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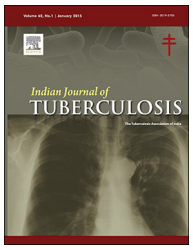

Abstracts

Angiopoietins as biomarkers of disease severity and bacterial burden in pulmonary tuberculosis

Kumar NP, Velayutham B, Nair D, Babu S. *Int J Tuberc Lung Dis* 2016; **21(1)**: 93–99. https://doi.org/10.5588/ijtld.16.0565

Background: Circulating angiogenic factors of the vascular endothelial growth factor family are important biomarkers of disease severity in pulmonary tuberculosis (PTB). However, the role of angiopoietins, which are also involved in angiogenesis, in PTB is not known.

Objective and design: To examine the association of circulating angiopoietins with TB disease or latent tuberculous infection (LTBI), we examined the systemic levels of angiopoietin (Ang) 1, Ang 2 and Tie-2 receptor in individuals with PTB ($n = 44$), LTBI ($n = 44$) or no tuberculous infection (NTBI) ($n = 44$).

Results: Circulating levels of Ang-1, Ang-2 and Tie-2 were significantly higher in PTB than in individuals with LTBI or NTBI. Moreover, Ang-1, Ang-2 and Tie-2 levels were significantly higher in PTB with bilateral disease. The levels of these factors also exhibited a significant positive relationship with bacterial burdens in PTB. Receiver operating characteristics curve analysis revealed Ang-2 as a marker distinguishing PTB from LTBI or NTBI. Finally, the circulating levels of Ang-1, Ang-2 and Tie-2 were significantly reduced following anti-tuberculosis chemotherapy.

Conclusions: Our data demonstrate that PTB is associated with elevated levels of circulating angiopoietins, possibly reflecting endothelial dysfunction. In addition, Ang-2 could prove useful as a biomarker to monitor disease severity, bacterial burden and therapeutic responses.

Conflicts of interest

The authors have none to declare.

Recent developments in genomics, bioinformatics and drug discovery to combat emerging drug-resistant tuberculosis

Swaminathan S, Sundaramurthi JC, Palaniappan AN, Narayanan S. *Tuberculosis* 2016; **101**. http://dx.doi.org/10.1016/j.tube.2016.08.002

Emergence of drug-resistant tuberculosis (DR-TB) is a big challenge in TB control. The delay in diagnosis of DR-TB leads to its increased transmission, and therefore prevalence. Recent developments in genomics have enabled whole genome sequencing (WGS) of *Mycobacterium tuberculosis (M. tuberculosis)* from 3-day-old liquid culture and directly from uncultured sputa, while new bioinformatics tools facilitate to determine DR mutations rapidly from the resulting sequences. The present drug discovery and development pipeline is filled with candidate drugs which have shown efficacy against DR-TB. Furthermore, some of the FDA-approved drugs are being evaluated for repurposing, and this approach appears promising as several drugs are reported to enhance efficacy of the standard TB drugs, reduce drug tolerance, or modulate the host immune response to control the growth of intracellular *M. tuberculosis*. Recent developments in genomics and bioinformatics along with new drug discovery collectively have the potential to result in synergistic impact leading to the development of a rapid protocol to determine the drug resistance profile of the infecting strain so as to provide personalized medicine. Hence, in this review, we discuss recent developments in WGS, bioinformatics and drug discovery to perceive how they would transform the management of tuberculosis in a timely manner.

Conflicts of interest

The authors have none to declare.

http://dx.doi.org/10.1016/j.ijtb.2017.01.008
0019-5707/

Identifying children with tuberculosis among household contacts in The Gambia

Egere U, Togun T, Sillah A, Mendy F, Otu J, Hoelscher M, Heinrich N, Hill PC, Kampmann B. *Int J Tuberc Lung Dis*. 2016;**21 (1)**:6–11. https://doi.org/10.5588/ijtld.16.0289

Setting: Greater Banjul Area of the Gambia.

Objectives: To identify co-prevalent tuberculosis (TB) among child contacts of adults with smear-positive TB.

Design: Child contacts aged <15 years in the immediate household and compound were prospectively enrolled and evaluated for TB disease using screening questionnaires and the tuberculin skin test (TST). Symptomatic and/or TST-positive (≤10 mm) contacts were further investigated.

Results: Of 4042 child contacts who underwent symptom screening and TST, 3339 (82.6%) were diagnosed as TB-exposed but not infected, 639 (15.8%) were latently infected and 64 (1.6%) had co-prevalent TB. Of the 64 TB cases, 50 (78.1%) were from within the immediate household of the index case, and 14 (21.9%) from within the same compound. Of the 27 asymptomatic but TST-positive children diagnosed with TB, 7 were microbiologically confirmed. The median age of the TB cases was 4.4 years (interquartile range 1.9–6.9); 53.1% were aged <5 years. Of the 4042 child contacts, 206 (5%) slept in the same bed as the index case; 28.1% of all TB cases occurred in this group. Symptom screening alone would have detected only 57.8% of the co-prevalent cases.

Conclusion: In our community setting, if contact tracing is restricted to symptom screening and immediate households only, nearly half of all co-prevalent TB disease in child contacts would be missed.

Conflicts of interest

The authors have none to declare.

Relationship between nutritional support and tuberculosis treatment outcomes in West Bengal, India

Samue B, Volkmann T, Cornelius S, Mukhopadhay S, Jose M, Mitra K, Kumar AMV, Oeltmann JE, Parija S, Prabhakaran AO, Moonan PK, Chadha VK. *Journal of Tuberculosis Research* 2016. https://doi.org/10.4236/jtr.2016.44023

Introduction: Poverty and poor nutrition are associated with the risk of developing tuberculosis (TB). Socioeconomic factors may interfere with anti-tuberculosis treatment compliance and its outcome. We examined whether providing nutritional support (monthly supply of rice and lentil beans) to TB patients who live below the poverty line was associated with TB treatment outcome.

Methods: This was a retrospective cohort study of sputum smear-positive pulmonary TB patients living below the poverty line (income of <$1.25 per day) registered for anti-tuberculosis treatment in two rural districts of West Bengal, India during 2012 to 2013. We compared treatment outcomes among patients who received nutritional support with those who did not. A log-binomial regression model was used to assess the relation between nutritional support and unsuccessful treatment outcome (loss-to-follow-up, treatment failure and death).

Results: Of 173 TB patients provided nutritional support, 15 (9%) had unsuccessful treatment outcomes, while 84 (21%) of the 400 not provided nutrition support had unsuccessful treatment outcomes ($p < 0.001$). After adjusting for age, sex and previous treatment, those who received nutritional support had a 50% reduced risk of unsuccessful treatment outcome than those who did not receive nutritional support (Relative Risk: 0.51; 95% Confidence Intervals: 0.30–0.86).

Conclusion: Under programmatic conditions, monthly rations of rice and lentils were associated with lower risk of unsuccessful treatment outcome among impoverished TB patients. Given the relatively small financial commitment needed per patient ($10 per patient per month), the national TB programme should consider scaling up nutritional support among TB patients living below the poverty line.

Conflicts of interest

The authors have none to declare.

Finding the right dose of rifampicin, and the right dose of optimism

Ruslami R, Menzies D. *The Lancet Infectious Diseases* 2017;**17 (1)**:2–3. http://dx.doi.org/10.1016/S1473-3099(16)30315-2

After the widespread introduction of rifampicin in the early 1970s, it took another two decades, and more than 50 randomised trials with more than 20,000 participants[1] to finalise the drugs, doses, and schedule for the currently recommended regimen for newly diagnosed patients with active tuberculosis. Yet this regimen has important drawbacks, most notably the 6 months duration, and frequent toxicity. These limitations have stimulated considerable research interest to find shorter and better-tolerated regimens.

New drug development is expensive, and progress in the past 20 years has been very slow. Investigators have re-examined current drugs and doses, including the dose of rifampicin, which was initially selected as the lowest effective dose because this drug was very expensive when first introduced. Bacterial clearance in mice,[2] extended early bactericidal activity in patients with pulmonary tuberculosis,[3] and 6-month survival in patients with tuberculosis meningitis[4] have all been improved with higher doses of rifampicin. In patients with tuberculosis, meningitis survival was closely related to serum concentrations.[5] In *The Lancet Infectious Diseases*, Martin Boeree and colleagues[6] report findings of a randomised controlled phase 2B trial of patients with drug-sensitive pulmonary tuberculosis. The trial assessed four experimental regimens given for 12 weeks followed by 14 weeks of isoniazid and rifampicin. The regimen with rifampicin dosage of 35 mg/kg (RIF_{35}) resulted in faster time to culture conversion compared with the standard regimen. This difference was not seen with the other experimental regimens (including two with rifampicin dose of 20 mg/kg), and was seen