

Anti-tuberculosis drugs resistance survey in West Nile, Uganda

Laurence Ahoua¹, Delphine Sauvageot¹, Daniel Edemaga²; Anandi Martin^{3,4}, Chantal Umuton², Alex Odama⁵, William Omale⁶, David Olson⁴, Laurence Bonte⁴, Francis Adatu-Engwau⁵, Maryline Bonnet¹

¹Epicentre, France; ²MSF, Uganda; ³Tropical Medical Institute, Antwerp Belgium; ⁴MSF, France; ⁵National Leprosy and Tuberculosis Program, Uganda; ⁶Arua Regional Referral Hospital, Uganda;

Background

- Multidrug resistance (MDR) in HIV co-infected patients
 - Increase of nosocomial transmission
 - High case fatality rate
- MDR poorly documented in Sub-Saharan countries where majority of TB cases are HIV co-infected
 - Emergence of MDR and Extreme-drug resistance (XDR) epidemics in Kwazulu Natal (Gandhi et al, Lancet.2006)
 - MDR-TB likely to be underestimated
- North western Uganda
 - National adult HIV prevalence rate was of 6.7% in 2005
 - Drug Susceptibility Testing survey in Uganda
 - 1996-97 (national): 0.5% MDR prevalence in new cases (NC) and 4.4% in previously treated cases (PTC)
 - 2000 (hospital-based study in Kampala): 4.7% MDR TB in NC, among those 70% HIV co-infected
 - HIV and TB program supported by Médecins Sans Frontières in West Nile region (north-western Uganda)
 - MDR treatment available in Arua regional referral Hospital

Objectives

- Primary objective**
 - To measure the MDR prevalence in overall new smear patients and HIV co-infected ones
- Secondary objectives**
 - To describe the 1st line drug resistance patterns of NC and PTC
 - To describe resistance to 2nd line drugs and XDR resistance among MDR-TB cases

Methods

- Cross-sectional survey of all consecutive smear positive patients in the TB centers of the Western Nile region
- TB Case and Drug resistance definitions based on WHO/IUATLD standards definitions (WHO, 2006)
- Sample size: N = 400 NC
- Laboratory procedures
 - Collection of 2 sputum samples
 - Samples shipped to the Tropical Medical Institute (Antwerp)
 - Culture & DST 1st line on Lowenstein Jensen (LJ) or MGIT
 - DST 2nd line on agar 7H11: proportion method

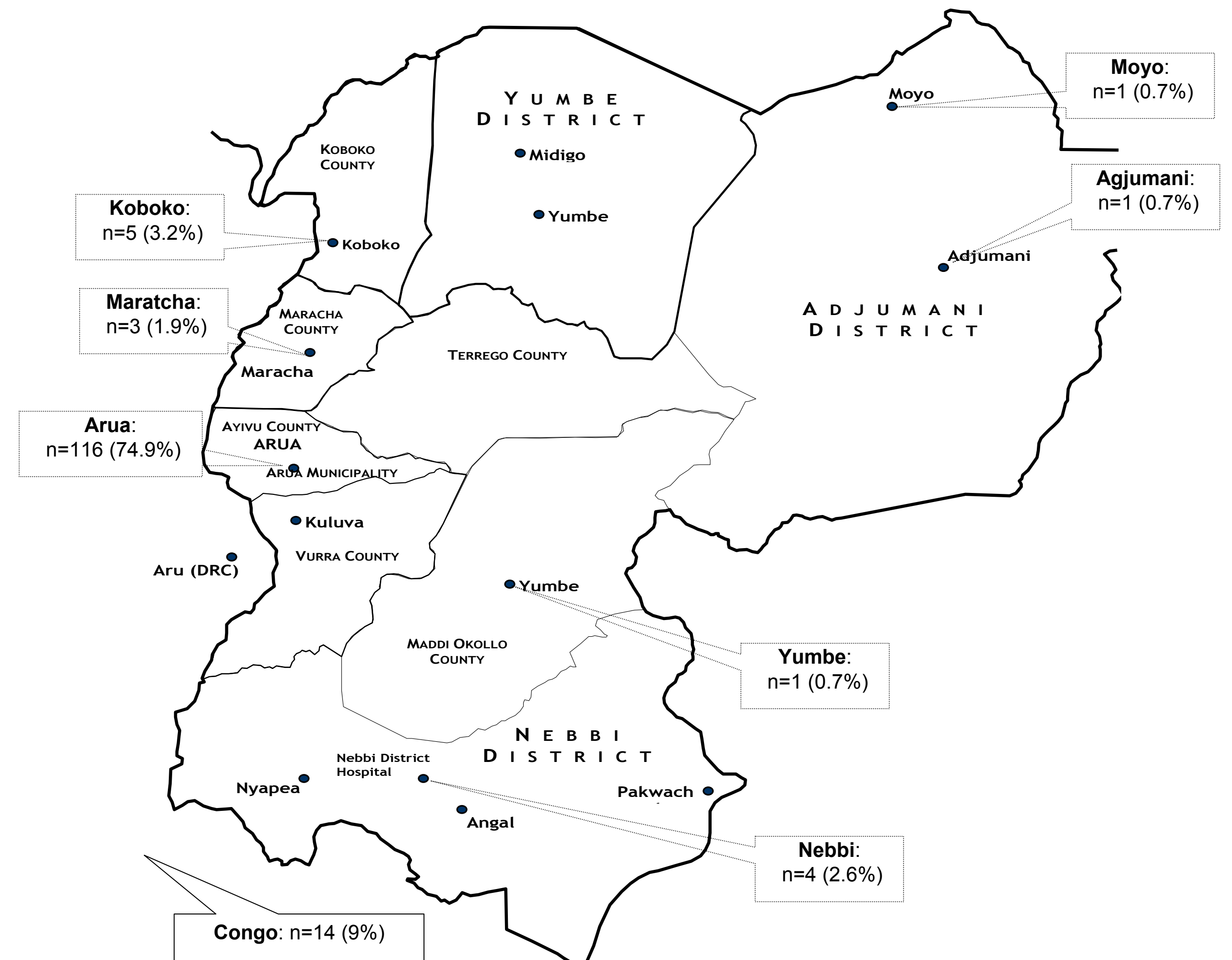
Preliminary results

Baseline patient characteristics

- A total of 169 patients were included in the DST survey (September 2007 - October 2008).
- Gender, age group and type of TB were not statistically different according to the HIV status.

Patients' characteristics	n (%)
Males	120 (71.0)
Age, year	
15-29	70 (41.4)
30-44	82 (48.5)
≥ 45	17 (10.1)
HIV status	
Positive	61 (36.1%)
Negative	94 (55.6%)
Refused testing	14 (8.3)
Type of TB	
New case	146 (86.4)
Previously treated case	23 (13.6)
<i>Failure</i>	2 (8.7)
<i>Relapse</i>	14 (60.9)
<i>RAD</i>	6 (26.0)
<i>Other</i>	1 (4.4)

Geographical origin (West Nile region)



Culture results

Of the 169 patients included: 16 had ongoing culture analysis, 2 had non analysable sputum samples.

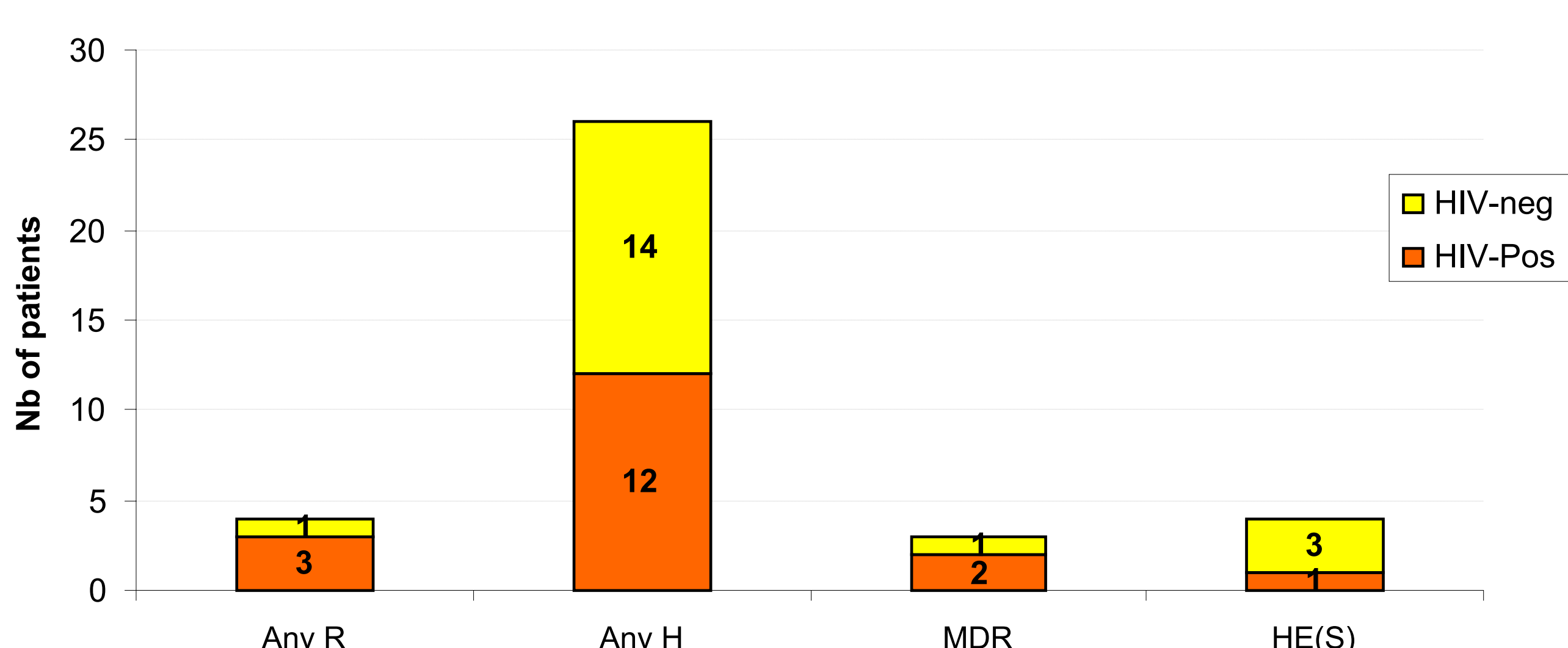
	MGIT			Total
	Pos	Neg	Contaminated	
LJ				
Pos	120	1	10	131
Neg	13	3	2	18
Contaminated	1	0	1	2
Total	134	4	13	151

Drug Sensitivity Testing results

	GLOBAL			NC			PTC	
	n	%	95%CI	n	%	95%CI	n	%
Nb of cases tested	145			123			22	
Full susceptible	101	69.7	61.6-76.7	89	72.4	63.7-79.6	12	54.6
MDR	3	2.1	0.6-6.3	0	0.0	-	3	13.6
HR	1	0.7	0.1 - 4.8	0	0.0	-	1	4.5
HRS	1	0.7	0.1 - 4.8	0	0.0	-	1	4.5
HRES	1	0.7	0.1 - 4.8	0	0.0	-	1	4.5
Other patterns								
Any H	27	18.2	13.0 - 25.9	18	14.6	9.4 - 22.2	9	40.9
Any R	4	2.8	1.0 - 7.2	0	0.0	-	4	18.2
Any E	7	4.8	2.3 - 9.9	6	4.9	2.2 - 10.5	1	4.5
Any S	22	15.2	10.2 - 22.1	19	15.4	10.0 - 23.1	3	13.6
H+E	1	0.7	0.1 - 4.8	1	0.8	0.1 - 5.7	0	0.0
H+S	6	4.1	1.8 - 9.0	6	4.9	2.2 - 10.5	0	0.0
H+E+S	3	2.1	0.1 - 6.3	3	2.4	0.8 - 7.4	0	0.0
R+E	0	0.0	-	0	0.0	-	0	0.0
R+S	1	0.7	0.1 - 4.8	0	0.0	-	1	4.5
R+E+S	0	0.0	-	0	0.0	-	0	0.0
MonoR	0	0.0	-	0	0.0	-	0	0.0
MonoH	14	9.3	5.8 - 15.7	8	6.5	3.3 - 12.6	6	27.3
MonoS	10	6.9	3.7 - 12.4	10	8.1	4.4 - 14.6	0	0.0
MonoE	2	1.4	0.3 - 5.4	2	1.6	0.4 - 6.4	0	0.0

- No XDR detected.
- Of the 3 MDR patients : 1 was resistant to Ethionamide and 1 was resistant to Pyrazinamide

Drug Sensitivity Testing by HIV status



Discussion

Main findings

- 86% NC and 36% being HIV co-infected
- Low MDR-TB prevalence, only in PTC
- No XDR
- High rate of primary isoniazid resistance (14.6%)
- No difference of drug sensitivity in HIV+ and HIV- patients

Operational issues for the National program

- Low MDR rate: DST would be recommended only in failures of standard 1st line drugs regimens
- 4 months RH continuation phase might be not enough to assure patients with primary H resistance and might induce R resistance amplification
- Completion of the survey end of 2009