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ANALYSIS OF RISK FACTORS FOR THE TRANSFER OF LATENT TUBERCULOSIS INFECTION TO ACTIVE TUBERCULOSIS IN CHILDREN LIVING IN FAMILY TUBERCULOSIS FACTORIES

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Abstract.

Relevance. According to the WHO definition, latent tuberculosis infection (LTBI) represents a state of persistence of Mycobacterium tuberculosis in the absence of clinical manifestations of the disease, which can only be detected through immunological tests. Experts estimate that about one-quarter of the world's population is infected with LTBI, with a lifetime risk of reactivation ranging from 5% to 15%, particularly within the first five years after infection and predominantly during childhood. Within the framework of the global tuberculosis control strategy after 2015, special attention has been directed to the early detection and prevention of LTBI as a key element in reducing the incidence of new cases. However, to date, no "gold standard" exists for diagnosing and differentiating latent and active forms of tuberculosis in children. **Objective**. To study the anamnestic and social indicators of latent tuberculosis infection development and active tuberculosis course in children. **Materials and Methods**. A retrospective-prospective cohort study was conducted in accordance with the international STROBE standard. A total of 60 children were included and divided into two groups: Group 1 consisted of 40 children with latent tuberculosis infection, and Group 2 included 20 children with active tuberculosis. **Results**. It was established that the key social risk factors for tuberculosis activation were living in low-income, large, and single-parent families, poor housing conditions, low parental education, unemployment, and harmful habits. Among biological factors, low birth weight, perinatal CNS lesions, early childhood anemia, as well as concomitant chronic conditions (helminthic invasions, gastrointestinal and endocrine disorders, myopia, rheumatism) were identified. Epidemiological factors included contact with bacillary patients, lack of chemoprophylaxis, non-compliance with sanitary measures in households, living in families with HIV infection, and a history of COVID-19. **Conclusions**. Thus, the study confirmed the multifactorial nature of the risk of LTBI activation in children, where social, biological, and epidemiological components play a significant role. The authors emphasize the necessity of a comprehensive assessment of risk factors and their justified differentiation for latent and active tuberculosis forms, which has practical significance for prevention, early diagnosis, and rational monitoring of children in risk groups.

Key words: latent tuberculosis infection, active tuberculosis, children, tuberculosis infection focus.

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Kirish: JSST tomonidan ta'riflanganidek, latent sil infektsiyasi (LTI) - sil kasalligi jarayoni faolligining klinik belgilari bo'lmaganda, inson organizmiga tuberkulyoz mikobakteriyalarining patogen shtammlarining kiritilishiga barqaror immunitet reaktsiyasining mavjudligi [9]. JSST ekspertlarining ta'kidlashicha, sayyoramiz aholisining qariyb 25 foizi LTBI tashuvchilardir [10]. Yashirin sil kasalligining inson hayoti davomida faollashishi xavfi 5 dan 15% gacha o'zgarib turadi, bunda eng yuqori xavf patogen inson tanasiga kirgan paytdan boshlab birinchi besh yil ichida sodir bo'ladi, ko'pincha bola yoki o'smirlarda kuzatiladi [1, 4].

"2015 yildan keyin silga qarshi kurashish bo'yicha global strategiya"ning ustuvor maqsadi profilaktika yo'nalishiga ega bo'lgan shaxsiylashtirilgan tibbiyot paradigmasi hisoblanadi. Strategiyaning bir qismi sifatida e'tibor LTBI rezervuari bilan ishlashga qaratilgan bo'lib, bu sil kasalligining yangi holatlarini kamaytirishga olib keladi, bu faol sil bilan kasallangan barcha bemorlarni adekvat davolash choralari bilan birgalikda ushbu yuqumli kasallikni yo'q qilishni kafolatlaydi [2,5,7,8]. Bugungi kun nuqtai nazaridan, ftiziopediatriyadagi ko'plab tadqiqotlarga qaramay, latent sil kasalligi jarayonining faollashuvi uchun xavf omillarini o'rganish davom etmoqda [3], shuningdek, LTBIni erta aniqlash va latent va faol sil infektsiyasini differentsial tashxislash uchun oltin standartlar mavjud emas [2,4,6,10]. Sil mikobacteriyasi bilan kasallangan bolalar xavf guruhini ifodalaydi, bir qator mualliflarning fikriga ko'ra, boshqa xarakterdagi xavf omillari

birlashganda sodir bo‘ladi. So‘nggi yillarda yashirin sil kasalligi jarayonini faollashtirishda har bir xavf omilining hissasi va bahosini aniqlashtirish zarurati paydo bo‘ldi.

Tadqiqot maqsadi: Bolalarda LTBI rivojlanishi va uning faollashishi davrida epidemiologik anamnezning xususiyatlari va somatik patologiyaning tuzilishini o‘rganish.

Materiallar va usullar: Tadqiqot Samarqand davlat tibbiyot universitetining ftiziatriya va pulmonologiya kafedrasida olib borildi. 60 nafar bola tanlab olindi va ikki guruhga bo‘lindi: 1-guruhga latent sil kasalligi bilan kasallangan 40 nafar, 2-guruhga faol sil kasalligi bilan kasallangan 20 nafar bola kiritildi.

Yashirin sil kasalligi bilan kasallangan 1-guruhda o‘rtacha yoshi 7,5±0,5 yoshni tashkil etgan bo‘lsa, guruhda 11 nafar (55,0%) o‘g‘il va 9 nafar (45,0%) qiz bola bo‘lgan. Biroq, bemorlarning ushbu guruhida jins bo‘yicha sezilarli farqlar aniqlanmagan (p>0,05). DiagnostikaLTBI tashxisi bolani sil kasalligining faol shakli bo‘lgan bemor bilan aloqa qilish uchun tekshirilganda, shuningdek immunodiagnostika natijalariga asoslanadi. 2TE PPD-L bilan Mantu testi bilan papulaning o‘lchami o‘rtacha 12,1±0,4 mm (95% CI 10,2-13,9 mm) va «Diaskintest» rekombinant sil allergeni bilan test bilan - 2,2± 0,5 mm (95) % CI 1,6-2,87 mm). Tekshirilayotgan bolalarning ushbu guruhida 2TE PPD-L bilan Mantu testi ko‘p hollarda ijobiy natijalarni ko‘rsatdi (n=40; 90,0%), Diaskintest preparati bilan test esa salbiy natijalarni (n=20; 80,0%) ko‘rsatdi. BCG emlash 40 ta bolada (100,0%) amalga oshirildi va 27 (69,3%) bolada samarali deb baholandi.

Sil kasalligining faol shakllari bo‘lgan 2-guruhda 20 nafar bola o‘rtacha yoshi 9,8 ± 0,3 yilni tashkil etdi. Jins bo‘yicha tekshirilgan guruhda 11 (55,0%) o‘g‘il va 9 (45,0%) qiz bola bor edi. Silning faol shakllari bo‘lgan bemorlarning ushbu guruhida jins bo‘yicha sezilarli farq yo‘q (p>0,05). Ushbu guruhdagi bemorlarni aniqlash usullari: respirator sil kasalligining faol shakli bilan og‘rigan bemorlar bilan aloqada bo‘lishi tufayli tekshirilganda 6 ta (30,0%), tibbiy yordamga murojaat qilishda 5 ta holatda (35), profilaktik ko‘ril paytida14 ta (70,0%). Shunday qilib, tekshirilgan 11 bolada (55,0%) aloqa mavjudligi aniqlangan, 10 tasida (n=11; 90,0%) yaqin oila va turar joy aloqasi ustunlik qilgan. 4 bolaning epidemiologik tarixi (n=11; 36,3%) sil kasalligidan o‘lim mavjudligini aniqladi, va bu «o‘lim o‘choqlari» sifatida qabul qilindi. Biz tekshirgan 2-guruhdagi 9 nafar bola (n=11; 81,8%) massiv bakterial ajraladigan o‘pka sili bilan og‘rigan bemorlar bilan aloqada bo‘lgan, ulardan 4 tasida (n=9; 44,4%) manbada patogenning bir nechta silga qarshi dorilarga nisbatan chidamliligi borligi aniqlangan.

2TE PPD-L bilan Mantu testi bilan papula o‘lchami o‘rtacha 12,8±0,7 mm (95% CI 12,9-13,4 mm) va «Diaskintest» rekombinant sil allergeni bilan test bilan - 14,66± 0,4 mm (95) % CI 14,1-15,9 mm). Tekshirilayotgan bolalarning ushbu guruhida 2TE PPD-L bilan Mantu testi ko‘p hollarda ijobiy natijalarni ko‘rsatdi (n=20; 65,0%) va Diaskintest preparati bilan test - giperergik natijalar (n=20; 85,0%). BCG emlash 40 ta bolada (100,0%) amalga oshirildi va 27 (69,3%) bolada samarali deb baholandi.

Silning faol shakli diagnostikasi markaziy tibbiy nazorat komissiyasi (CMCC) tomonidan keng qamrovli klinik, radiologik laboratoriya tekshiruvi va bemorlarning immunodiagnozi ma’lumotlari asosida tasdiqlangan. Bemorlarning ushbu guruhida tuberkulyozning birlamchi shakllari ustunlik qildi: 6 (30,0%) bemorda birlamchi sil kasalligi kompleksi, 7 (35,0%) bemorda ko‘krak ichi limfa tugunlari sili, shu bilan birga 4 bemorda (20,0%) infiltrativ o‘pka sili tashxisi qo‘yilgan. sil, 2 (10,0%) tarqoq o‘pka sili, 1 (5,0%) silli plevrit. Bemorlarning 95,0%da (n=19) sil kasalligining o‘pkada joylashgan shakli, faqat 1 nafar bemorda (5,0%) o‘pka va son suyagining kombinatsiyalangan sil kasalligi bo‘lgan. I guruhidagi bolalarning sil jarayonining infiltratsiya bosqichi respondentlarning 12 (60,0%), parchalanish va tarqalish bosqichi - 1 (5,0%), so‘rilish bosqichi - 1 (5,0%), petrifikatsiya bosqichi - 2 (10,0) da aniqlandi. Postvaksinal belgisi ushbu guruhning barcha bolalarida topilgan, ammo uning samaradorligi faqat 7 bolada (n=20, 35,0%) aniqlangan. Statistik ma’lumotlarni qayta ishlash SPSS Statistics dasturi yordamida amalga oshirildi. O‘rtacha arifmetik (M), p=0,95 darajasidagi ishonch oralig‘i, o‘rtachaning standart xatosi (±SEM), median (ME) Farqlarning ahamiyati Student testi (t) yordamida hisoblangan.

Natijalar va uning muhokamasi: Ijtimoiy tarixni tahlil qilganda, sil kasalligining faol jarayonining namoyon bo‘lishida hal qiluvchi xavf omillari bolaning kam ta’minlangan (RR 5,500), ko‘p bolali oilada (RR 4,667), to‘liq bo‘lmagan oilada (RR 3,200) yashashi bo‘lgan. Bolaning va uning oilasining qoniqarsiz yashash sharoitlarida yashashi (RR 4,857), otasining doimiy ish yo‘qligi (RR 3,467), ota-onalarning o‘rta yoki o‘rta maxsus ma’lumot darajasi borligi (RR 3,000), onaning ishsizligi (RR 2,308), ota-onalarning alkogolizm va chekish kabi zararli odatlarni mavjudligi (RR 2,000), shuningdek, bizning tadqiqotimizda bolaning MTM ga “uyushmaganligi” ijtimoiy omili ko‘pincha mavjud edi (RR 2,000).

Ijtimoiy tarix natijalari 1-jadvalda keltirilgan ijtimoiy xavf omillarini aniqlashga imkon berdi.

Jadval-1

I va II guruhlaridagi ijtimoiy xavf omillari

Ijtimoiy tarix ma'lumotlari	Faol TB n=20	LTI n=40	RRTB-LTI, 95% CI	χ2TB-LTBI, p
	Abs (%)	Abs (%)		
To'liq bo'lmagan oilada yashash	8 (40,0)	5 (12,5)	3,200; 8.526-1.201	5,941; 0,015
Katta oilada bola bilan yashash	7 (35,0)	3 (7,5)	4,667;15,150-1,348	7,260; 0,008
Kam ta'minlangan oilada bola bilan yashash	11 (55,0)	4 (10,0)	5.500; 15.111-2.002	14 400;<0,001
Ota-onalar uchun o'rta yoki o'rta maxsus ta'lim darajasi	18 (90,0)	12 (30,0)	3000; 4.924-1.828	19 200;<0,001
Onaning doimiy ish joyi yo'q	15 (75,0)	13 (37,5)	2.308; 3.856-1.381	9,676; 0,002
Otaning doimiy ishi yo'q	10 (66,7) n=15	5 (19,2) n=26	3,467; 8.235-1.459	8,077; 0,005
Ota-onalarning alkogolizm, chekish va giyohvandlik	11 (55,0)	11 (27,5)	2000; 3.795-1.054	4,342; 0,038
Bola va uning oilasi uchun qoniqarsiz yashash sharoitlari	17 (85,0)	7 (17,5)	4,857; 9.758-2.418	25.313;<0,001
Bola tartibga solinmagan	5 (25,0)	5 (12,5)	2000; 6.114-0.654	1,500; 0,221

Faol, hamda yashirin sil kasalligi uchun keng tarqalgan antenatal xavf omili o'tmishda oilada sil kasalligining mavjudligi edi (RR 7,192 va RR 4,987). Rossiya Federatsiyasining LTBI bo'yicha federal klinik ko'rsatmalariga ko'ra, faol yoki yashirin sil infektsiyasi uchun biologik ekstrauterin xavf omillari iloji boricha ishonchli tarzda taqdim etilmagan [9]. Biroq, biz faol sil kasalligi uchun xavf omillarini aniqladik: tug'ilishda tana vazni 2500 g dan kam (RR 1,677), tug'ilish paytida markaziy asab tizimining perinatal shikastlanishi (RR 1,753) va 1 yoshda temir tanqisligi anemiyasining mavjudligi (RR 4.023) ahamiyatga ega ekanligi aniqlandi. Yashirin sil infektsiyasining rivojlanishi uchun xavf omillari hayotning 1-yilida tez-tez O'RVI epizodlari (RR 1,588), hayotning 1 yilida bolaning psixomotor rivojlanishining kechikishi (RR 4,576), rivojlanishning nuqsonlarining mavjudligi (RR 2,667), bolalik infektsiyalari (RR 1,870) mavjudligi ham bo'ldi.

Faol va yashirin sil kasalligi uchun xavf omillari emlashdan keyingi BCG belgisining yo'qligi (RR 1,734), shuningdek, silga qarshi vaktsina samaradorligining pastligi (RR 2,901) edi. Aktiv sil rivojlanishi uchun xavf omillari bo'lishi mumkin bo'lgan somatik kasalliklarni hisobga olgan holda, biz quyidagi natijalarga erishdik: gijja invaziyasi (RR 3,000), temir tanqisligi anemiyasi (RR 1,900), endokrinologik patologiya va metabolik kasalliklar (RR 1,200), miopiya (RR 1,429), gastrit va kolit (RR 2,286), revmatizm va osteomielit (RR 2,000), pielonefrit (RR 1,333), buyrak gidronefrozi (RR 3,000). Shuni ta'kidlash kerakki, yuqorida sanab o'tilgan patologik sharoitlar, shuningdek, yashirin sil infektsiyasiga moyil bo'lgan omillar bo'lib xizmat qilgan. 2-jadvalda bemorlarning ikkala guruhida aniqlangan patologiya to'g'risidagi ma'lumotlar ko'rsatilgan:

Jadval-2

I va II guruh bemorlaridagi somatik kasalliklar

Kasalliklarning tuzilishi	Faol sil n=20	LTI n=40	RR TB-LTBI, 95% CI	χ2TB-LTBI, p
	Abs (%)	Abs (%)		
Gijjalar bilan zararlanish	3 (15,0)	2 (5,0)	3000; 16.534-0.544	1,745; 0,187

Temir tanqisligi anemiyasi	19 (95,0)	20 (50,0)	1900; 2.632-1.372	11.868; 0,001
Boladagi endokrin patologiya va metabolik kasalliklar	3 (15,0)	5 (12,5)	1200; 4.523-0.318	0,072; 0,789
Miopiya	10 (50,0)	14 (35,0)	1,429; 2.626-0.777	1250; 0,264
Nafas olish tizimining patologiyasi, O‘RVI va sil kasalligidan tashqari	3 (15,0)	12 (30,0)	0,500; 1,572-0,159	1600; 0,206
Gastrit va kolit	8 (40,0)	7 (17,5)	2,286; 5.406-0.967	3600; 0,058
Revmatizm va osteomielit	3 (15,0)	3 (7,5)	2000; 9.032-0.443	0,833; 0,362
Piyelonefrit	4 (20,0)	6 (15,0)	1,333; 4.193-0.424	0,240; 0,625
Buyraklarning gidronefrozi	3 (15,0)	2 (5,0)	3000; 16.534-0.544	1,745; 0,187

Ishimiznind davomida, biz I va II guruhdagi bemorlarda epidemiologik xavf omillarini ko‘rib chiqdik (3-jadval).

Jadval-3

I va II guruh bemorlarida epidemiologik xavf omillari

Xavf omillari	**Faol sil n=20**	**LTI n=40**	**RR TB-LBTI, 95% CI**	**χ2TB-LTBI, p**
	Abs (%)	**Abs (%)**		
Faol sil kasalligi bilan og‘rigan bemor bilan aloqa qilish	20 (100,0)	35 (87,5)	1,143; 1.285-1.017	2,727; 0,009
Yakuniy dezinfektsiya yo‘qligi	15 (75,0)	3 (7,5)	10 000; 30.568-3.271	28,929; 0,001
Kimyoprofilaktikaning etishmasligi	2 (10,0)	25 (62,5)	0,160; 0,609-0,042	14.848; 0,001
OIV infektsiyasi o‘chog‘ida yashash	8 (40,0)	2 (5,0)	8 000; 34.227-1.870	11 760; 0,001
Covid-19 o‘chog‘ida yashash	3 (15,0)	19 (47,5)	0,316; 0,942-0,106	6,065;0,014

Epidemiologik tarixni tahlil qilish sil infektsiyasi o‘chog‘ida yashashda yashirin va faol sil kasalligini rivojlanish xavfi yuqori ekanligini ko‘rsatdi (RR 1,143). Muayyan jarayonning faollashishi uchun xavf omili sil kasalligi o‘chog‘ida yakuniy dezinfeksiyaning yo‘qligi (RR 10,000) bo‘lsa, latent jarayon uchun oilada sil bilan kasallangan bemor aniqlanganda kimyoprofilaktikaning etishmasligi muhim edi (RR 0,160).

Faol sil kasalligining rivojlanishi uchun qo‘shimcha epidemiologik xavf omillarining ahamiyatini baholashda OIV infektsiyasi o‘chog‘ida yashash kabi omilning ahamiyati aniqlandi (RR 8,000). OIV bilan kasallangan infektsiya manbalarining aksariyati asotsial turmush tarzini olib borishi va sanitariya-gigiyena me’yorlariga mos kelmasligini hisobga olsak, bunday o‘choqlarda bolalarning yuqishi xavfi ushbu omil mavjud bo‘lmagan epidemiyalarga qaraganda ancha yuqori (p≤ 0,005). Yashirin sil kasalligi bilan kasallangan bolalar guruhi uchun epidemiologik xavf omili Covid-19 epidemiyasida yashagan (RR 0,316). Bizning taxminlarimizga ko‘ra, bunday epidemiya o‘choqlarida yashash bolada yashirin koronavirus infektsiyasiga ham duchor bo‘lganligini anglatadi, bu umumiy qarshilik va infektsiyaning pasayishiga ta`sir etadi.

Xulosa: Adabiyotda faol va latent sil infektsiyasi uchun xavf omillari alohida bo‘linishi yo‘q. Bizning fikrimizcha, bunday bo‘linish zarur va dolzarbdir, chunki sil kasalligi infektsiyasining faol bo‘lmagan shaklida faollashishi yoki davom etishiga xavf omillarining ta’siri teng emas.

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