

Anti-tuberculosis drugs resistance survey in West Nile, Uganda

Laurence Ahoua¹, Delphine Sauvageot¹, Daniel Edemaga², Anandi Martin^{3,4}, Chantal Umutohi², 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

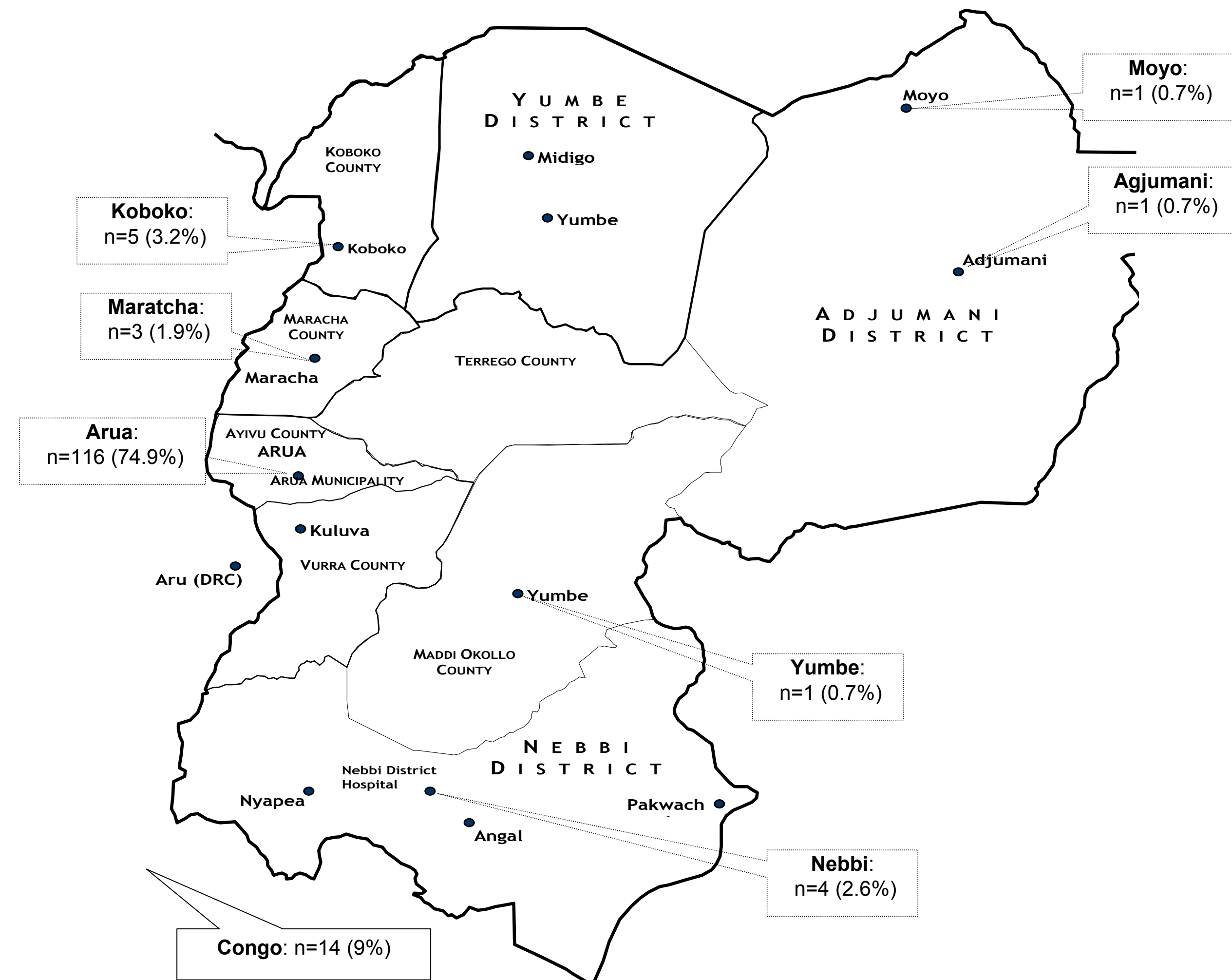
Preliminary results

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)

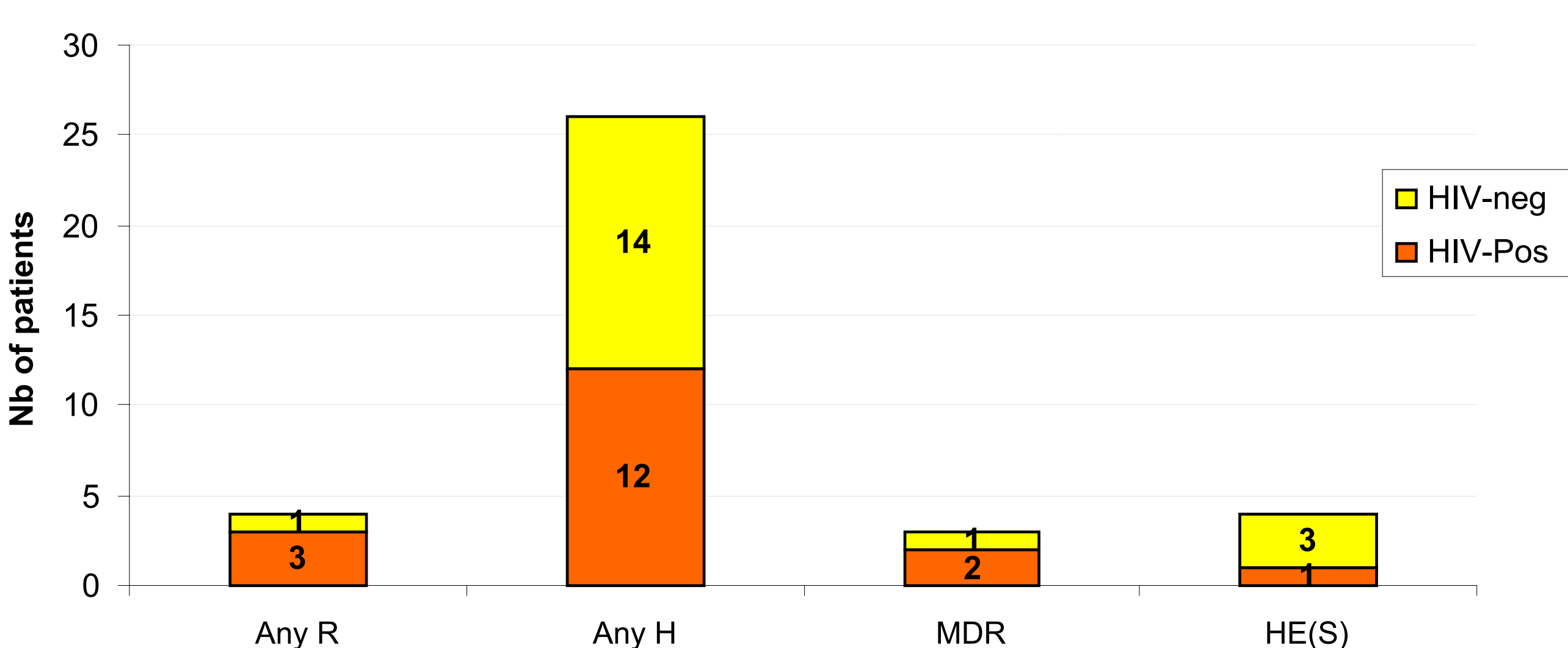


Culture results

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 by HIV status



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

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