Yılın makaleleri-Tüberküloz

Doç. Dr. Erkan Çakır
Bezmialem Üniversitesi Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları Anabilim Dalı
Çocuk Göğüs Hastalıkları Bilimdalı

A blood RNA signature for tuberculosis disease risk: a prospective cohort study

Daniel E Zak*, Adam Penn-Nicholson*, Thomas J Scriba*, Ethan Thompson†, Sara Suliman†, Lynn M Amon, Hassan Mahomed, Mzwandile Erasmus, Wendy Whatney, Gregory D Hussey, Deborah Abrahams, Fazlin Kafaar, Tony Hawkridge, Suzanne Verver, E Jane Hughes, Martin Ota, Jayne Sutherland, Rawleigh Howe, Hazel M Dockrell, W Henry Boom, Bonnie Thiel, Tom H M Ottenhoff, Harriet Mayanja-Kizza, Amelia C Crampin, Katrina Downing, Mark Hatherill, Joe Valvo, Smitha Shankar, Shreemanta K Parida, Stefan H E Kaufmann, Gerhard Walzl, Alan Aderem, Willem A Hanekom, for the ACS and GC6-74 cohort study groups‡

Lancet 2016; 387: 2312–22
Published Online March 23, 2016
http://dx.doi.org/10.1016/S0140-6736(15)01316-1

See Comment page 2268

*Contributed equally

†Contributed equally

‡Members listed at the end of p

The Center for Infect Disease Research, Seattle, USA (D E Zak, E Thompson, L M Amon PhD, J Valv, S Shankar M S, A Aderem P; South African Tuberculosis Vaccine Initiative, Institute of Infectious Disease and Molecular Medicine & Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa (A Penn-Nicholson PhD, T J Scriba PhD, S Suliman PhD, H Mahomed M D, M Erasmus BSc, W Whatney BSc Hons, Prof G D Hussey FFCH(SA), D Abrahams DipMT, F Kafaar DipNur, T Hawkridge FCPHM, E J Hughes BSc Hons, K Downing PhD, M Hatherill M D,

Summary

Background Identification of blood biomarkers that prospectively predict progression of *Mycobacterium tuberculosis* infection to tuberculosis disease might lead to interventions that combat the tuberculosis epidemic. We aimed to assess whether global gene expression measured in whole blood of healthy people allowed identification of prospective signatures of risk of active tuberculosis disease.

Methods In this prospective cohort study, we followed up healthy, South African adolescents aged 12–18 years from the adolescent cohort study (ACS) who were infected with *M tuberculosis* for 2 years. We collected blood samples from study participants every 6 months and monitored the adolescents for progression to tuberculosis disease. A prospective signature of risk was derived from whole blood RNA sequencing data by comparing participants who developed

TB enfeksiyonunun aktif hastalığa ilerleyip ilerlemeyeceğini gösteren genler var mıdır?

Findings Between July 6, 2005, and April 23, 2007, we enrolled 6363 participants from the ACS study and 4466 from independent South African and Gambian cohorts. 46 progressors and 107 matched controls were identified in the ACS cohort. A 16 gene signature of risk was identified. The signature predicted tuberculosis progression with a sensitivity of 66·1% (95% CI 63·2–68·9) and a specificity of 80·6% (79·2–82·0) in the 12 months preceding tuberculosis diagnosis. The risk signature was validated in an untouched group of adolescents (p=0·018 for RNA sequencing and p=0·0095 for qRT-PCR) and in the independent South African and Gambian cohorts (p values <0·0001 by qRT-PCR) with a sensitivity of 53·7% (42·6–64·3) and a specificity of 82·8% (76·7–86) in the 12 months preceding tuberculosis.

Interpretation The whole blood tuberculosis risk signature prospectively identified people at risk of developing active tuberculosis, opening the possibility for targeted intervention to prevent the disease.

Funding Bill & Melinda Gates Foundation, the National Institutes of Health, Aeras, the European Union, and the South African Medical Research Council.

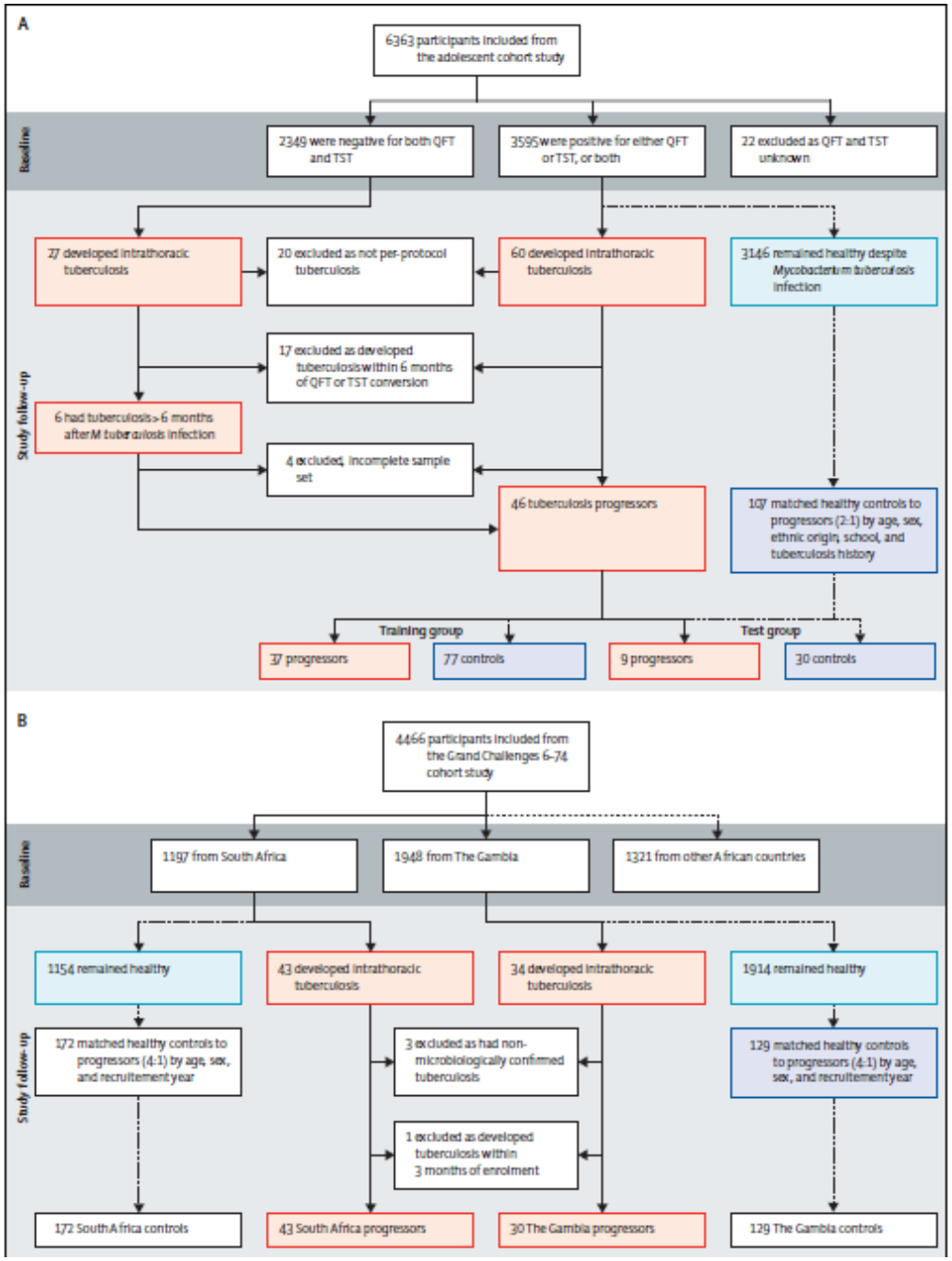
A blood RNA signature for tuberculosis disease risk: a prospective cohort study

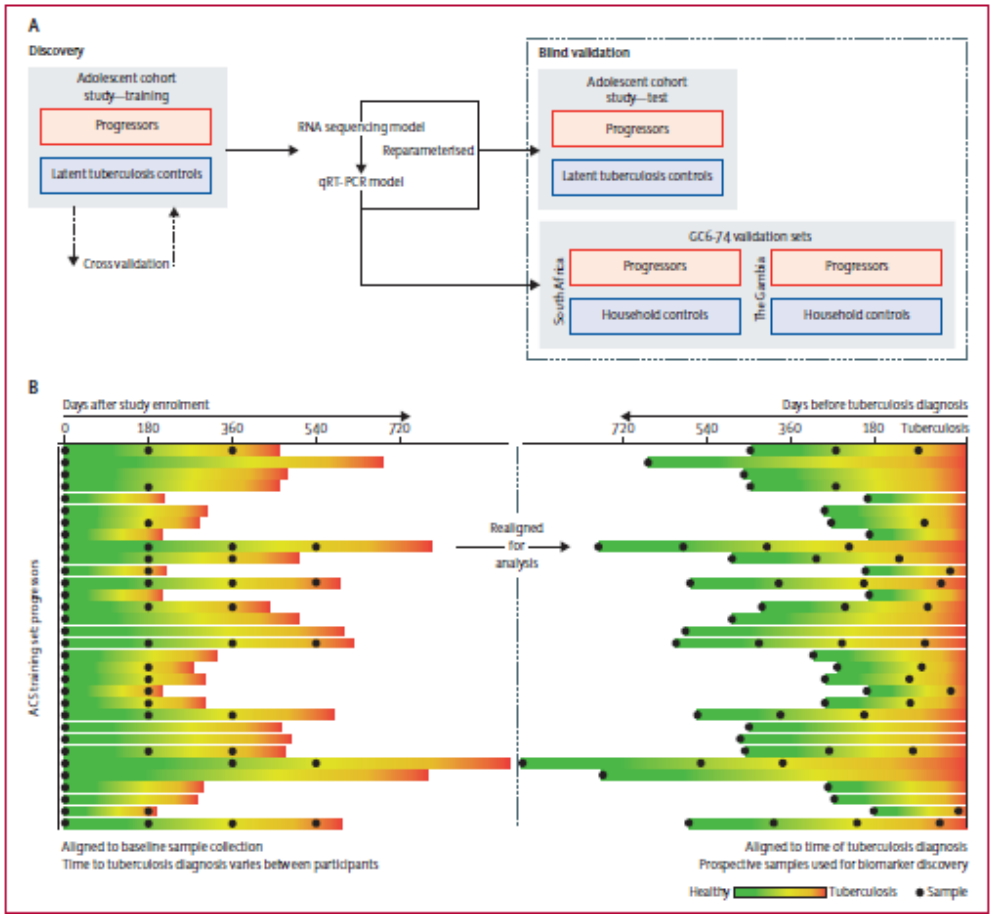
- Güney Afrika'dan yapılmış prospektif kohort çalışma
- 2005-2007 yılları arasında hastalar alınmış
- TB enfekte 12-18 yaş arası adolesanlar (Güney afrika Adolesan kohort çalışmasından 6323 kişi alınmış)
- Güney Afrika ve Gambia'dan ayrıca bağımsız 4446 kişi alınmış
- 6 ayda bir kan örnekleri incelenmiş ve RNA sekanslarına bakılmış
- Latent tüberkülozu olanları hastalığa ilerleme açısından kontrol etmişler
- Hastalığa ilerleyenlerle sağlıklı kalanlar karşılaştırılmış

46 aktif hastalığa ilerlemiş olgu

107 kontrol olgunun sonuçları

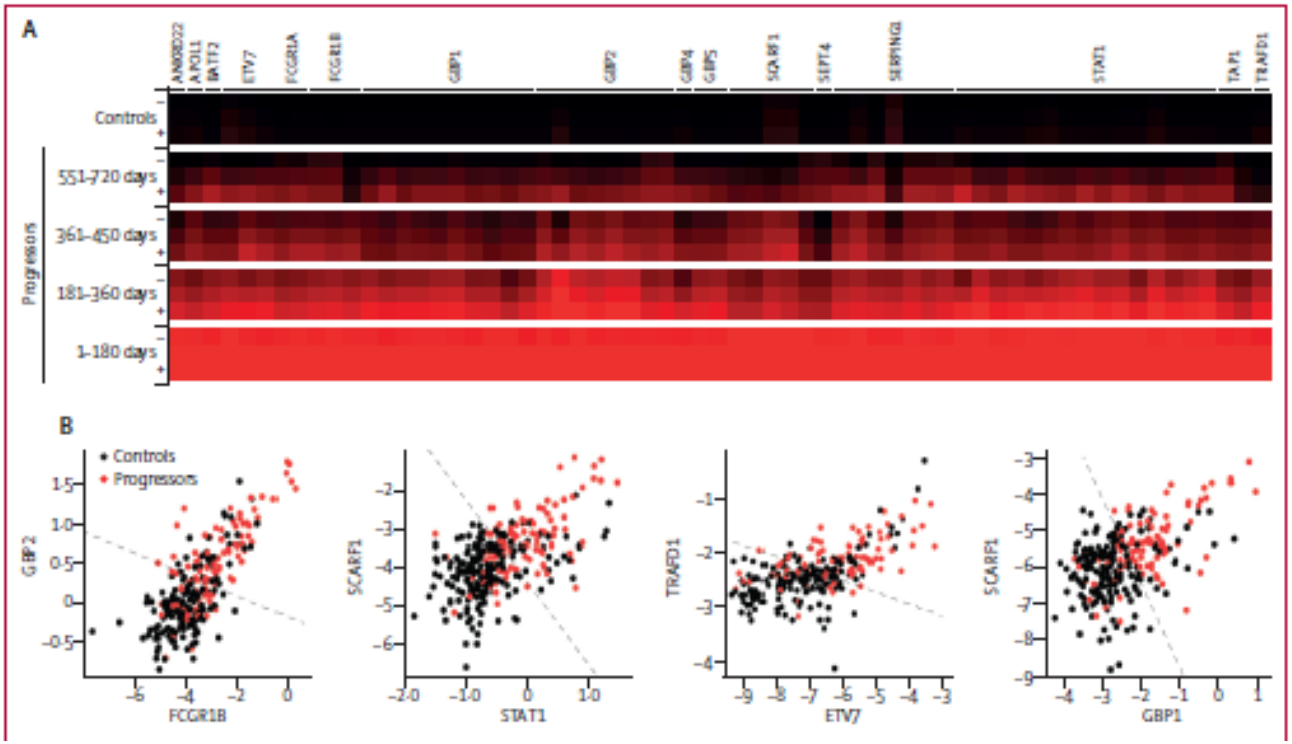
karşılaştırılmış





Latent TB olanların hastalığa ilerleme süreci kaydedilmiş

A blood RNA signature for tuberculosis disease risk: a prospective cohort study



- TB hastalığına ilerlemeyi önceden gösterebilen 16 adet genetik işaretleyici tespit edilmiş
- Hastalık gelişmeden 12 ay öncesinde TB hastalığına ilerlemeyi göstermedeki sensitiviteleri % 66 (%95 CI 63-68.9), spesifiteleri % 80.6 (%95 CI 79.2-82.0) bulunmuş

A blood RNA signature for tuberculosis disease risk: a prospective cohort study

Sonuç

- Çalışma, latent TB enfeksiyonu olan ya da TB ile karşılaşmış bireylerde RNA işaretleyicilerinin aktif hastalığa ilerlemeyi önceden gösterebileceğini ispatlamıştır.
- Sonuçlar ilerideki diğer çalışmalara da ışık tutmuştur
- Profilaktik tedavi alması gereken grupları belirlemede bu işaretleyicilerin kullanılıp kullanılamayacağı araştırılabilir.

OPEN ACCESS

ORIGINAL ARTICLE

The impact of BCG vaccination on tuberculin skin test responses in children is age dependent: evidence to be considered when screening children for tuberculosis infection

James A Seddon,[1] James Paton,[2] Zohreh Nademi,[3,4] Denis Keane,[1] Bhanu Williams,[5] Amanda Williams,[5] Steven B Welch,[6] Sue Liebeschutz,[7] Anna Riddell,[8] Jolanta Bernatoniene,[9] Sanjay Patel,[10] Nuria Martinez-Alier,[11] Paddy McMaster,[12] Beate Kampmann[1,13]

For numbered affiliations see end of article.

Correspondence to
Professor Beate Kampmann, Department of Paediatrics, Centre of International Child Health, Imperial College London, Norfolk Place, London W2 1PG, UK; b.kampmann@imperial.ac.uk

Received 10 August 2015
Revised 6 March 2016
Accepted 28 March 2016
Published Online First 22 June 2016

ABSTRACT

Background Following exposure to TB, contacts are screened to target preventive treatment at those at high risk of developing TB. The UK has recently revised its recommendations for screening and now advises a 5 mm tuberculin skin test (TST) cut-off irrespective of age or BCG status. We sought to evaluate the impact of BCG on TST responses in UK children exposed to TB and the performance of different TST cut-offs to predict interferon γ release assay (IGRA) positivity.

The impact of BCG vaccination on TST positivity was evaluated in IGRA-negative children, as was the performance of different TST cut-offs to predict IGRA positivity.

Results Of 422 children recruited (median age 69 months; IQR: 32–113 months), 300 (71%) had been vaccinated with BCG. BCG vaccination affected the TST response in IGRA-negative children less than 5 years old but not in older children. A 5 mm TST cut-off demonstrated good sensitivity and specificity in BCG-unvaccinated children, and an excellent negative predictive value but was associated with low specificity

Key messages

What is the key question?

- The impact of BCG vaccination on tuberculin skin test response is poorly understood in children; we set out to determine the impact of previous BCG vaccination on tuberculin skin test response in UK children following

Why read on?

- The revised UK national guidance of using a 5 mm tuberculin skin test cut-off results in impaired specificity in BCG-vaccinated children.

BCG aşısının TST sonuçlarına ve rehberlerdeki yorumlara etkisi araştırılmış

tuberculosis. This is usually manifest as a positive immune test in either the skin or blood.[1] TB infection implies that organisms are dormant within the body and are not causing disease; the child is clinic-

- İngiltere'de yaşa ve BCG aşılamasına bakılmaksızın TDT için pozitif değer halen 5 mm olarak alınmaktadır
- Çalışmada BCG aşılamasının bu değer üzerine etkisine bakılmış
- 2011-2014 yılları arasında 15 yaş altı TB temaslısı çocuklar alınmış
- Median yaşı 66 ay olan 422 çocuk (300'ü aşılı)
- TDT ve IGST uygulanmış
- BCG aşılılar ve aşısızların TST değerlerine bakılmış

Table 1 Demographic and clinical characteristics of children in the study

	IGRA status		BCG status		
Characteristic	IGRA negative (%)	IGRA positive (%)	BCG unvaccinated (%)	BCG vaccinated (%)	Total (%)
Total	314 (100)	108 (100)	122 (100)	300 (100)	422 (100)
Gender					
Male	164 (52.2)	52 (48.2)	64 (52.5)	152 (50.7)	216 (51.2)
Female	150 (47.8)	56 (51.9)	58 (47.5)	148 (49.3)	206 (48.8)
Median age in months (IQR)	60 (25–104)	94 (61–136)	71 (37–118)	68 (30–110)	69 (32–113)
Ethnicity					
White	69 (22.0)	36 (33.3)	84 (68.9)	21 (7.0)	105 (24.9)
Indian	38 (12.1)	10 (9.3)	3 (2.5)	45 (15.0)	48 (11.4)
Pakistani	60 (19.1)	18 (16.7)	8 (6.6)	70 (23.3)	78 (18.5)
Bangladeshi	34 (10.8)	4 (3.7)	2 (1.6)	36 (12.0)	38 (9.0)
Black Caribbean	2 (0.6)	0	0	2 (0.7)	2 (0.5)
Black African	68 (21.7)	27 (25.0)	12 (9.8)	83 (27.7)	95 (22.5)
Black Other	8 (2.6)	6 (5.6)	5 (4.1)	9 (3.0)	14 (3.3)
Chinese	1 (0.3)	0	0	1 (0.3)	1 (0.2)
Mixed/other	34 (10.8)	7 (6.5)	8 (6.6)	33 (11.0)	41 (9.7)
HIV status*					
Negative	280 (89.2)	90 (83.3)	100 (82.0)	270 (90)	370 (87.7)
Positive	0	0	0	0	0
Not tested	34 (10.8)	18 (16.7)	22 (18.0)	30 (10)	52 (12.3)
Born in the UK					
No	36 (11.5)	25 (23.2)	12 (9.8)	49 (16.3)	61 (14.5)
Yes	278 (88.5)	83 (76.9)	110 (90.2)	251 (83.7)	361 (85.6)
Type of IGRA					
QuantiFERON-TB Gold	190 (60.7)	71 (65.7)	84 (68.9)	177 (59.2)	261 (62.0)
T-SPOT.TB	124 (39.3)	37 (34.3)	38 (31.2)	122 (40.8)	161 (38.0)

*HIV status was known in 370 children. No children were known to be HIV positive.
IGRA, interferon γ release assay.

- Latent TB'yi göstermede özgüllük ve duyarlılığın
- BCG aşısı olmayanlarda TDT için pozitiflik sınırı 5 mm,
- BCG aşılılarda ise TDT için pozitiflik sınırı 10 mm alınmasının

daha uygun olduğu bulunmuş

- BCG'nin 5 yaş ve üzeri çocuklarda TDT endurasyonunu belirgin etkilemediği gösterilmiş

Sonuç

BCG aşılaması TDT değerlendirmede

dikkate alınmalı ve rakamlar yeniden gözden geçirilmelidir.

Journal of Biomarkers
Volume 2016, Article ID 5643853, 6 pages
http://dx.doi.org/10.1155/2016/5643853

Research Article

Determination of Urinary Neopterin/Creatinine Ratio to Distinguish Active Tuberculosis from Latent *Mycobacterium tuberculosis* Infection

Michael Eisenhut,[1] Dougal S. Hargreaves,[2] Anne Scott,[1] David Housley,[1] Andrew Walters,[1] and Rohinton Mulla[1]

[1] *Luton & Dunstable University Hospital NHS Foundation Trust, London LU4 ODZ, UK*

İdrar neopterin/kreatinin oranının aktif- latent TB ayırımı üzerine etkisi araştırılmış

Academic Editor: Mark Molloy

Background. Biomarkers to distinguish latent from active *Mycobacterium (M.) tuberculosis* infection in clinical practice are lacking. The urinary neopterin/creatinine ratio can quantify the systemic interferon-gamma effect in patients with *M. tuberculosis* infection. *Methods*. In a prospective observational study, urinary neopterin levels were measured by enzyme linked immunosorbent assay in patients with active tuberculosis, in people with latent *M. tuberculosis* infection, and in healthy controls and the urinary neopterin/creatinine ratio was calculated. *Results*. We included a total of 44 patients with *M. tuberculosis* infection and nine controls. 12 patients had active tuberculosis (8 of them culture-confirmed). The median age was 15 years (range 4.5 to 49). Median urinary neopterin/creatinine ratio in patients with active tuberculosis was 374.1 micromol/mol (129.0 to 1072.3), in patients with latent *M. tuberculosis* infection it was 142.1 (28.0 to 384.1), and in controls it was 146.0 (40.3 to 200.0), with significantly higher levels in patients with active tuberculosis ($p < 0.01$). The receiver operating characteristics curve had an area under the curve of 0.84 (95% CI 0.70 to 0.97) ($p < 0.01$). *Conclusions*. Urinary neopterin/creatinine ratios are significantly higher in patients with active tuberculosis compared to patients with latent infection and may be a significant predictor of active tuberculosis in patients with *M. tuberculosis* infection.

Determination of Urinary Neopterin/Creatinine Ratio to Distinguish Active Tuberculosis from Latent *Mycobacterium tuberculosis* Infection

- Neopterin; (2-amino-4 hidroksi-6-pteridinin) guanosin trifosfat siklohidrolaz 1 tarafından aktive edilen guanosin trifosfat ürünüdür.
- Aktif makrofaj, monosit, dentritik hücreler ve endotel hücreleri tarafından üretilir.
- Az miktarda da olsa interferon gama uyarısı ile böbrek epitel hücreleri, fibroblastlar ve vasküler düz kaslar tarafından da üretilir.
- Üretimi sonrası değişikliğe uğramadan idrarda toplanır.
- Elisa yöntemiyle idrarda ölçülebilir bir biyolojik ajandır.

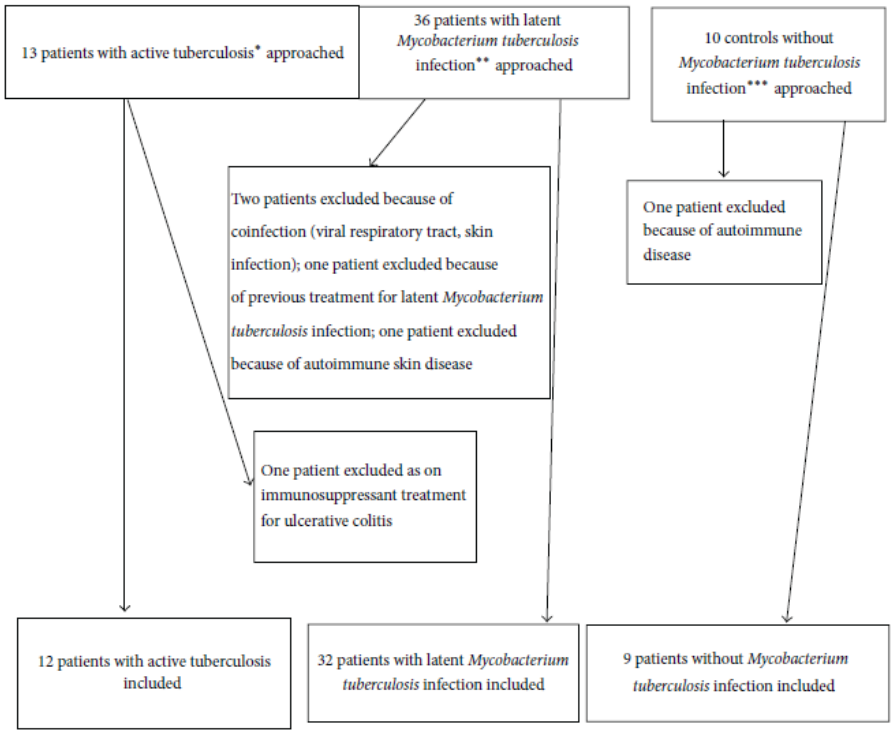
Determination of Urinary Neopterin/Creatinine Ratio to Distinguish Active Tuberculosis from Latent *Mycobacterium tuberculosis* Infection

Daha önceden neopterinin TB hastalığında tedavi etkinliği ve relapstaki yeri araştırılmış fakat aktif-latent TB ayrımında hiç araştırılmamış

I. Yuksekol, M. Ozkan, O. Akgul et al., "Urinary neopterin measurement as a non-invasive diagnostic method in pulmonary tuberculosis," *International Journal of Tuberculosis and Lung Disease*, vol. 7, no. 8, pp. 771–776, 2003.

R. S. Wallis, T. M. Doherty, P. Onyebujoh et al., "Biomarkers for tuberculosis disease activity, cure, and relapse," *The Lancet Infectious Diseases*, vol. 9, no. 3, pp. 162–172, 2009.

Determination of Urinary Neopterin/Creatinine Ratio to Distinguish Active Tuberculosis from Latent *Mycobacterium tuberculosis* Infection

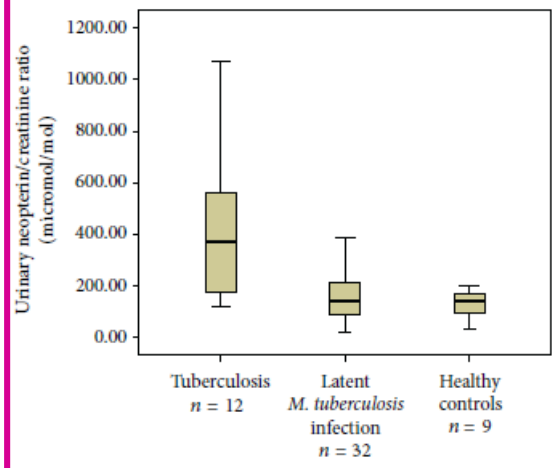


- 12 aktif TB hastası
- 32 latent TB hastası
- 9 kontrol hastası alınmış

Table 1

	Patients with tuberculosis ($n = 12$)	Patients with latent *Mycobacterium tuberculosis* infection ($n = 32$)	Healthy controls ($n = 9$)
Age in years (median (range))	14.7 (5.8 to 37)	14.7 (4.5 to 49)	24 (9 to 40)
Gender (female)	7	19	6
Manifestations of disease	9 pulmonary tuberculosis, 3 extrapulmonary tuberculosis (1 each lymphadenitis, mandibular, and peritoneal)	No disease manifestations	No disease manifestations
Isolation of *Mycobacterium tuberculosis*	6/9 patients with pulmonary tuberculosis, and one each with tuberculous lymphadenitis, and mandibular tuberculosis	N/A	N/A
Urinary neopterin/creatinine ratio (micromole/mol, median (range))	374.1 (129.0 to 1072.3)	142.1 (28.0 to 384.1)	146.0 (40.3 to 200.0)

- İdrar neopterin/kreatinin oranı aktif TB olanlarda belirgin yüksek bulunmuş (p>0.01)
- Latent TB ve kontrol arasında fark saptanmamış
- Aktif TB'lilerde tedavi ile belirgin azalsa da istatistiki fark yok (p=0.17) (Sayı yetersizliği?)



Determination of Urinary Neopterin/Creatinine Ratio to Distinguish Active Tuberculosis from Latent *Mycobacterium tuberculosis* Infection

Sonuç

- İdrar neopterin/kreatinin oranı aktif TB- Latent TB ayrımında güvenilir bir ayraçtır
- Sonraki çalışmalar cut-off değer belirleme üzerine yapılmalıdır.

PLOS ONE

RESEARCH ARTICLE

The Use of Interferon Gamma Inducible Protein 10 as a Potential Biomarker in the Diagnosis of Latent Tuberculosis Infection in Uganda

Irene Andia Biraro[1,2]*, Simon Kimuda[1,2], Moses Egesa[1,2], Stephen Cose[2,3], Emily L. Webb[4], Moses Joloba[1], Steven G. Smith[5], Alison M. Elliott[2,3], Hazel M. Dockrell[5], Achilles Katamba[1]

1 Makerere University College of Health Sciences, Kampala, Uganda, **2** Medical Research Council/Uganda Virus Research Institute, Uganda Research Unit on AIDS, Entebbe, Uganda, **3** Department of Clinical Research, London School of Hygiene & Tropical Medicine, London, United Kingdom, **4** Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, United Kingdom, **5** Department of Immunology and Infection, London School of Hygiene & Tropical Medicine, London, United Kingdom

* andiaodanga@yahoo.com

OPEN ACCESS

Citation: Biraro IA, Kimuda S, Egesa M, Cose S, Webb EL, Joloba M, et al. (2016) The Use of

Abstract

IP-10'un latent TB belirlemede ajan olup olamayacağı üzerine çalışılmış

- Latent TB tanısında altın standart bulunmamaktadır

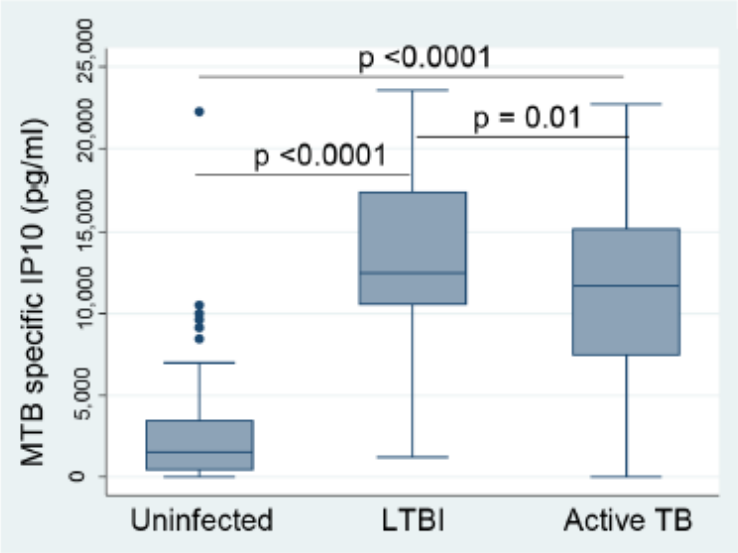
✓ TDT

✓ IGST (QuantiFERON – Elispot)

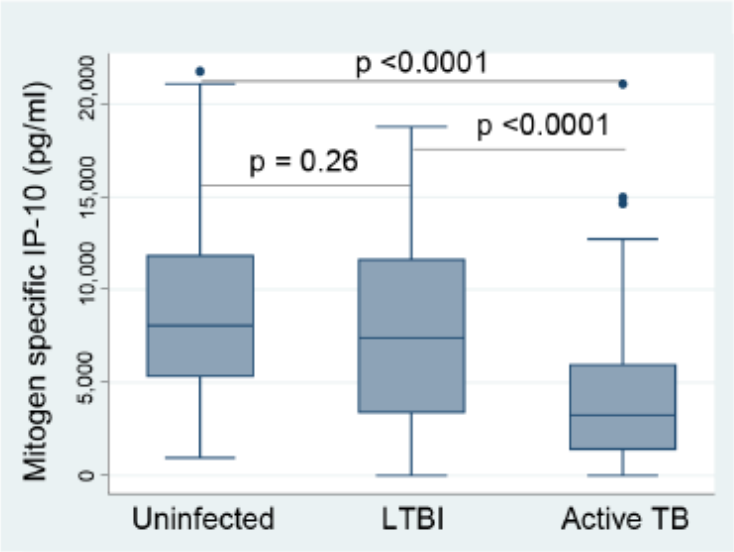
- Yeni aday: İnterferon tarafından indüklenen protein-10 (IP-10)
- IP-10 İnterferon ve diğer sitokinler tarafından uyarılan ve makrofajlardan salınan bir kemokindir.
- IP-10 monosit ve aktif Th1 hücrelerinin enflamasyon bölgesine hareketini sağlar
- *M. Tuberculosis* antijenlerine karşı oluşumu artan IP-10 bir enfeksiyon belirteci olarak kullanılabilir.

- Çalışmada IP-10- TDT ve Quantiferonun latent TB ve aktif TB deki cevapları değerlendirilmiş.
- 102 aktif TB hastası ve bunların 237 temaslısı çalışmaya alınmış
- TDT 5 mm HIV +, 10 mm HIV – lerde kabul edilmiş
- 76 enfeksiyon yok: QFN -, TDT –
- 62 latent enfeksiyon: QFN +, TDT +
- 99 şüpheli sonuç: [92 (QFN+, TDT -), 7 (QFN-, TDT +)]

A)

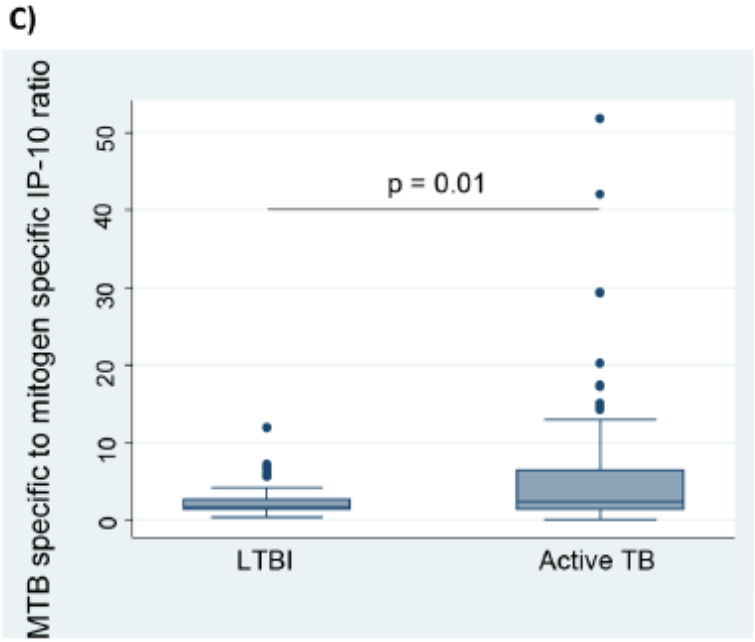


B)



Mycobacterum tuberculosis spesifik IP-10 değerleri latent TB'de diğerlerine göre daha yüksek bulunmuş

Mitojen spesifik (Fitohemaglutinin ile indüklenen) IP-10 değerleri enfeksiyonu olmayanlar ve latent TB olanlarda aktif TB olanlara göre daha yüksek



Mycobacterum tuberculosis spesifik IP-10/Mitojen spesifik IP-10 oranı aktif TB'lilerde daha yüksek

Sonuç

- IP-10 latent TB olanlarda enfeksiyonu olmayanlara göre belirgin yüksek
- Aktif TB- latent TB ayırımını yapmada yetersiz
- MTB spesifik IP-10/mitojen spesifik IP-10 oranı HIV negatif erişkinlerde aktif TB'yi göstermede etkin
- IP-10'un Latent TB'yi göstermede QFN ile uyumu, TST ile uyumundan daha iyi

PLOS ONE

RESEARCH ARTICLE

A Novel Sample Processing Method for Rapid Detection of Tuberculosis in the Stool of Pediatric Patients Using the Xpert MTB/RIF Assay

Xpert MTB/RIF gaita örneklemesi

Padmapriya P. Banada[1☯], Uvistra Naidoo[2☯¤], Srinidhi Deshpande[1], Farina Karim[2], JoAnne [illegible][2],

[illegible], New Jersey, United States of America, **2** KwaZulu-Natal Research Institute for TB/HIV (K-RITH), Durban, South Africa, **3** Department of Microbiology and Molecular Genetics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, United States of America, **4** Cepheid, 904 Caribbean Drive, Sunnyvale, California, United States of America, **5** Cepheid, Bothell, Washington, United States of America

☯ These authors contributed equally to this work.
¤ Current address: Department of Pediatrics and Child Health, University of Cape Town, Cape Town, South Africa
* allandda@rutgers.edu

OPEN ACCESS

Citation: Banada PP, Naidoo U, Deshpande S, Karim F, Flynn JL, O'Malley M, et al. (2016) A Novel Sample Processing Method for Rapid Detection of Tuberculosis in the Stool of Pediatric Patients Using the Xpert MTB/RIF Assay. PLoS ONE 11(3): e0151980. doi:10.1371/journal.pone.0151980

Abstract

Background

A Novel Sample Processing Method for Rapid Detection of Tuberculosis in the Stool of Pediatric Patients Using the Xpert MTB/RIF Assay

•XPERT MTB/RIF testi için toplanması

daha kolay olan gaita örneklerinin valide

edilmesi için çalışma yapılmış

•0.2 gr, 0.6 gr ve 1,2 gr gaita test edilmiş

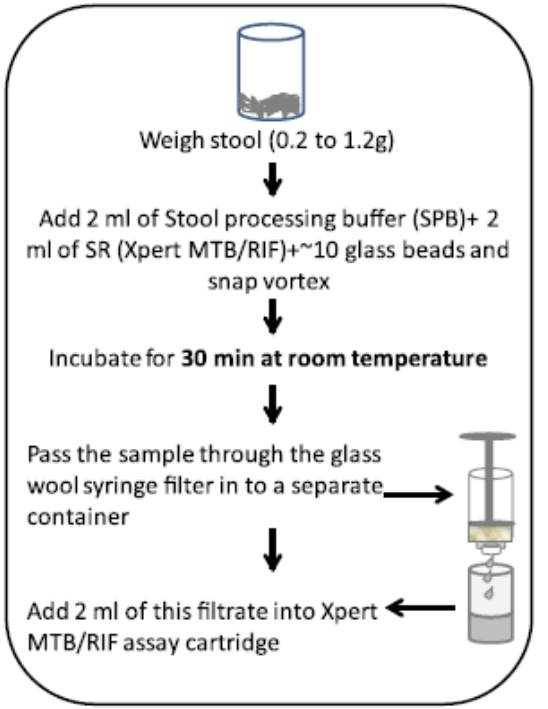


Fig 1. Flow diagram showing how stool was processed in this study.

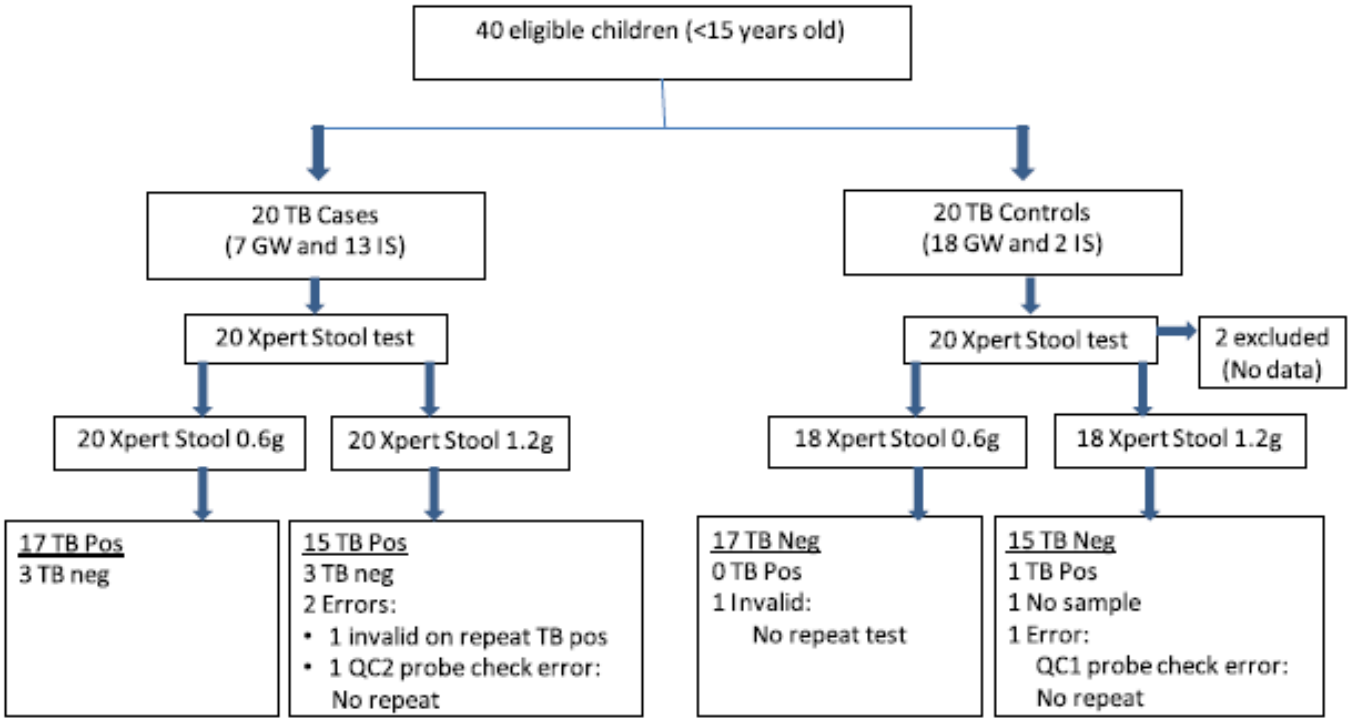


Fig 4. Study flow diagram. Xpert stool testing of 0.6g and 1.2g volume from Xpert induced sputum (IS) and gastric washing (GW) results was performed on above recruited participants. As indicated, repeat testing was performed on a limited stool number of samples that were initially negative.

doi:10.1371/journal.pone.0151980.g004

A Novel Sample Processing Method for Rapid Detection of Tuberculosis in the Stool of Pediatric Patients Using the Xpert MTB/RIF Assay

Sonuç

- 0.6 gr gaita örneklerinin diğerlerine göre TB göstermede hassasiyeti ve özgüllüğü daha iyi bulunmuş
- Sonuç: Gaita hızlı ve güvenilir şekilde TB tanısında kullanılabilir.

INTERNATIONAL JOURNAL OF MYCOBACTERIOLOGY 5 (2016) 111–119

Asian - African society Of Mycobacteriology

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/IJMYCO

Association of plasma cytokines with radiological recovery in pulmonary tuberculosis patients

Najeeha Talat Iqbal [a,b,*], *Rabia Hussain* [c], *Firdaus Shahid* [c], *Ghaffar Dawood* [d]

[a] *Department of Pediatrics and Child Health, Aga Khan University, Karachi, Pakistan*
[b] *Department of Biological and Biomedical Sciences, Aga Khan University, Karachi, Pakistan*
[c] *Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi, Pakistan*
[d] *Masoomeen General Hospital, Kharadar, Karachi, Pakistan*

Plazma sitokin düzeylerinin radyolojik iyileşme ile korelasyonu

Association of plasma cytokines with radiological recovery in pulmonary tuberculosis patients

- Yeni tanı ARB pozitif 15 hasta
- Kronik hastalığı olanlar dışlanmış
- 43 kontrol hastası
- TH1/TH2 sitokin kit 2 (BD Bioscience, CA, USA)
- IL-2, IL-4, IL-6, IL-10, TNFα, IFNγ

Table 1 – Demographics of study groups.

TB cases	Age (y) (Mean ± SD)	Sex M/F	MT (Mean ± SD)
PTB ($n = 15$)	32.06 ± 12.03	3/12	16.53 ± 9.07
EC ($n = 43$)	29.41 ± 10.69	19/25	7.80 ± 8.00*

Note: EC = endemic control; MT = Montoux test; PTB = pulmonary tuberculosis; SD = standard deviation.
* $p = .001$ using Student t test.

Radyolojik iyileşme 3 grup

- Hızlı iyileşenler (n:5): 6 ayın altında
- Orta iyileşenler (n: 4): 6-12 ay arası
- Yavaş iyileşenler (n: 6): 12 ay üstü

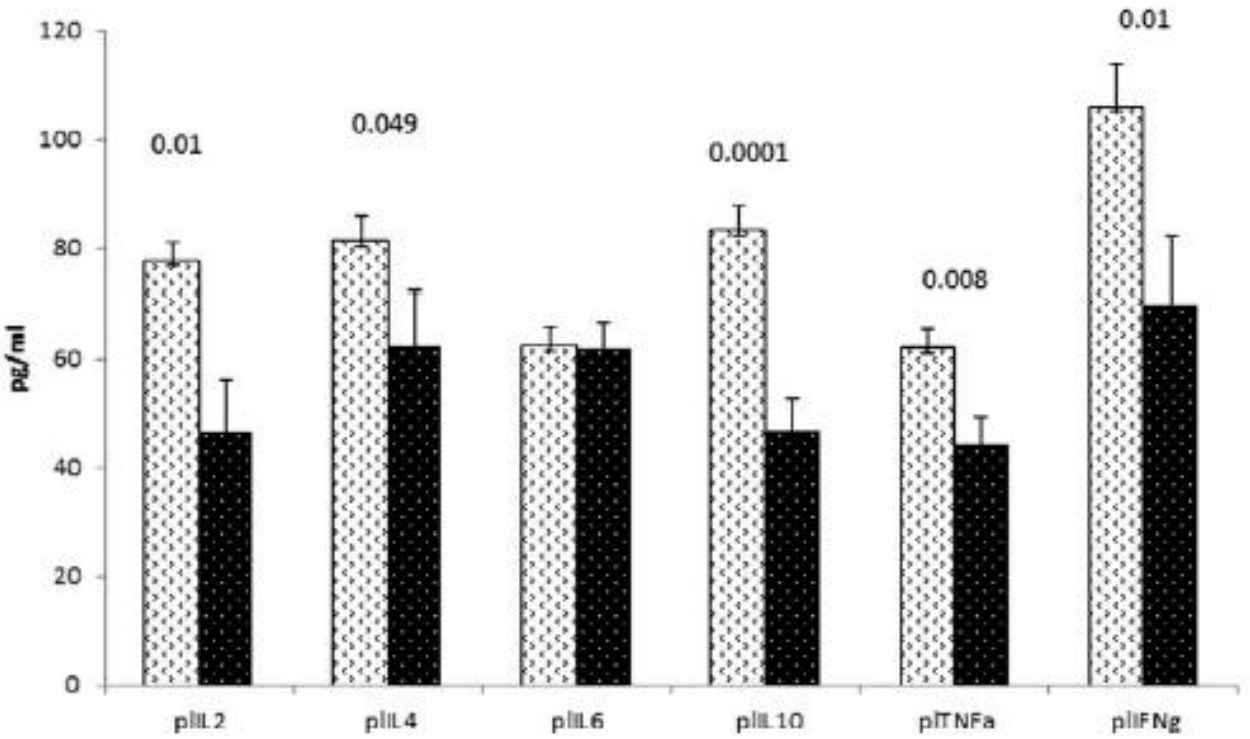
Table 3 – Radiological recovery in relation to extent of pulmonary disease at intake.

TB cases (*N*)	Fast	Intermediate	Slow
PMN (1)	0	0	1
PMD (8)	1	4	3
PMD-HLN (4)	4	0	0
PMD-PE (1)	0	0	1
PAD-HLN-PE (1)	0	0	1
Total	5	4	6

Note: HLN = hilar lymph node; PE = pulmonary effusions; PMD = presents with minimal disease.

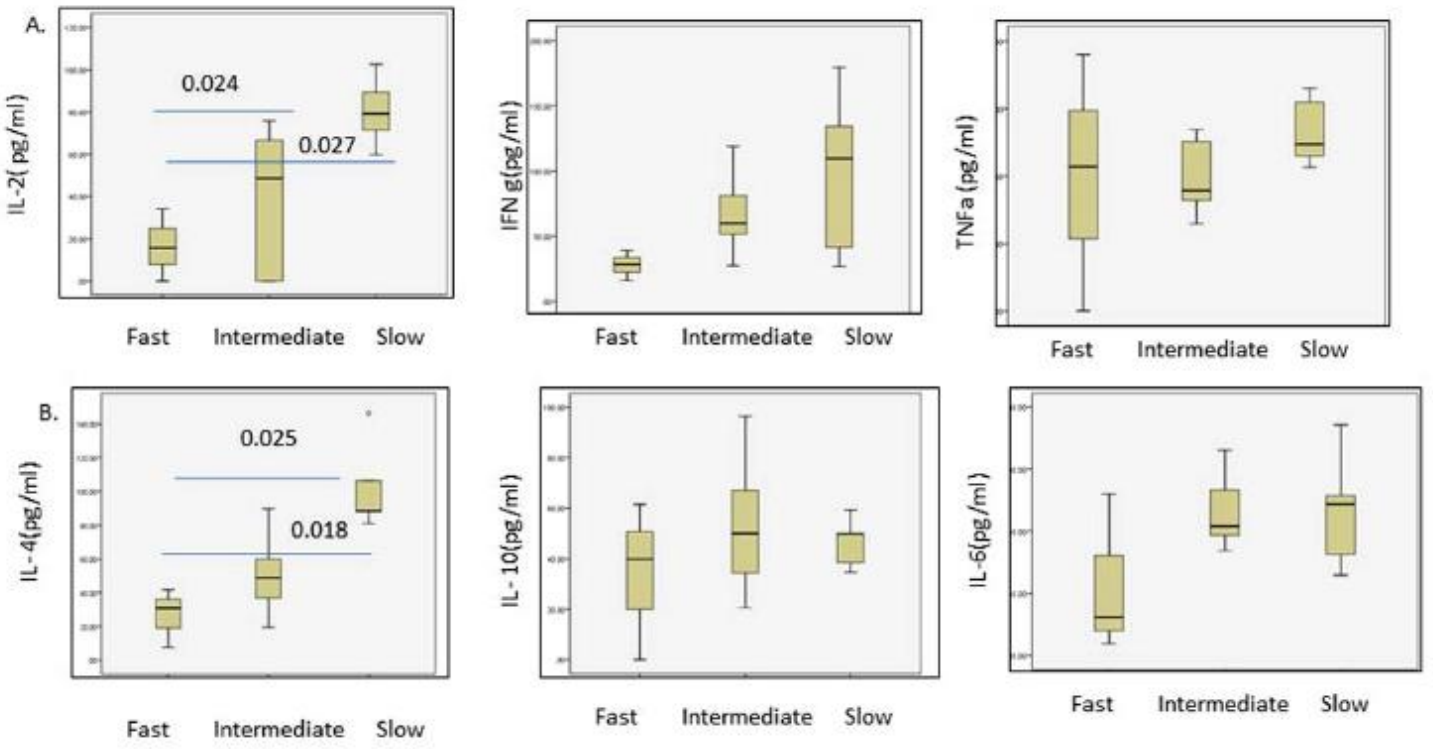
PMN: minimal hastalık
PMD: Minimal hastalık ve en az 1 kaviter lezyon
PAD: İlerlemiş hastalık

Başlangıç sitokin düzeyleri



TB gruplarında (Açık renk bar) tüm sitokinler sağlıklı kontrolden (koyu bar) daha yüksek

Radyolojik iyileşmeye göre sitokin düzeyleri



IL-2 ve IL-4 düzeyleri yavaş iyileşen ve orta iyileşenlerde hızlı iyileşenlere göre istatistiki olarak daha yüksek.
Diğerlerinde de yükseklik var fakat istatistiki anlamlı değil

Sonuç

•Sitokin analizleri radyoljik iyileşmenin takibi ve tahmin edilmesinde önceden belirleyici olabilirler.

•Sitokin analizleri hem hastalığın takibinde iyileşme göstergesi olarak hem de hastalığın başında prognoz göstergesi olarak kullanılabilirler.

•İleride TB kontrol programlarına dahil edilebilirler.

Cochrane Library

Cochrane Database of Systematic Reviews

Nutritional supplements for people being treated for active tuberculosis (Review)

Grobler L, Nagpal S, Sudarsanam TD, Sinclair D

Beslenme desteğinin aktif TB üzerine etkisi

Grobler L, Nagpal S, Sudarsanam TD, Sinclair D.
Nutritional supplements for people being treated for active tuberculosis.
Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD006086.
DOI: 10.1002/14651858.CD006086.pub4.

www.cochranelibrary.com

WILEY

Nutritional supplements for people being treated for active tuberculosis (Review)

Grobler L, Nagpal S, Sudarsanam TD, Sinclair D

- Aktif TB'de beslenme desteğinin, ölüm, kür oranı, tedavi tamamlama, hayat kalitesi ve kilo alımı üzerine etkileri araştırılmış
- Kriterlere uygun 35 çalışma bulunmuş
- Toplam katılımcı 8283 kişi
- Makro (beslenme ve enerji desteği) ve mikro beslenme ürünlerinin (Multi vitamin, vitamin A, D, E, selenyum, Çinko, arginin) yukarıdaki paremetreler üzerine etkisi incelenmiş

Nutritional supplements for people being treated for active tuberculosis (Review)

Grobler L, Nagpal S, Sudarsanam TD, Sinclair D

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Multi-micronutrient supplementation compared with placebo for patients with active tuberculosis

Patient or population: adults and children with active tuberculosis
Settings: low- and middle-income countries
Intervention: multi-micronutrient supplements
Comparison: placebo or no intervention

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Multi-micronutrients				
Death	HIV-negative participants		RR 0.86 (0.46 to 1.6)	1219 (4 trials)	⊕⊕◯◯ low[1,2,3]	Multi-micronutrient supplements may have little or no effect on mortality in HIV-neg-
	40 per 1000	34 per 1000 (18 to 64)				
	HIV-positive participants		RR 0.92 (0.69 to 1.23)	1429 (3 trials)	⊕⊕⊕◯ moderate[4,5]	Multi-micronutrients probably have little or no effect on mortality in HIV-positive tuberculosis patients not on ARV therapy
	357 per 1000	328 per 1000 (246 to 439)				
Cure rate	-	-	-	(0 trials)	-	We don't know if multi-micronutrients improve cure in tuberculosis patients
Treatment completion	970 per 1000	960 per 1000 (920 to 101)	RR 0.99 (0.95 to 1.04)	302 (1 trial)	⊕◯◯◯ very low[6,7]	We don't know if multi-micronutrients improve treatment completion in tuberculosis patients

Beslenme desteklerinin ölüm oranı, kür oranı ve tedavi tamamlama üzerine etkisi yok

Nutritional supplements for people being treated for active tuberculosis (Review)

Grobler L, Nagpal S, Sudarsanam TD, Sinclair D

Remaining sputum positive (at 4 weeks)	**309 per 1000**	**312 per 1000** (263 to 371)	**RR 0.92** (0.63 to 1.35)	1020 (2 studies)	⊕◯◯◯ **very low**[8,9,10]	We don't know if multi-micronutrients reduce the proportion of patients still sputum positive at 4 weeks
Weight gain	-	-	Not pooled	2940 (5 trials)	⊕⊕◯◯ **low**[11]	Multi-micronutrient supplements may not improve weight gain in tuberculosis patients
Quality of life	-	-	-	(0 trials)	-	We don't know if multi-micronutrients improve quality of life in tuberculosis patients

*The **assumed risk** is taken from the risk in the control groups of the included studies. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
Abbreviations: CI = confidence interval; RR = risk ratio; GRADE = Grading of Recommendations Assessment, Development and Evaluation

Beslenme desteklerinin kilo alımı ve hayat kalitesi üzerine belirgin etkisi yok

Nutritional supplements for people being treated for active tuberculosis (Review)

Grobler L, Nagpal S, Sudarsanam TD, Sinclair D

Sonuç

•Bazı çalışmalarda kilo alımı üzerine pozitif etkisi olsa da beslenme ve enerji desteğinin tüberküloz tedavi sonuçlarına etkisine dair yeterli araştırma yok

•TB tedavisi öncesi bazı vitamin düzeyleri düşük bulunsa da, önerilen günlük miktarın üzerinde rutin vitamin desteğinin klinik faydasına ait yeterli destek yok

Dikkatiniz ve sabrınız
için teşekkürler