Prevalence and risk factors for drug-resistant tuberculosis in HIV-infected patients - a Romanian single-centre experience

Irina Ianache[1], Simona Erscoiu[1,2], Manuela Nica[1], Gratiela Tardei[1], Emanoil Ceausu[1,2], Petre Calistru[2], Cristiana Oprea[1,2]
1. "Victor Babes" Hospital for Infectious and Tropical Diseases, Bucharest, Romania; 2."Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Objective:

Primary: to assess the prevalence of drug resistant (DR)-TB in HIV/TB co-infected patients from a Romanian tertiary health care facility.
Secondary: to estimate the risk factors for survival in this group

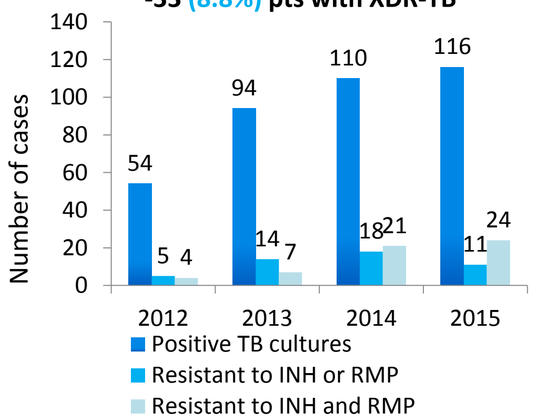
Methods:

- Prospective study on HIV-infected patients diagnosed with DR-TB at "Victor Babes" Clinical Hospital for Infectious Diseases, Bucharest, between January 2012 and December 2015.
- DR-TB strains were classified in **MDR-TB** (resistance to INH and RIF), **pre-XDR** (MDRTB and resistance to either quinolones or an injectable) and **XDR-TB** (MDR and resistance to both aminoglycosides and quinolones).
- Statistical analysis was performed using SPSS 20.0, survival being compared using Kaplan Meier curves

Results:

MDR-TB incidence among HIV-infected patients

9,012 person-years (PY): 374 pts with positive TB cultures and drug susceptibility testing performed: - 48 (12.8%) strains resistant to at least one drug (INH or RMP)
- 56 (14.9%) pts with overall MDR-TB (incidence 6.21/1000 PY)
- 23 (6.1%) pts with MDR-TB;
-33 (8.8%) pts with XDR-TB



MDR-TB	2012	2013	2014	2015	*P value*
Incidence /year	7.4%	7.4%	19.0%	20.6%	0.04

Socio-demographic and clinical characteristics		Total (n=56)
Gender – male	n(%)	39 (69.6)
Age (years) at HIV diagnosis	median (IQR)	29 (22-35)
Age (years) at TB-diagnosis	median (IQR)	31 (26-37)
Concomitant MDR-TB and HIV	n(%)	15 (26.7)
Modes of HIV acquisition sexual parenteral injecting drug use	n(%)	14 (29.0) 9 (16.0) 33 (59.0)
Homelessness	n (%)	23 (41.0)
History of imprisonment	n(%)	26 (46.4)
Previously treated for TB	n(%)	27 (48.2)
Non-adherence to cART	n(%)	24 (42.8)
CD4+/mm^3 at MDR-TB diagnosis	median (IQR)	31 (12-100)
Nadir CD4+/mm^3	median (IQR)	14 (5-38)
HIV-RNA $\log_{10}$ (copies/mL)	median (IQR)	5.20 (3.46-5.73)
All-cause mortality	n(%)	38 (67.8)

Comparison between age at HIV infection and age at MDR-TB diagnosis by modes of HIV acquisition

Age (years)		HSX n=14	PI n=9	IDU n=33	*P value*	Pulmonary TB n=26	Disseminated TB n=30	*P value*
HIV diagnosis	median (IQR)	24 (24, 35)	**11** (10, 14)	31 (27, 37)	**<0.0001**	31 (25, 39)	**27** (20, 33)	0.19
MDR-TB diagnosis	median (IQR)	35 (26, 40)	**26** (24, 26)	31 (29, 38)	**0.01**	31 (28, 40)	**29** (25, 36)	**0.03**

Comparison between median survival time (months) and mortality rate in HIV-infected patients diagnosed with MDR-TB by HIV-modes of transmission and DR -strains

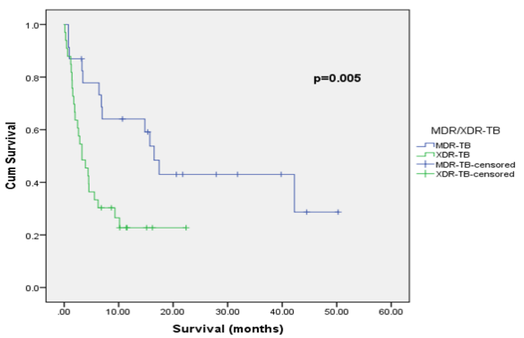
	HSX n=14	P n=9	IDUs n=33	*P value*
Mortality rate n(%)	6 (42.8)	8 (88.8)	24 (72.7)	**0.04**
Early mortality rate n(%)	2 (14.2)	2 (22.2)	14 (42.4)	0.13
Survival median (IQR)	10.8 (4.2,20.4)	9.3 (3.2,17.4)	4.4 (1.5,10.1)	**0.04**

	MDR-TB n=23	XDR-TB n=33	*P value*
Mortality rate n (%)	13 (56.5)	24 (72.7)	0.2
Early mortality rate n (%)	3 (13.0)	15 (45.4)	0.01
Survival time (months) median (IQR)	15.3 (5.6, 28.1)	3.2 (1.5, 9.3)	**<0.0001**

Correlation between risk factors and survival in patients with MDR TB co infected with HIV

Risk factor		Survival time mts median (IQR)	*P value*
Homelessness (n=23)	Yes	4.5 (1.3-6.9)	0.01
	No	9.3 (2.7-16.9)	
Imprisonment (n=26)	Yes	4.1 (1.2-7.6)	0.01
	No	9.7 (3.1-18.5)	
Injectable drugs (n=33)	Yes	4.4 (1.5 -10.1)	0.03
	No	10.2 (3.2-21.7)	
CD4+ < 50/mm^3 at TB diagnosis (n=35)	Yes	3.9 (1.8-6.8)	0.01
	No	11.2 (2.2-25.1)	

Survival in patients with MDR-TB and XDR-TB



Conclusions

- The prevalence and mortality rate in patients with HIV infection and DR-TB were high.
- Severe immunosuppression, history of imprisonment, homelessness and injecting drug use were associated with a lower-survival.
- Rapid TB diagnosis methods, enhanced direct observed treatment, proper isolation facilities and new anti TB drugs are needed in order to limit the spread of TB.

Prevalence and survival in HIV infected patients diagnosed with MDR TB - a Romanian single center experience

Irina Ianache[1], Simona Erscoiu[1,2], Manuela Nica[1], Gratiela Tardei[1], Emanoil Ceausu[1,2], Petre Calistru[2], Cristiana Oprea[1,2]

1. "Victor Babes" Hospital for Infectious and Tropical Diseases, Bucharest, Romania; 2."Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Objective:

We aimed to assess the prevalence of DR-TB and to estimate the risk factors for survival in HIV/TB co-infected patients from a Romanian tertiary health care facility

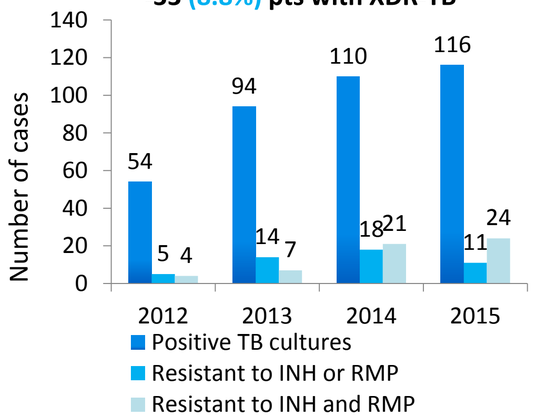
Methods:

- Prospective study on HIV-infected patients diagnosed with DR-TB at "Victor Babes" Clinical Hospital for Infectious Diseases, Bucharest, between January 2012 and December 2015.
- Drug resistant (DR)-TB strains were classified in **MDR-TB** (resistance to INH and RIF), **pre-XDR** (MDRTB and resistance to either quinolones or an injectable) and **XDR-TB** (MDR and resistance to both aminoglycosides and quinolones).
- Statistical analysis was performed using SPSS 20.0, survival being compared using Kaplan Meier curves

Results:

MDR-TB incidence among HIV-infected patients

9,012 person-years (PY): 374 pts with positive TB cultures and drug susceptibility testing performed: - 48 (12.8%) strains resistant to at least one drug (INH or RMP)
- 56 (14.9%) pts with overall MDR-TB (incidence 6.21/1000 PY)
- 23 (6.1%) pts with MDR-TB;
-33 (8.8%) pts with XDR-TB



MDR-TB	2012	2013	2014	2015	*P*
Incidence /year	7.4%	7.4%	19.0%	20.6%	0.04

Socio-demographic and clinical characteristics		Total (n=56)
Gender – male	n(%)	39 (69.6)
Age (years) at HIV diagnosis	median (IQR)	29 (22-35)
Age (years) at TB-diagnosis	median (IQR)	31 (26-37)
Concomitant MDR-TB and HIV	n(%)	15 (26.7)
Modes of HIV acquisition sexual parenteral injecting drug use	n(%)	14 (29.0) 9 (16.0) 33 (59.0)
Homelessness	n(%)	23 (41.0)
History of imprisonment	n(%)	26 (46.4)
Previously treated for TB	n(%)	27 (48.2)
Non-adherence to cART	n(%)	24 (42.8)
CD4+/mm^3 at MDR-TB diagnosis	median (IQR)	31 (12-100)
Nadir CD4+/mm^3	median (IQR)	14 (5-38)
HIV-RNA $\log_{10}$ (copies/mL)	median (IQR)	5.20 (3.46-5.73)
All-cause mortality	n(%)	38 (67.8)

Comparison between age at HIV infection and age at MDR-TB diagnosis by modes of HIV acquisition

Age (years)		HSX n=14	PI n=9	IDU n=33	*P value*	Pulmonary TB n=26	Disseminated TB n=30	*P value*
HIV diagnosis	median (IQR)	24 (24, 35)	**11** (10, 14)	31 (27, 37)	**<0.0001**	31 (25, 39)	**27** (20, 33)	0.19
MDR-TB diagnosis	median (IQR)	35 (26, 40)	**26** (24, 26)	31 (29, 38)	**0.01**	31 (28, 40)	**29** (25, 36)	**0.03**

Comparison between median survival time (months) and mortality rate in HIV-infected patients diagnosed with MDR-TB by HIV-modes of transmission and DR -strains

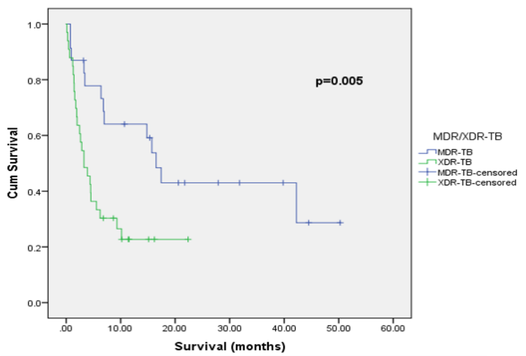
	HSX n=14	P n=9	IDUs n=33	*P value*
Mortality rate n(%)	6 (42.8)	8 (88.8)	24 (72.7)	**0.04**
Early mortality rate n(%)	2 (14.2)	2 (22.2)	14 (42.4)	0.13
Survival median (IQR)	10.8 (4.2,20.4	9.3 (3.2,17.4)	4.4 (1.5,10.1)	**0.04**

	MDR-TB n=23	XDR-TB n=33	*P value*
Mortality rate n (%)	13 (56.5)	24 (72.7)	0.2
Early mortality rate n (%)	3 (13.0)	15 (45.4)	0.01
Survival time (months) median (IQR)	15.3 (5.6, 28.1)	3.2 (1.5, 9.3)	**<0.0001**

Correlation between risk factors and survival in patients with MDR TB co infected with HIV

Risk factor		Survival time mts median (IQR)	*P value*
Homelessness (n=23)	Yes	4.5 (1.3-6.9)	0.01
	No	9.3 (2.7-16.9)	
Imprisonment (n=26)	Yes	4.1 (1.2-7.6)	0.01
	No	9.7 (3.1-18.5)	
Injectable drugs (n=33)	Yes	4.4 (1.5 -10.1)	0.03
	No	10.2 (3.2-21.7)	
CD4+ < 50/mm^3 at TB diagnosis (n=35)	Yes	3.9 (1.8-6.8)	0.01
	No	11.2 (2.2-25.1)	

Survival in patients with MDR-TB and XDR-TB



Conclusions

- The prevalence and mortality rate in patients with HIV infection and DR-TB were high.
- Severe immunosuppression, history of imprisonment, homelessness and injecting drug use were associated with a lower-survival.
- Rapid TB diagnosis methods, enhanced direct observed treatment, proper isolation facilities and new anti TB drugs are needed in order to limit the spread of TB.