371. MDR- and XDR-TB: clinical and public health experiences

P3316
Poor treatment outcomes of XDR-TB patients in resource-limited settings

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Background: According to the last report of the World Health Organization, 60 countries have diagnosed at least one case of extensively drug-resistant tuberculosis (XDR-TB). Treatment success rates for XDR-TB have been highly variable. To gain further insight into this issue we compared outcomes in a low (LI) versus middle/high income (MHI) countries.

Objective: To compare XDR-TB-related treatment outcomes (i.e. culture conversion and mortality) in MHI vs. LI countries

Methods: A comparative retrospective evaluation of data from a European (Estonia and Italy) vs. South-African datasets, which included only culture-confirmed XDR-TB cases. Treatment success rates for XDR-TB have been highly variable. To gain further insight into this issue we compared outcomes in a low (LI) versus middle/high income (MHI) countries.

Results: A total of 235 XDR-TB patients were enrolled (61 from Europe (70.5%, males) and 174 (51.2% males) from South Africa). Their mean (standard deviation) age was 47.0 (12.2) and 35.2 (11.2) years, respectively (P < 0.001). HIV co-infection was significantly more frequent in the South-African cohort (28/174, 16.1%, vs. 0/235, 0%; P < 0.001). HIV co-infection was significantly associated with death, but not culture conversion, in the combined cohort (aOR: 2.37; P < 0.008).

Conclusion: Unfavorable outcomes, although common in both settings, are more frequent in a resource-poor setting. These data can inform prevention and treatment strategies for XDR-TB in different settings.

P3317
The incidence of multi drug resistant tuberculosis among patients receiving standardized treatment regimen for suspected MDR-TB

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The LCP-PMDT started the implementation of Standardized treatment regimen for all smear positive Drug Resistant Tuberculosis suspects. The appropriateness of these regimens need to be evaluated. This is a Descriptive prospective cohort study, the objective is to determine the Incidence of MDR-TB among patients receiving Standardized treatment regimen for suspected MDR-TB.

256 patients received standardized treatment regimen, 180 patients have available culture and DST results. 76 patients still have pending culture and DST results. Of the 180 patients with available culture and DST results, 113 were confirmed MDR-TB. 55 (76.3%) patients belonging to the others Non-DOTS multiple treatment group were confirmed MDR-TB compared to 7 (33.3%) patients with Non-DOTS with single treatment. 17 of 18 (94%) patients who belonged to category I failure group were confirmed MDR-TB. 5 of 11 (45.5%) patients under category I relapse, 8 (33.3%) of 24 patients under category I relapse were confirmed MDR-TB. 11 of 20 (55%) patients under category II relapse and 10 (90.1%) of 11 patients under category II failure were confirmed MDR-TB.

Conclusion: MDR-TB occurs more frequently among the standardized regimen II group (category I failure, category II failure, and other Non-DOTS with multiple treatment). Recommendations: Initiation of standardized regimen for MDR-TB for patients with Category I failure, Category II failure, category II relapse and those with Non-DOTS with multiple treatment while awaiting the results of the DST. Category II treatment regimen, should be used in category I RAD and category I Relapse pending culture and DST results.

P3318
Non-pharmacological factors for the emergence of drug resistance in patients of pulmonary tuberculosis: An Indian overview

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Aim: To evaluate the impact of or non pharmacological factors on the emergence of drug resistant tuberculosis in eastern Uttar Pradesh.

Material and methods: 150 diagnosed cases of drug resistance pulmonary tuberculosis via culture and sensitivity were evaluated of their socio-economic background with special reference to their literacy, annual income, housing, reason of discontinuation of treatment, migration status etc. Data was collected and analysed statistically.

Observation: Prevalence of drug resistance was more in large families(76%), with lower housing area per person(62%), with at least one migration history(75.33%), having at least one member previously sputum positive(65.33%) and lower annual income(66%). Also was more in illiterates(58%). The reason of discontinuation of treatment, migration status etc. Data was collected and analysed statistically.

Table 1: Reason of discontinuation of drugs

<table>
<thead>
<tr>
<th>Reason of discontinuation of drugs</th>
<th>No and percentage of total patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No discontinuation</td>
<td>10, 6.66%</td>
</tr>
<tr>
<td>Adverse effect</td>
<td>27, 18%</td>
</tr>
<tr>
<td>Resolution of basic symptom (early asymptomatics)</td>
<td>60, 40%</td>
</tr>
<tr>
<td>Advised by unqualified doctors</td>
<td>18, 12%</td>
</tr>
<tr>
<td>Fear of related social stigma</td>
<td>12.8%</td>
</tr>
<tr>
<td>Can’t afford expenditure of treatment</td>
<td>23, 15.33%</td>
</tr>
</tbody>
</table>

Conclusion: Role of socioeconomic factors can’t be denied in emergence of drug resistance. Patient centered approach especially proper counselling may help in this regard.
P3319 The efficacy of a rifabutin-containing regimen for rifabutin-susceptible multidrug-resistant tuberculosis
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Objective: We investigated the efficacy of a rifabutin (RBU)-containing regimen for the treatment of rifabutin-susceptible multidrug-resistant tuberculosis (MDR-TB).

Methods: From 256 patients diagnosed with MDR-TB at Asan Medical Center in South Korea between January 2006 and December 2010, 39 patients (15.2%) were susceptible to RBU. Of these 39 patients, nine patients who were appropriately treated with a RBU-containing regimen were included, and the outcomes of both groups were retrospectively compared.

Results: In the nine patients with RBU-susceptible MDR-TB, their mean age was 43.7 years and the proportion of extensively drug-resistant TB (XDR-TB) was 44.4% (4/9). Baseline characteristics and the drug resistance pattern (except RBU) did not differ between the two groups. Treatment success was achieved in all nine patients in the RBU group: cure in six (66.7%), and treatment completion in three (33.3%). On the other hand, the treatment success rate was 48.1% (13/27) and treatment failed in 14 (51.9%) of the 27 patients in the control group (p = 0.012).

Conclusions: RBU seems to be useful in the treatment of MDR-TB patients who are susceptible to RBU.

P3320 Treatment outcomes of MDR-TB cases registered in Bucharast sector 4 during 2004-2008
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Introduction: Although the TB incidence rate declined significantly in Romania in the last decade, from 142.2/100,000 in 2002 to 90.2/100,000 in 2010, the MDR-TB-remains at a rate of attention (2.9% in new and 10.9% in retreated cases).

Objective: To analyze the treatment outcomes of MDR-TB cases registered in the TB Dispensary of Bucharast Sector 4, in order to optimize the TB control in its territory.

Material and methods: We conducted an observational retrospective study of TB MDR-TB cases registered in Bucharast Sector 4 since December 2004-December 2008. Data have been collected from the TB register of the dispensary, TB information system, treatment records and epidemiological surveys.

Results: Out of 78 patients 35 have been included in the DOTS Plus project financed by the Global Fund (GLC group) and 43 have been treated from NTP resources (NTP group). Chronic patients represented 11.5% in GLC group and 30.9% in NTP group. 19% of all the patients treated in GLC group and 46.5% from NTP group have been treated with second line anti-TB drugs in the past. Overall success rate was 3 times higher in the GLC group (82.8%) than in the other (27.9%). New cases had a success rate of 95% in the GLC and only 66.6% in the NTP group. The relapses had a success rate of 72.7% in the GLC compared to 36.8% in the NTP group. The cases with second line medication in their histories have a success rate of 57.1% in the GLC and just 5% in the NTP group.

Conclusion: The favorable outcome of MDR-TB patients in DOTS Plus project demonstrates the real benefit brought by this project and its extension to all MDR-TB patients in the country should be required.

P3321 Treatment outcome of multi drug resistant tuberculosis patients in modified DOTS-PLUS: A new strategy
Rajendra Prasad1, Abhijeet Singh2, Rahul Srivastava3, Ramawadh

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1Pulmonary Medicine, CSM Medical University (Erstwhile King Georges Medical University), Lucknow, UP, India; 2Microbiology, CSM Medical University (Erstwhile King Georges Medical University), Lucknow, UP, India

Background: Multi Drug Resistant Tuberculosis is a global problem and growing threat to human health with notoriously difficult and challenging treatment. Aims and objective: To study the treatment outcome with second line drugs in patients of MDR-TB in modified DOTS-PLUS strategy.

Methods: A prospective cohort study analysis was done on consecutive patients with MDR-TB attending the Dept of Pulmonary, CSMSKU, between June 2009 to Feb 2010 with follow-up till February 2012. All the patients were given multidrug therapy free of cost as per DOTS PLUS Protocol of Revised National Tuberculosis Control Programme (RNTCP). Treatment included monthly follow up, adherence check up, radiological and bacteriological assessment (sputum smear advised monthly till conversion then quarterly; culture for MTB at 0.6,12,18,24 months);intense health education and monitoring of adverse effects. Patients outcome considered as cure when atleast 2 of the last 3 cultures were negative and as failure when the same were positive.

Results: All the patients had resistance to at least Isoniazid and Rifampicin with mean no. of 3.02 drugs and were seroergicive for HIV. Default rate and expiry rate at the completion of 24 months of treatment were observed to be 7(17.2%) and 10(10.2%) respectively. Mean smear and culture conversion time were 3.4±2.1 months (1-11) and 4.6±2.5 months (4-12) respectively. Spu tum smear and culture conversion rate were 75/84(92.5%) and 71/84(87.5%) respectively with only 10(10.2%) patients remained culture positive. Significant side effects were experienced in only 17.4% patients.

Conclusions: Modified DOTS-PLUS strategy can be model for treatment of MDR-TB in private sector.

P3322 Failures in treatment of patients according DOTS-PLUS program: Medico-social predictors
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The problem of treatment patients who suffering from multi drug resistance tuberculosis of lungs (MDR) remains one of the main problems of phthisiology now. Efficiency of treatment of this group patients according the program DOTS-PLUS fluctuates in a range 61%-77%, and failure in treatment is registered in 3%-14% of cases in different countries. The purpose of our research is revealing predictors of failure in treatment of the patients suffering MDR TB.

200 MDR TB patients who were treated under program DOTS-PLUS in the Tomsk region (from 2000 to 2008) have been included in case-control study. Patients with failure in treatment (n=100) were in the main group, and patients (n=100) who were cured were in the comparison group. The age of patients varied from 16 till 75 years. The deficiency of body weight (weight <15.9 and less) has brought about the increase of treatment failures in treatment (OR 11.0). Revealing cavernous tuberculosis at the initial stage increased risk of failure more than in 5 times (OR 5.69). The complications increasing risk of failure in treatment were respiratory insufficiency (OR 3.25), anemia (OR 13.78) and hemoptysis (OR 3.80). For therapy failure following accompanying diseases had prognostic value: pathology of urinary system (OR 6.62), chronic not obstructive bronchitis (OR 2.43), pathology of gastrointestinal tract (OR 3.23) and pathology of cardiovascular system (OR 3.52).

Thus development of MDR TB and efficiency of its treatment depends from both social, and medical factors which are necessary to consider at the initial stage of treatment and to apply measures for their minimization.

P3323 Success of the patient-oriented approach to MDR-TB treatment in Tomsk Oblast, Russia, 2000-2009
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In 2000-2009, 1141 MDR TB patients were treated in Tomsk Oblast (civilian sector). MDR-TB treatment effectiveness: 63.1% - cured, 12.6% - failed. 8.3% - died, 15.9 - defaulted. Since 2005, a patient-oriented approach has been developed (daily food packages for patients’ motivation, treatment at home, Red Cross volunteers, alcohol program, searching for patients who miss treatment using social and psychological support - “Spuktnik” program etc.). This approach resulted in default decrease from 29.3% (2003) to 10.4% (2009). MDR-TB reservoir decreased from 823 patients (2002) to 380 (2011), including 291 patients who are still on treatment. From 2004 to 2011: TB incidence among new cases (per 100 000) decreased from 105.6 to 75.3 (by 28.6%). TB prevalence - from 205.2 to 104.9 (by 48.9%). TB mortality - from 17.7 to 5.8 (by 67.2%). “Spuktnik” (smear negative, without lung destruction) among new cases increased from 25% (2005) to 40% (2011).

Conclusions: The patient-oriented approach significantly improved TB situation in Tomsk Oblast. We are concerned that patients with “Spuktnik” who are not provided with in-depth examination might be admitted to general health care settings and treated for pneumonia using fluoroquinolones.

P3324 Long term treatment outcome in multi drug resistant tuberculosis
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Background: Multi Drug Resistant Tuberculosis (MDR-TB) is an increasing worldwide problem which is difficult to treat and has greater risk of relapse.

Aims and objective: To analyze long term treatment outcome with second line drugs in patients with MDR-TB.

Abstract printing supported by Chiesi Visit Chiesi at Stand B2.10
Methods: A descriptive analyses of 93 consecutive patients with MDR-TB attending the Dept of Pulmonary Medicine, CSMUU, between June 1998 to February 2008 with follow-up till December 2010. All patients were admitted for average duration of 70 days and received a regimen chosen from Kanamycin, PAS, Ethionamide, Cycloserine, Fluoroquinolone, Isoniazid, Ethambutol and Pyrazinamide. Patients outcome was considered as cure when at least two of the last three (At 12, 18 & 24 m) cultures were negative and if failure when the same were positive. 

Results: All the patients had resistance to at least Isoniazid and Rifampicin with mean no. of 3.38 drugs. Average duration of pretreatment chemotherapy was 34.5 (10-62) months. Out of 93 patients enrolled, 75 completed the treatment as planned, 5 patients died during treatment, and 13 patients abandoned it or lost to follow up. Considering the best scenario cure rate was 93.33% (70/75) and in worst planned, 5 patients died during treatment, and 13 patients abandoned it or lost to follow up. The control of tuberculosis is facing challenges with the development of drug resistance as more and more drugs are used. Complex MDR-TB has recently emerged as a global patient with a similar issue. In Taiwan, there are around 600-1000 MDR-TB cases with 1.0% new TB cases, 6.2% treatment cases and 10.0% XDR-TB. Treating MDR-TB has become much more difficult, a new treatment regimen is mandatory.

Conclusion: The control of tuberculosis is facing challenges with the development of drug resistance as more and more drugs are used. Complex MDR-TB has recently emerged as a global patient with a similar issue. In Taiwan, there are around 600-1000 MDR-TB cases with 1.0% new TB cases, 6.2% treatment cases and 10.0% XDR-TB. Treating MDR-TB has become much more difficult, a new treatment regimen is mandatory.

Poster Discussion
Room A1 - 10:45 - 12:45
Background: Isoniazid-resistant tuberculosis is the most common form of mono drug resistance in tuberculosis (TB). There has been an outbreak of isoniazid-resistant TB in North London. An outbreak committee has made recommendations. Aim: To study isoniazid resistant TB patients attending Newham community chest clinic. Methods: The notes of 31 isoniazid-resistant TB patients treated between 2004 to 2009 were studied. The reference laboratory gave confirmation of resistance.

Results: The age range was 17 to 73 (median 32). Male: female 2.1:1. 7(23%) patients had North London outbreak strain. Of the 31 patients, 20(65%) had pulmonary involvement, 11(35%) had extensive disease and 8(26%) were sputum smear positive. The extra-pulmonary presentations were lymphadenopathy, abscesses and miliary TB. Six(19.3%) patients had risk factors for resistance. HIV was present in 1 patient. The majority of our patients were not associated with the outbreak. Conclusion: Treatment completion rates were satisfactory, and exceeded the target (90%) set by the TB outbreak control committee. There was no difference in treatment completion rates between the two regimes. Reference: [1] Maguire H, Forrester S, Adam S. Progress report and updated recommendations of the London Outbreak Control Committee May 2006.

P3311

Drug resistance trends and patterns of mycobacterium tuberculosis isolates from pulmonary tuberculosis patients at a tertiary care hospital in Turkey

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Objective: To determine the proportions and patterns of resistance to commonly used tuberculosis (TB) drugs (isoniazid [INH], rifampicin [R], ethambutol [E] and streptomycin[S]) among pulmonary TB patients and assess potential risk factors for drug resistance.

Methodology: Strains were collected from 1584 sputum smear negative or positive pulmonary TB patients with culture positive in tertiary care hospital of Turkey. Specimens were cultured in liquid and solid media, and drug susceptibility tests were performed for first-line drugs including isoniazid, rifampicin, streptomycin, ethambutol and pyrazinamide.

Results: Drug susceptibility testing (DST) has been obtained from all samples 442 (27.9%) of 1584 isolates were resistant to at least one of five antibiotics tested. 380 (18.9%) isolates were resistant to isoniazid; 168 (10.6%) to streptomycin; 137 (8.6%) to ethambutol; 203 (13.9%) to rifampicin. 146 isolates (9.2%) were multidrug resistant. Results also showed 49% of patients were below the age of 40 years.

Conclusion: Regardless of previous treatment history, the high resistance observed in isoniazid, which is a first-line drug. Treating culture-positive TB patients based on DOTs together with strengthened control programs should therefore be considered in the management of TB patients.

P3332

How big is the problem with MDR-TB cases in Macedonia?

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Multidrug resistant tuberculosis (MDR-TB) is defined as pulmonary tuberculosis caused by isoniazid and rifampicin resistant. Fluoroquinolones must be involved in standard treatment regimen of MDR-TB. Effect of old and the new generation fluoroquinolones are compared on sputum conversion to treat MDR-TB. 63 MDR-TB patients included. Patients were divided into two groups according to usage of ofloxacin and moxifloxacin. 26 patients used moxifloxacin and 37 patients used ofloxacin. Mean age was 32.7±12.3 in moxifloxacin group and 38.1±14.9 in ofloxacin group. Gender distribution (M/F) in moxifloxacin and ofloxacin group was 22/4, 14/23, respectively. All patients were HIV negative. Sputum conversion, culture conversion and treatment period were compared between two groups.

Table 1. Comparison of sputum conversion, culture conversion and treatment time with use of Moxifloxacin and Ofloxacin

<table>
<thead>
<tr>
<th></th>
<th>Moxifloxacin (mean ± SD)</th>
<th>Ofloxacin (mean ± SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum conversion</td>
<td>1.81±1.58</td>
<td>1.78±1.08</td>
<td>0.276</td>
</tr>
<tr>
<td>Culture conversion</td>
<td>1.96±1.31</td>
<td>1.81±0.81</td>
<td>0.857</td>
</tr>
<tr>
<td>Treatment time</td>
<td>21.6±5.43</td>
<td>21.68±5.43</td>
<td>0.545</td>
</tr>
</tbody>
</table>

Mann-Whitney U test 95% confidence interval.

There was no significant difference in sputum and culture conversion and treatment time between two group (p>0.05).

Conclusion: In spite of the declared information that moxifloxacin is more efficient than ofloxacin in treatment of MDR-TB; in this study there was no significant difference in sputum conversion, culture conversion and treatment time. Although patient number is not a lot, this result can make us think that economic reasons are important when selecting the quinolone group for the treatment.