

TUBERCULOSIS IN ADOLESCENCE – IDENTIFICATION AND TREATMENT OF HIGH RISK GROUPS AND HIGH RISK INDIVIDUALS

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Summary. Tuberculosis (TB) in teenagers has recently been an increasing phenomenon in our clinical practice. During the study, 37 (3.4%) teenage TB patients (pts) were analyzed retrospectively, from January 1992 – December 2001. Two groups of TB cases were registered: 15 pts in the period 1992 -1996, when we used only the old National Tuberculosis Program (NTP) and 22 pts in 1997-2001 when we used the new NTP by WHO recommendations and DOTS strategy. Generally, 94.6% were new cases and 5.4% defaulters. By the social status most of the pts 59.5% were students, 40.5% had bad habits (alcohol, drug abuse) with the village / city ratio of 67.6% / 32.3%. BCG scar hadn't been seen in 27.1% of the pts, while 86.5% had positive tuberculin skin test. Chronic cough and weight loss were dominant symptoms (91.9% pts), while parenchyma cavities were the leading radiological feature (75.8%). Extrapulmonary TB lesions, mostly on pleura (16.2%) and kidney (5.4%) had been noticed in 32.4% of the pts. Close contact; smear conversion rate and only the culture positive pts registered significance ($p < 0.05$). The pts (67.5% of them) were treated by Isoniasid (H), Rifampicin (R), Pyrazinamide (Z), Streptomycin (S) / Ethambutol (E), 29.7% H, R, Z and 2.8% H, R, Z, S, E. Most frequent therapy side effects were liver dysfunction (16.2%), while 10.8% pts had allergy on Z.

The increasing frequency of TB among teenagers (up to 6% of new cases annually, due to close contact with defaulters/treatment failures) does not seem to be a problem (successful conversion rate), but reflects the need for an effective implementation of NTP.

Key words: Tuberculosis, adolescences, directly observed therapy, antitubercotics

Introduction

It is an already established a fact that 10% of all infected people with Mycobacterium tuberculosis will develop an active disease throughout their life - 5% in first year since the infection and in the rest 5%, after a while, during the period of low immunity due to different circumstances in presence, or absence of various diseases (1). What form of tuberculosis (TB) will appear, among the other causes, depends on the age of infection too. Its an undoubtable fact that in puberty and adolescence, the organism is more sensitive to the tuberculosis bacillus and this sensitivity is rising amidst poor social and economic circumstances, as well as some diseases which compromise immunity (measles, whooping cough) (2).

Puberty and adolescence represent a special period of life when the development of sexual organs and secondary sexual characteristics, with its peak in ejaculation and menstruation start (1,2). In other words, it is one of the most dynamic phases of physiological growth in which morphological changes of the organism are the most visible. A special focus in phtysiogenesis during the puberty is on endocrine glands. Its function induces a significant immune deficiency in teenagers and adolescents during the puberty. In Europe and

North America, in times of higher incidence and morbidity of TB, the peak of case notification rate was found in young adults- teenagers with postprimary forms of fibrocaseous tuberculosis (1-3).

Basic characteristics of TB in adolescence are the postprimary forms. A prerequisite is in the lower natural defence mechanisms, which is partly conditioned by the genetic inheritance (4-6). Theoretically, superinfection by the TB bacilli is possible only in frequently treated infections, so home infections are often more extensive due to the renewed contact with ill person (5). Nevertheless, a high contact rate in those patients made a doubt about possible genetic inclination on TB infection, consider the higher incidence in some families among the others (as well infected) (5,6). A cohort of familiar studies by Homenko et al., in 1988 and 1990, show the inheritance of susceptibility to TB (from parents to children) associated with inheritance of some HLA halotips, precisely HLA-DR2 and HLA-B7 antigenes, whose owners had higher serum level of IgG antigenes on purified protien deriviate (PPD), especially in higher frequency in anergic patients (4). Moreover, in those patients, clinical and radiological features were so extensive, that specific immune reaction on TB made the impression of no control (6,7).

In recent years, the morbidity of TB among the adolescents in our county has slightly increased and considering its epidemiological, clinical, radiological and bacteriological characteristics, represents a special phenomenon in our clinical practice, which we try to explore in the light of the new National Tuberculosis Program (NTP).

Patients and methods

The clinical data of 1090 TB patients (pts), who were in period from January 1992-December 2001 diagnosed and initially treated at our Clinic, were retrospectively analyzed. Among those pts, 37 were between 15 and 19 years of age (teenagers-adolescents). Those pts were divided in two groups: first (I) of 15 pts who were hospitalized in the period of January 1992-December 1996, when we used old NTP and second (II) of 22 pts who were hospitalized in the period from January 1997 - December 2001, when we used the new NTP according to the recommendations of World Health Organisation (WHO) and Directly Observed treatment-Short Course (DOTS) strategy (7-10).

All pts were divided by the gender, age, presence or absence of bad habits (smoking and alcohol consumption, drug abuse), positive familiar history on TB (close contact with tuberculosis patient in family), social and economic status, presence/absence of BCG scar and category according to NTP. Presence/absence of fever, chronic cough and haemoptysis as well as its average duration till the moment of diagnosis/ hospitalisation were registered based on the clinical symptoms.

From diagnostic procedures we analyzed the results of:

- Postero-anterior chest radiography including the computed tomography in the presence of unreliable diagnosis, for sorts and extensivity of pulmonary lesions,
- Microbiological sputum examination (microscopy and culture (Lowenstein-Jensen)), with average conversion rates,
- Tuberculin skin test (0.1 ml or 3 I.U. intradermal application of Purified Protein Derivate (PPD) (upper third of volar of brachium), with reprimanding after the period of 72 hours), while the diameter of induration above 6mm and more was considered as a positive reaction and,
- In order to explore the pulmonary function status, sprometry was performed with flow-volume curve, and in the case of obstructive disturbances of pulmonary ventilation the bronchodilatator test was performed (two inhalation with metered-dose Salbutamol, repeating the spirometry after the 15 minutes).

During the antituberculous treatment there were observed:

- Sort of antituberculosis treatment,
- Presence/absence of allergic /toxic manifestations on antituberculous and,

- Result of initial phase of treatment (clinical, radiological and bacteriological).

All obtained results were analyzed by the method of descriptive and analytic statistics (nonparametric tests). Significances were estimated by the student's t-test between proportion of small independent specimens. Time series (cohorts) of incidence and sputum conversion are done on a year and a week level. All statistical calculations were done with Statistical Package for Social Sciences softwer, version 8.0, for Windows.

Results

In the ten-year period of observation (January 1992-December 2001), 1090 pts were treated from active pulmonary TB at our Clinic. From this number 37 (3.4%) pts were adolescents (teenagers), persons from 15 to 19 years of age. The case notification rates of those pts varied from 2.3% in 1992 to 5.14% in 2001 (Figure1 and 2).

Male pts were 21 (56.76% overall-54.54% in I group of pts and 60.0% in II), while 14 (37.84%) were female (45.46% in I and 40.0% in II), with average age of 18.35±1.55 y in I group of pts and 17.4±1.6 y in II. Overall age were 18.35±1.55 y. Most of them, 22 (59.46%) were students and pupils, 11 (29.74%) unemployed, 2 (5.4%) farmers and 2 (5.4%) factory workers. 15 (40.54%) had bad habits (alcohol and narcotic abuse, smoking cigarettes), with average pack/year ratio of 1.27±0.42/ 3.53±1.38. The village/city ratio was 67.6% / 32.3% (p> 0.05).

The BCG scar wasn't noticed in 10 (27.1%) of the pts, while 32 (86.49%) had positive tuberculin skin test. Tempestuous reactors were 12 (32.43%) with diameter of skin induration's bigger than 15 mm. Only 27.02% were tuberculin negative.

Among newly confirmed TB (I category) there were 35 (94.59%) pts, while 1 (2.7%) had relapse (II category) and 1 (2.7%) was a chronic case with multi-drug resistant (MDR) TB (IV category). A familiar close contact with TB patient was registered in 21 (56.76%), with significance in II group (p<0.05) and ratio between those two groups of 72.72%/33.33%. Extrapulmonary TB was in 12 (32.42%) pts, mostly on pleura (16.22%) and kidney (5.4%).

The most common respiratory symptoms were: haemoptysis in 11 (29.73%) pts, fever in 28 (75.68%), chronic cough in 30 (81.08%) and weight loss in 34 (91.89%). Radiologically, 9 (24.32%) pts had unilateral infiltrative lesions, 26 (70.27%) bilateral, while 28 (75.68%) had cavities which were often significant (p<0.05), among the other radiological forms. Spirometry showed the obstructive ventilation disturbances in 7 (18.92%) pts, while in 5 (13.51%) restrictive. Only 1 (2.7%) patient had positive bronchodilatator test.

Microbiological sputum examination showed 12 (32.43%) smear-positive cases and 25 (65.57%) on culture, while 13 (35.13%) were only on culture positive-significantly more in II group of pts. Average sputum conversion rates in II group of pts had significance (p<0.05) (Table 1 and Figure 3).

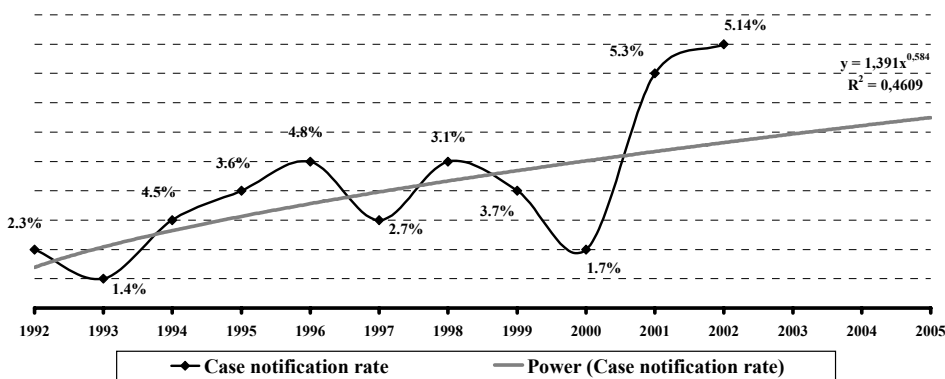


Fig. 1. Trendlines of teenage case notification rates

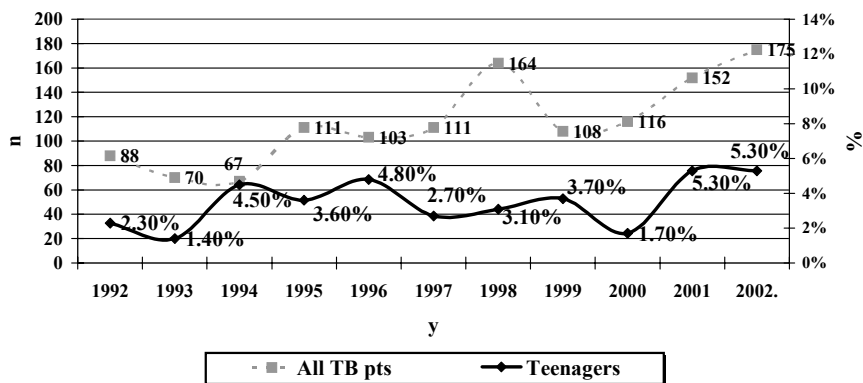


Fig. 2. Teenagers among all hospitalized TB patients

In order of category of TB (case definition), 11 (29.75%) pts were treated with Isoniasid (H), Rifampicin (R) and Pyrazinamide (Z) or Ethambutol (E), 25 (65.57%) with H, R, Z and Streptomycin (S) (59.46%) or E, while 1 (2.7%) was treated with H, R, Z, S and E. Significant number ($p < 0.05$) of pts from II group (65.57%) were treated with oral Prednisolone in the dose of 40/60 mg daily for four weeks period together with antituberculotics. Most frequent therapy side effects were liver dysfunction (16.2%), while 10.8% pts had allergy on Z (Table 2).

Table 1. Bacteriological sputum characteristics with average conversion rate on microscopy and culture.

	Bacteriological sputum characteristics with average conversion rate on microscopy and culture				
	Smear + (%)	Smear conversion rate (days)	Culture + (%)	Culture conversion rates (weeks)	Only on Culture +
I group (1992-1996)	40	4.66±1.51	66.1	5.1 ± 0.64	26.6
II group (1997-2001)	27.27 *	11.0 ± 5.6 *	68.1	3.73±1.33*	40.9 *
Overall	32.4	10.67±2.44	67.6	4.28±0.87	35.13

* $p < 0.05$

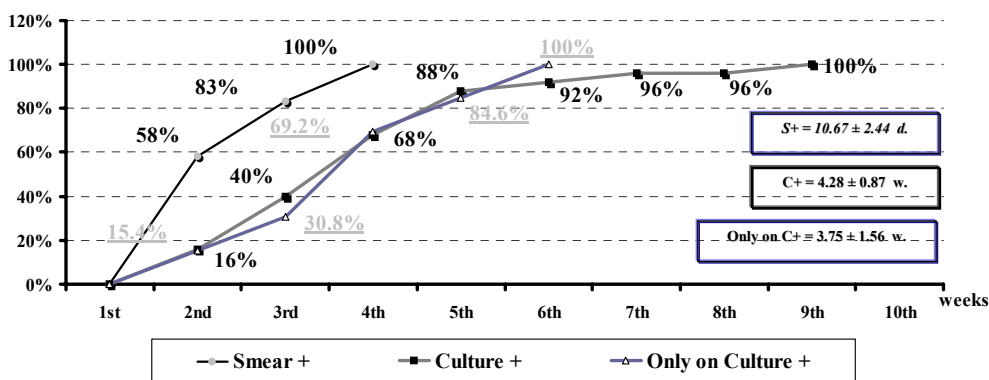


Fig. 3. Sputum conversion rates

Table 2. Initial treatment and toxic effects of antituberculous drugs

	Antituberculosis regimens			Oral Prednisolone (40/60 mg daily/4 weeks) (%)	Toxic effects – functional disturbances			
	H, R, Z / E (n / %)	H, R, Z, S / E (n / %)	H, R, Z, S, E (n / %)		Liver n/%	Hearing n/%	Arthritis n/%	Allergy (Z) n/%
I group (1992 –1996)	7 / 46.6% *	7 / 46.6	1 / 6.6	46.66	2 / 13.3	0 / 0	1 / 6.66	2 / 13.3
II group (1997 –2001)	4 / 18.8	18 / 81.8 *	0 / 0	65.57 *	4 / 18.18	3 / 13.63	3 / 13.63	2 / 9.09
Overall	11 / 29.75	25 / 67.57	1 / 2.7	56.76	6 / 16.22	3 / 8.1	4 / 10.81	4 / 10.81

* p < 0.05

Discussion

Puberty and adolescence represent the most dynamic phase of physiological growth in which morphological changes of the organism are the most visible (1,2,4). A special place in pathogenesis of TB as well as pathogenesis lies in lower natural immunity (5, 6). In recent years, incidence and morbidity of TB has slightly arisen and considering its epidemiological, clinical, radiological and bacteriological characteristics, represents a unique phenomenon in our clinical practice, which we try to explore, according to the implementation of new NTP (7-10).

The higher incidence and morbidity of TB among the adolescents is present in most of the middle- and high-incidence countries, as a consequence of social and economic circumstances, the migration of population and insufficient implementation of national programs (11-14). We analyzed clinical data of 37 adolescents among 1090 TB pts who were diagnosed and treated at our Clinic from January 1992 – December 2001, and divided them in two groups in order to evaluate effects of implementation of new NTP through the framework of initial (hospital) phase of antituberculosis treatment (7, 10,12,15).

Most of the pts were male (56.76%) with similar gender ratio between groups, while the average age was 18.35 ± 1.55 y. Among those pts the majority were students and 40.54% had the history of bad habits (alcohol and drug abuse, smoking habits) with average pack/year ratio of $1.27 \pm 0.42 / 3.53 \pm 1.38$, which is characteristic for the population in the East European transition countries with low annual personal income (8,16,17). The city/village ratio among those pts is also according to those data. Positive tuberculin reaction was noticed in 86.49% pts and they were also in I category of TB patients according to the NTP and WHO recommendation, while 10% didn't had a BCG scar at all (17,18).

Close contact in high percentage with active TB pts in a family, with statistical significance of the same among pts in II group, tells about the poor implementation of NTP in the period before 1997, while respiratory symptoms, extensivity of radiological features and sputum smear status confirm those findings similar to the results of Cojacariu et al. (16,19,20).

Therefore, the fast sputum conversion rate and adequate diagnostic and therapeutic tools in treatment of those pts, nevertheless of antituberculous side effects (allergy, toxic effects) epidemiologically made the population of TB teenager pts "non-complicated", but show on certain, specific number of unrevealed relapses and defaulters/treatment failures, who represents a "TB infection reservoirs", most probably resistant one and alarm for effective implementation of NTP and faster introduction of DOTS strategy on all levels of antituberculous treatment especially in extended phase of treatment (21-24).

As a conclusion, we can say that the increasing frequency of TB among adolescents up to 6% of new cases annually on our material, represents a unique phenomenon in our clinical practice. The main causes for those are close contact with relapses and defaulters/treatment failures inside the family, lower natural immunity in puberty and adolescence, poor socially status and social unacceptable habits. These factors contribute to the development of TB with extensive radiological features, often with extrapulmonary lesions, which results in the bad clinical condition of pts and many complications in the antituberculous treatment (25,26). The implementation of the new NTP and DOTS strategy does have its effects in a faster sputum conversion rate and provides a more rational screening of the high-risk family and individuals (27,28). So, TB in teenagers and adolescents does not seem to be a bigger epidemiological and clinical problem (successful and fast sputum conversion rate), but reflects the need for effective and sufficient implementation of NTP.

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TUBERKULOZA U ADOLESCENATA – IDENTIFIKACIJA VISOKO RIZIČNIH GRUPA I POJEDINACA

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Kratak sadržaj: Tuberkuloza (TB) u tinejdžera (12-19 godina starosti), poslednjih godina beleži lagani porast. Retrospektivnom analizom kliničkih podataka 1090 TB bol koji su tokom 1992.-2001. dijagnostikovani i lečeni u Klinici za plućne bolesti i tuberkulozu, 37 (3,4%) bili su adolescenti. Prvu grupu činilo je 15 bolesnika (1992-1996), kada je primenjivan stari Nacionalni Program za TB (NTP), i drugu 22 bolesnika (1997-2001.) kada smo koristili nov NTP po preporukama SZO (WHO) i DOTS strategiju. Ukupno, 94,6% bolesnika su bili novooboleli slučajevi, a 5,4% recidivi/hroničari. Bilo je 59,5% studenata, a 40,5% imalo loše navike, sa odnosom selo / grad - 67,6% / 32,3%. Bez BCG ožiljka je bilo 27,1% bolesnika, a 86,5% je imalo pozitivan tuberkulinski test. Vodeći simptom u 91,9% je bio hronični kašalj, dok su radiološki dominirale kavitacije u plućnom parenhimu (75,8%). Ekstrapulmonalne TB lezije su bile u 32,4% bolesnika, uglavnom na pleuri (16,2%). Bliski kontakt s obolelim od tb, samo na kulturi sputum pozitivni bol. i konverzija sputum pozitivnih bol. direktnom mikroskopijom, pokazivali su značajnost između ispitivanih grupa

($p < 0,05$). 67,5% je tretirano Isoniasidom (H), Rifampicinom (R), Pyrazinamidom (Z) i Streptomycinom (S) / Ethambutolom (E), 29,7% H, R, Z / E i 2,8% H, R, Z, S, E. Disfunkciju jetrenih enzima je imalo 16,2% bolesnika, a 10,8% alergijske manifestacije na Z.

Povećana incidenca TB u adolescentata - do 6% novootkrivenih slučajeva godišnje, izgleda ne predstavlja veći epidemiološki problem, obzirom na uspešnu i brzu konverziju sputuma, ali ukazuje na potrebu efektivnijeg sprovođenja NTP.

Ključne reči: Tuberkuloza, adolescencija, direktno kontrolisano lečenje, antituberkulotici