official Statistical Reporting Form No. 8 on tuberculosis" approved by the State Statistical Committee of the Republic of Azerbaijan over the past three years (2021–2023).

Over the past three years (2021–2023), 686 children and adolescents with primary tuberculosis have been registered in the Republic of Azerbaijan. Among the newly identified children and adolescents, the study examined age, gender, pulmonary tuberculosis, extrapulmonary tuberculosis and their clinical forms (form No. 8). The statistical method of Student variation was used to determine the accuracy of the differences between the results obtained in the study.

$$t = \frac{M_1 - M_2}{\sqrt{(m_1^2 + m_2^2)}}$$

The differences were considered statistically significant at $t \geq 2$ ($p < 0.05$) [2].

Results of the study. Over the past three years (2021–2023), 7839 patients with primary tuberculosis have been registered. Children and adolescents make up 8.7 % (686 people) from the number of newly diagnosed patients. 70.4 % (483 people) of the newly registered children and adolescents had pulmonary tuberculosis, and 29.6 % (203 people) had extrapulmonary tuberculosis. 56.3 % of the identified patients were men, 43.7 % were women. The study analyzed the clinical forms of the disease in initially registered children and adolescents by age and gender. Table 1 shows the absolute indicators of clinical forms of pulmonary tuberculosis by age and gender.

Table 1

Absolute indicators of clinical forms of pulmonary tuberculosis by age and gender among children and adolescents with tuberculosis, first registered in the Republic of Azerbaijan over the past three years (2021–2023)

Pulmonary tuberculosis	gender	up to 1 year old	1–4 years old	5–13 years old	14 years old	15–17 years old	Total
Of these:	m	1	–	11	5	39	56
	f	–	–	8	2	15	25
Focal	m	4	5	27	18	131	185
	f	4	2	47	27	103	183
Infiltrative	m	–	–	–	1	1	2
	f	–	–	–	1	3	4
Cavernous	m	–	–	–	–	1	1
	f	1	–	–	1	2	4
Fibrous-cavernous	m	–	1	–	1	1	3
	f	–	3	–	1	2	6
Disseminated	m	1	4	2	–	2	9
	f	–	3	1	1	–	5
Primary tuberculosis complex of respiratory organs	m	–	–	–	–	–	–
	f	–	–	–	–	–	–

An analysis of table 1 shows that among children and adolescents with pulmonary tuberculosis who were first registered over the past three years, 53±2.3 % (256 people) were boys, and 47±2.3 % (227 people) were girls.

An analysis of the clinical forms of pulmonary tuberculosis by gender showed that the focal form was statistically more common in boys than in girls ($t=3.16$; $p<0.01$). On the contrary, the infiltrative

form was more common in girls, and the difference was statistically significant ($t=2.30$; $p<0.05$).

16.8±1.7 % (81 people) of the registered patients had focal tuberculosis (of which: 69.1 % (56 people) were boys, 30.9 % (25 people) were girls). Focal tuberculosis was detected in 66.7 % (54 people) of adolescents aged 15–17 years, in 1.2 % (1 person) of children under 1 year, in 23.5 % (19 people) of children aged 5–13 years and in 8.6 % (7 people) of children aged 14 years. Infiltrative tuberculosis

accounts for 76.2±1.9 % (368 people) of patients with pulmonary tuberculosis. 50.3 % (185 people) of patients with this clinical form were men, 49.7 % (183 people) were women. 75.8 % (279 people) of those with infiltrative tuberculosis were adolescents, 20.1 % (74 people) were children aged 5–13 years, 1.9 % (7 people) were children aged 1–4 years, and 2.2 % (8 people) were children under 1 year old. Of the initially registered patients, 6 (1.2±0.5 %) had cavernous tuberculosis, of which: 66.7 % (4 people) were adolescents, and 33.4 % (2 people) were children aged 14 years. The prevalence of fibrous-cavernous tuberculosis, which is considered one of the most severe clinical forms of pulmonary tuberculosis, was 1.0±0.5 % (5 people), of which: 60 % (3 people) were adolescents, 20 % (1 person) were 14 years old, 20 % (1 person) were children under 1 year old. The prevalence of disseminated tuberculosis is 1.9±0.6 % (9 people). Of these: – 33.4 % (3 people) are adolescents, 22.2 % (2 people) are children under 14 years old, and 44.4 % (4 people) are children aged 1 to 4 years. Primary tuberculosis complex of respiratory organs was detected in 14 patients (2.9±0.8 %), of which: – 2 people (14.3 %) are adolescents, 1 person (7.1 %) is 14 years old, 3 people (21.4 %) are children aged 5–13 years, 7 people (50 %) are children aged 1–4 years and 1 person (7.1 %) is children under 1 year old. Although

men predominate in general, the incidence of cavernous, fibrous-cavernous and disseminated forms of tuberculosis is higher among women. The analysis shows that the incidence among adolescents is 74.1 % (358 people). The incidence among children under one year of age was 2.3 % (11 people), among children aged 1–4 years – 3.7 % (18 people), and among children aged 5–13 years – 19.9 % (96 people).

The frequency of the infiltrative form was significantly higher than the focal one ($t=24.5$; $p<0.001$). In addition, the infiltrative form was statistically more common than the cavernous ($t=37.7$; $p<0.001$), fibrous-cavernous ($t=38.0$; $p<0.001$), disseminated ($t=36.8$; $p<0.001$) and primary respiratory tuberculosis complex ($t=34.1$; $p<0.001$). The clinical structure of pulmonary tuberculosis in children and adolescents was dominated by the infiltrative form, which was statistically significantly more common than other clinical forms ($p<0.001$). Destructive forms, cavernous and fibrocavernous tuberculosis, were rarely observed.

The study also analyzed the clinical forms of extrapulmonary tuberculosis in children and adolescents who were initially registered. The status of clinical forms of extrapulmonary tuberculosis depending on age and body type is presented in Table 2.

Table 2

Absolute indicators of clinical forms of extrapulmonary tuberculosis among children and adolescents with tuberculosis, first registered in the Republic of Azerbaijan over the past three years (2021–2023), by age and gender

Tuberculosis of extrapulmonary organs	gender	up to 1 year old	1–4 years old	5–13 years old	14 years old	15–17 years old	Total
Among them: Tuberculosis of the intrathoracic lymph nodes	m	1	5	7	2	4	19
	f	–	3	6	3	4	16
Tuberculous pleurisy	m	1	2	12	3	34	52
	f	1	1	5	4	10	21
Tuberculosis of the central nervous system and meninges	m	3	5	6	1	1	16
	f	2	6	4	–	–	12
Tuberculosis of bones and joints	m	–	1	4	–	1	6
	f	–	–	1	–	1	2
Tuberculosis of the genitourinary system	m	–	1	2	–	1	4
	f	–	–	2	–	1	3
Tuberculosis of peripheral lymph nodes	m	1	4	13	3	6	27
	f	1	4	6	1	3	15
Tuberculosis of the intestine, peritoneum and mesenteric lymph nodes	m	–	–	2	2	2	6
	f	–	–	2	–	2	4

An analysis of table 2 shows that in the period 2021–2023, 203 people with extrapulmonary tuberculosis were registered among children and adolescents. Of these, 64±3.4 % (130 people) were men and 36±3.4 % (73 people) were women. Of these, 17.2±2.6 % (35 people) had tuberculosis of the intrathoracic lymph nodes, 36±3.4 % (73 people) had tuberculous pleurisy, 13.8±2.4 % (28 people) had tuberculosis of the central nervous system (CNS) and meninges, 3.9±1.4 % (8 people) – tuberculosis of bones and joints, 3.4±1.3 % (7 people) – tuberculosis of the genitourinary system, 20.7±2.8 % (42 people) – tuberculosis of peripheral lymph nodes and 4.9±1.5 % (10 people) – tuberculosis of the intestine, peritoneum and mesenteric lymph nodes. Among the

clinical forms of extrapulmonary tuberculosis, tuberculous pleurisy was more common than others. Tuberculosis of the peripheral lymph nodes was in second place in terms of morbidity. Tuberculosis of bones and joints is a less common clinical form. The incidence among adolescents is 38.7 % (89 people), in children aged 5–13 years – 35.5 % (72 people), in children aged 1–4 years – 15.8 % (32 people), and in children under 1 year – 4.9 % (10 people). Tuberculous pleurisy is more common in the age group of 15–17 years, tuberculosis of the central nervous system (CNS) and meninges — in the age group of 1–4 years, tuberculosis of the intrathoracic lymph nodes, tuberculosis of bones and joints, tuberculosis of the genitourinary tract, tuberculosis of

peripheral lymph nodes, tuberculosis of the intestine, peritoneum and mesenteric lymph nodes – in the age group of 5–13 years.

It was found that tuberculous pleurisy is more common than tuberculosis of peripheral lymph nodes ($t=3.6$; $p<0.001$). At the same time, it was found that tuberculous pleurisy is more common than tuberculosis of the intrathoracic lymph nodes ($t=4.9$; $p<0.001$), tuberculosis of the central nervous system and meninges ($t=6.3$; $p<0.001$), tuberculosis of bones and joints ($t=9.1$; $p<0.001$) and tuberculosis of the genitourinary tract ($t=9.5$; $p<0.001$).

It was also found that tuberculosis of the peripheral lymph nodes is more common than tuberculosis of bones and joints ($t=5.8$; $p<0.001$) and tuberculosis of the genitourinary tract ($t=6.1$; $p<0.001$).

Discussion. Our results are consistent with the data of Ikeda S., et al. Their study also showed that pulmonary tuberculosis is prevalent in children and adolescents, and that the disease is especially common in adolescence. In our study, 74.1 % of the patients were adolescents aged 15–17 years, which confirms these results [5].

Marais B.J., et al. noted that the existing difficulties in the early diagnosis of tuberculosis in children lead to the development of severe clinical forms. Our results also indicate that the presence of

cavernous and fibrous-cavernous tuberculosis, as well as tuberculosis of the central nervous system and meninges, indicates the existence of certain problems in early diagnosis and the persistence of epidemiological tension [8].

In studies conducted by Sousa G.B., et al. it was also reported that infiltrative pulmonary tuberculosis prevails among adolescents. In our study, the infiltrative form accounted for 76.2 % of all cases of pulmonary tuberculosis and was statistically significantly higher than other clinical forms ($p<0.001$) [10].

Verkuijl S., et al. emphasized that cases of tuberculosis in children are not fully documented worldwide and that late diagnosis remains an urgent problem. The fact that severe clinical forms, especially tuberculosis of the central nervous system and tuberculosis of the meninges, accounted for 13.8 % in our study confirms these ideas and indicates the need to further strengthen early detection programs [12].

In addition, according to the World Health Organization, children make up approximately 10–12 % of the total number of tuberculosis patients. In our study, this figure was 8.7 %, which, in addition to being close to global figures, confirms the epidemiological significance of childhood tuberculosis in the country [13].

Conclusion

As can be seen from the analysis, the identification of severe clinical forms, such as cavernous, fibrous-cavernous tuberculosis, as well as tuberculosis of the central nervous system and meninges in children and adolescents, indicates deficiencies in early diagnosis, as well as the presence of epidemiological tension. Our study showed that 70.4 % (483 people) of the newly registered children and adolescents had pulmonary tuberculosis, and 29.6 % (203 people) had extrapulmonary tuberculosis.

56.3 % (386 people) of the identified patients were men, and 43.7 % (300 people) were women. The infiltrative form prevailed among patients with pulmonary tuberculosis (76.2 %), whereas in cases of extrapulmonary tuberculosis, tuberculous pleurisy was the most common clinical form (36 %).

Prospects for further research. It is planned to further strengthen measures for early diagnosis, examination of contact persons and detection of latent tuberculosis infection, as there is a relatively high incidence of severe clinical forms among children and adolescents in Azerbaijan.

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DIAGNOSTIC CRITERIA FOR LOCALIZED SCLERODERMA

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Localized scleroderma remains a complex diagnostic challenge due to diverse clinical manifestations and a lack of prognostic markers. A study of 113 individuals analyzed demographic, clinical, and laboratory parameters, including vascular endothelial growth factor levels, to assess vascular dysfunction. The disease demonstrates significant gender and age specificity, with onset peaks among young men and older women. Most lesions are plaque forms at the induration stage, indicating late clinical detection. Vascular endothelial growth factor has been shown to be an objective severity indicator, correlating directly with the extent of fibrosis. Based on these results, a novel multilevel prognostic model was developed that integrates risk factors, morphology, and angiogenesis markers. This model holds significant value for global dermatology, enabling the timely identification of high-risk patients, predicting the clinical course, and preventing irreversible tissue changes through early, personalized treatment.

Keywords: localized scleroderma, vascular endothelial growth factor, prognostic model, disease severity, endothelial dysfunction, risk factors.

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ДІАГНОСТИЧНІ КРИТЕРІЇ ЛОКАЛІЗОВАНОЇ СКЛЕРОДЕРМІЇ

Локалізована склеродермія залишається складною діагностичною проблемою через різноманітність клінічних проявів і відсутність чітких прогностичних маркерів. У дослідженні за участю ста тринадцяти осіб було проаналізовано демографічні, клінічні та лабораторні показники, зокрема рівень фактора росту ендотелію судин для оцінки дисфункції судин. Встановлено, що хвороба має суттєву гендерну та вікову специфіку, з піками дебюту серед молодих чоловіків і жінок старшого віку. Більшість уражень представлена пляшковою формою на стадії ущільнення, що вказує на пізні клінічне виявлення. Доведено, що фактор росту ендотелію судин є об'єктивним індикатором тяжкості патології, адже його концентрація прямо корелює з площею фіброзу. Спираючись на ці результати, розроблено новітню багаторівневу прогностичну модель, яка об'єднує фактори ризику, морфологію та показники ангіогенезу. Ця модель має вагомое значення для світової дерматології, оскільки дозволяє своєчасно виокремлювати пацієнтів із високим рівнем ризику, прогнозувати клінічний перебіг та запобігати незворотним змінам тканин шляхом ранньої персоналізації лікування.

Ключові слова: локалізована склеродермія, фактор росту ендотелію, прогностична модель, тяжкість захворювання, ендотеліальна дисфункція, фактори ризику.

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Scleroderma is a complex autoimmune disease that affects the skin, joints, blood vessels, and internal organs [15]. At a certain stage, the body begins to actively synthesize antibodies directed against the

vascular endothelium (the inner lining of blood vessels). Subsequent inflammation of the endothelial lining of small capillaries leads to thrombosis. Consequently, the tissues supplied by these vessels