

63% of the increase in case notification by DOTS programs between 2002 and 2003.

Conclusions: Without DOTS and Public awareness program, it is highly unlikely that countries will be able to develop effective and sustainable tuberculosis program. With the introduction of DOTS, achieving the global targets for tuberculosis control has now become a realistic proposition.

OL-036 Incidence of multi drug resistant tuberculosis (MDR-TB) in extrapulmonary tuberculosis cases in Northern India

A.K. Maurya^{1*}, S. Kant¹, V.L. Nag², R.A.S. Kushwaha¹, M. Kumar², S. Jain², T.N. Dhole². ¹Department of Pulmonary Medicine, Chhatrapati Shahuji Maharaj Medical University (Erstwhile King George Medical University) Lucknow, India, ²Department of Microbiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Background: The importance of extrapulmonary tuberculosis (EPTB) among all forms of tuberculosis has not yet been ascertained in developing countries. Multi drug resistant tuberculosis (MDR-TB) is an increasing worldwide problem as well as in India. The transmission of resistance strains is increasing day-by-day because of the rising load of MDR-TB patients. The aim of the study to know incidence of MDR-TB in extra pulmonary tuberculosis cases in tertiary care hospitals in Northern India.

Materials and Methods: A total of 789 specimens from patients of EPTB cases with varied presentation were studied. All the samples were processed for ZN staining for Acid Fast bacilli and radiometric BACTEC culture for Mycobacteria. Identification of *M. tuberculosis* complex (MTBC) was done by BACTEC NAP (p-nitro- α -acetylamino- β -hydroxy propiophenone) differentiation test. All *M. tuberculosis* isolates were recovered for radiometric based drug susceptibility pattern against streptomycin, isoniazid, rifampicin and ethambutol (SHRE) using the proportion method.

Results: 165 (20.7%) of 797 patients clinically suspected to have extra pulmonary tuberculosis were BACTEC culture positive for mycobacteria. Out of 165 cases, 127 (77%) were newly diagnosed and 38 (23%) previous treated cases. On Biochemical characterization, 123 (74.5%) of the 164 isolates were identified as *Mycobacterium tuberculosis* complex by NAP Test. A total of 123 (74.5%) *M. tuberculosis* isolates for firstline antitubercular drug susceptibility pattern. We observed that MDR strains (resistance to rifampicin and isoniazid) were found in 15 (12.1%) of 123 isolates. Overall results shown that incidence of MDRTB in EPTB case was 12.1%.

Conclusion: *M. tuberculosis* was present in 20.7 percent samples. The maximum numbers of *M. tuberculosis* were isolated from lymph node aspiration. Our study originates that multi drug resistant tuberculosis is gradually increased in extrapulmonary tuberculosis cases.

OL-037 Analysis of microRNA expression profiling identifies two microRNAs as potential diagnostic markers for active tuberculosis

J. Wu^{1*}, C.Y. Lu¹, W.H. Zhang¹. ¹Department of infectious disease, Huashan Hospital, Fudan University, China

Background: The biological behaviors and disease relevance of microRNAs in the development of active tuberculosis (ATB) are still unknown.

Methods: The expression profile of microRNA under the challenge of *mycobacterium tuberculosis* PPD was first measured using microarray in PBMCs isolated from

ATB patients and health controls (HC). The remarkably reactive microRNAs were further validated in other cohorts by quantitative real-time PCR (qRT-PCR). The receiver operating characteristic (ROC) curve was plotted to evaluate the diagnostic value of the determined PPD-responsive microRNAs.

Result: It turned out that 14 out of 866 human microRNAs showed significantly higher increased expression after PPD stimulation in ATB than in HC groups. The qRT-PCR study validated the findings from microarray-based screen, in which, upon PPD stimulation, miR-155 had fold change of 1.4 in HC group and 3.7 in ATB group ($p < 0.0001$); miR-155* had 1.9 in HC and 4.6 in ATB group ($p < 0.005$). In ROC plots, area under the curve (AUC) was 0.8972 for miR-155 and 0.7945 for miR-155*.

Conclusion: MiR-155 and miR-155* exhibited characteristic expression by TB-specific antigen, suggesting that they can be potential diagnostic markers under the challenge of specific MTB antigens.

OL-038 Efficiency of RD-1 antigen-specific interferon- γ release assays (IGRAs) blood-based tests for the diagnosis of *Mycobacterium tuberculosis* infection in Pott's disease at a tertiary care hospital

M. Kumar^{1*}, R. Kumar², V.L. Nag³, N. Krishnani⁴, U. Singh⁵, T.N. Dhole³, A.K. Maurya³, S.G. Babu¹. ¹Department of Biotechnology, Babasaheb Bhimrao Ambedkar University, Lucknow, India, ²Department of Neurosurgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ³Department of Microbiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ⁴Department of Pathology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ⁵Department of Biostatic, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Objective: QuantiFERON-TBGold (QFT-G) test is a recent method in the diagnosis of latent or active tuberculosis and shows better results. This assay based on the detection of interferon-gamma; produced by stimulated T lymphocytes with tuberculosis specific antigens. In this study we evaluate the degree of usefulness of this method in detecting the Pott's disease.

Methods: A total of 83 cases were included in this study. Among them few were confirmed tuberculosis patients as evidenced by the traditional clinical techniques like Ziehl Nelsen smear, BACTEC culture, PCR *IS6110* gene and histopathology as well as they undergone surgery for treatment. In this study nonsurgical cases were also included, their confirmation was done with the TB ELISA. The above all cases were compared with the recent QFT-G assay for its efficacy, sensitivity and specificity in confirming the cases of both suspected and confirmed tuberculosis.

Results: The study comprised of 83 cases, however 5 cases were excluded in this as they were found to be malignant. Among the 52 surgical cases, it was found that 39 were tested to be tuberculosis and 13 were found to be negative by the traditional clinical techniques. However, the QFT-G assay gives the result that among the 39 active tuberculosis samples only 24 found to be positive. Interestingly, 1 has given tuberculosis positive from the samples observed to be negative by the traditional tests. Then, the sensitivity and specificity was 62% and 92%, (p value = 0.001), 56% and 100%, (p value = 0.009) surgical and nonsurgical patient correspondingly. The overall 60% sensitivity and 95% specificity (p value ≤ 0.001).

Conclusion: By analyzing the obtained results we can say that the specificity of QFT-G was high but its sensitivity

was low. Further, the result needs to be verified by other laboratory diagnosis methods in case of Pott's disease.

OL-039 Can *Mycobacterium tuberculosis* DNA be detected in plasma/serum samples from tuberculosis patients?

D. Chen^{1*}, B. Gu¹, S.Y. Pan¹, H. Wang¹, Z.H. Yan¹, C. Zhao¹, G.Y. Liu¹. ¹Department of Laboratory Medicine, the First Affiliated Hospital of Nanjing Medical University, China

Background: Tests based on PCR have shown promise for the detection of *M. tuberculosis* in different clinical samples except plasma/serum. The purpose of this study was to know that whether *M. tuberculosis* DNA can be detected in plasma/serum samples.

Methods: 43 serums and 94 plasma were collected from 124 clinical diagnosed TB patients. Four different *M. tuberculosis* DNA extraction methods, including phenol-chloroform method, Qiagen kit, Omega kit and magnetic bead method were compared to get higher sensitivity. One quantitative fluorescent PCR designed by this study was used for the detection of *M. tuberculosis* DNA.

Results: The highest DNA extraction efficiency (52.8%) and the best reproducibility (CV=26.7%) were seen in the magnetic bead method. And *M. tuberculosis* DNA can really be detected in some samples, and 39 of the 124 (31.5%) TB patients showed *M. tuberculosis* DNA positive in plasma/serum samples. Interestingly, 35.3% (12/34) smear negative cases demonstrate *M. tuberculosis* DNA positive.

Conclusion: In conclusion, this is the first study to report the existence of circulating *M. tuberculosis* DNA in plasma/serum from tuberculosis patients and showed that the detection of *M. tuberculosis* DNA may provide valuable information for the diagnosis of AFB negative TB patients.

OL-040 Rapid identification and molecular characterization of drug resistant *Mycobacterium tuberculosis* isolates circulating in China by multilocus PCR and electrospray ionization mass spectrometry

F.F. Wang^{1*}, D.J. Ecker², W.H. Zhang¹, Y.-W. Tang³. ¹Department of Infectious Diseases, Huashan Hospital, Fudan University, Shanghai, China, ²Ibis Biosciences, Inc., a subsidiary of Abbott Molecular, Inc., Carlsbad, CA, ³Departments of Pathology and Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

Objective: The emergence of multidrug-resistant (MDR)-TB and more recently, of extensively drug-resistant (XDR)-TB is a real threat to achieve TB control and elimination. Quick detection of drug resistance is an urgent clinical need for personalized treatment to control MDR-TB or XDR-TB.

Methods: We used multilocus PCR and electrospray ionization mass spectrometry (PCR/ESI-MS) to determine the genotype and drug resistance profiles for 96 *Mycobacterium tuberculosis* isolates circulating in low and high endemic regions (Shanghai, n=49; Chongqing, n=47) in China.

Results: The mutation profiles obtained by the PCR/ESI-MS assay indicated that Principal Genetic Group 1 (PGG1) profile (87.5%) was dominant across the isolates tested in China. The results revealed that a cluster of 11 isolates with *katG* S315T & *inhA* promoter C-15T, *rpoB* S531L, and *embB* M306I in Chongqing, the high TB endemic region, which was not observed in Shanghai, the low endemic region. In addition, another resistance mutation profile with *katG* S315T & *inhA* promoter T-8C, *rpoB* D516G & P564R/A, was detected in 10 isolates in high endemic region in comparison to one in low endemic region. Drug-resistant gene mutations were

more diversified in the low endemic region than in the high endemic region.

Conclusion: PCR/ESI-MS can provide another rapid and accurate laboratory diagnostic tool for antituberculosis drug resistance determination. This new technique has potential to facilitate rapid determination of MDR-TB in China, allowing timely guidance for individualized treatment.

Free Paper Presentation 6: Hepatitis B
Saturday, July 16, 2011, 15:30–17:00
Meeting Room 310

PL-006 HBV infection modeling and numerical simulation for anti-HBV infection personalized combination therapy

X. Chen¹, L.Q. Min^{1*}, Y.A. Ye², Q. Zhang¹. ¹University of Science and Technology Beijing, ²Traditional Chinese Internal Medicine Key Laboratory of China Education Ministry, Dongzhimen Hospital, Beijing University of Chinese Medicine, China

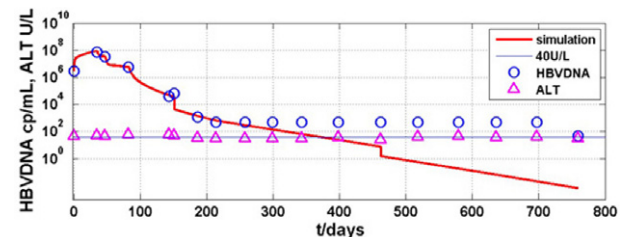
Background: Some chronic HBV (CHB) patients have normal ALTs and hepatic injuries. Chinese herbal medicine and nucleosides combination treatments may be effective for some of such kind patients. It needs to develop an anti-HBV infection treatment model to interpret the mechanism for curable CHB patients with near normal liver functions.

Methods: A 57 years old male chronic HBeAg positive patient (nucleosides-native) received Chinese Herbal Medicine (CHM 15–23 ingredients, 450–600g) treatment two times daily for 24 weeks, switched to CHM + Adefovir Dipivoxil for 53 weeks, then switched to CHM + Entecavir for 21 weeks. A new differential equation model is introduced to describe the dynamics of anti-HBV infection treatment, in which a *term* is in charge of killing virus rather than infected hepatocytes.

Results: His HBeAg got seroconversion at week 98. The numerical simulation of the model and his HBV DNA, ALT are shown in following figure.

Conclusions: Analysis shows that a treated CHB patient with infective number $R_0 < 1$ will eventually be cured. Large value of that *term* makes patient's virus be eventually cleared without damaging hepatocytes.

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OL-041 Evaluation of serum level changes of sCD26 & sCD30 before and after treatment with interferon among naïve chronic hepatitis B patients

M. Alavi-Moghaddam^{1*}. ¹Shahid Beheshti University Of Medical Sciences, Iran

Propose: To evaluate the role of serum levels of sCD26 and sCD30 in predicting the outcome of therapy with IFN α among naïve chronic hepatitis B patients.