Supplemental Digital Content 1. Diagnostic criteria.

Prospective etiological investigation of community-acquired pulmonary infections in hospitalized people living with HIV.

Authors: Claudia Figueiredo-Mello, Pontus Naucler, Marinella D. Negra, Anna S. Levin.

Bacteria

The definitive etiological diagnosis of a bacterial infection was made by identification of a microorganism by culture of a sterile site (blood or pleural fluid) or a respiratory sample. Endotracheal aspirate cultures were considered positive if the number of colonies were $\geq 10^6$ ufc/ml and for bronchoalveolar lavage cultures if the number of colonies were $\geq 10^4$ ufc/mL. The agents identified by these methods were considered the causative agents if they were not usual colonizers of the upper airways, such as coagulase negative staphylococci, and if there were no other agent more likely identified in blood cultures or by molecular tests.

Positive IgM in blood sample (semi-quantitative IgG and IgM, RIDASCREEN®, *R-Biopharm AG, Darmstat*, Germany) or presence of positive polymerase chain reaction (PCR) in a respiratory sample or nasopharyngeal swab (*Film Array, BioFireDiagnostics, Salt Lake City*, UT) was considered confirmatory for *Chlamydophila pneumoniae* and *Mycoplasma pneumonia* infection.

A positive PCR in nasopharyngeal swab was confirmatory for *Bordetella pertussis* infection (semi-quantitative IgG and IgM, RIDASCREEN®, *R-Biopharm AG, Darmstat*, Germany). A positive PCR in blood confirmed *S. pneumoniae* and *H. influenza*e infection.

*Legionella pneumophilla* infection was defined by the presence of a positive PCR in a respiratory sample or a positive urinary antigen (SAS™ *Legionella Test, SA Scientific, San Antonio*, TX).

Fungi

The definitive diagnosis of a fungal infection was made by identification of a microorganism by culture of a sterile site (blood or pleural fluid) or a positive culture in respiratory sample for one of these agents: *Cryptococcus neoformans, Histoplasma capsulatum, Coccidioides immitis* or *Blastomyces dermatitidis* or through the characterization of the agent in histopathology.

Direct visualization or a positive PCR in a respiratory sample for *Pneumocystis jirovecii* was considered confirmatory, unless the patient had documented CD4+ T cell count over 200 cells/mm³ and did not receive therapy directed against this agent.

Probable diagnosis of *Histoplasma capsulatum* was considered in the presence of a positive serology plus a compatible clinical condition plus treatment initiated by the attending physician.

Mycobacteria

*Mycobacterium tuberculosis* was confirmed by culture in any sample (blood, pleural fluid or respiratory sample).

A positive smear or a histopathologic finding, without a positive culture, was considered confirmatory for a mycobacterial infection without species identification.

Identification in blood culture or in two cultured respiratory samples was confirmatory for non-mycobacterial species.

Virus

Positive PCR in a respiratory sample or in a nasopharyngeal swab confirmed adenovirus infection. Positive PCR in nasopharyngeal swab was considered confirmatory of parainfluenza viruses 1-3, respiratory syncytial virus, influenza viruses A and B, human coronaviruses CoV NL63, HKU1, OC43 and229E, enterovirus, rhinovirus, adenovirus, bocavirus, human metapneumovirus infection (*Film Array, BioFireDiagnostics, Salt Lake City*, UT). Cytomegalovirus and herpes virus 8 were characterized based on histopathological studies.

Non-infectious causes

Pulmonary thromboembolism was diagnosed based on computed tomography. Suggestive lesions observed in bronchoscopy were defined as Kaposi´s Sarcoma.

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SUPPLEMENTARY TABLE 1.
Baseline characteristics of 224 patients living with HIV admitted to the hospital with community-acquired pulmonary infections (September 2012-July 2014)

| | |
|---|---|
| Age (years) mean (SD) | 40.3 (11.6) |
| Male sex | 154 (69%) |
| Comorbidities | 67 (30%) |
| Hypertension | 26 (12%) |
| Liver disease | 22 (10%) |
| Neoplastic disease | 10 (4%) |
| Diabetes mellitus | 9 (4%) |
| Cardiac insufficiency | 9 (4%) |
| Renal disease | 5 (2%) |
| Chronic obstructive pulmonary disease dependent on oxygen | 3 (1%) |
| Cerebrovascular disease | 2 (<1%) |
| Drug use (n=223*) | 131 (59%) |
| Tobacco use (n=222*) | 91 (41%) |
| Alcoholism (n=220*) | 83 (38%) |
| Inhaled drug use (n=223*) | 67 (30%) |
| Intravenous drug use (n=223*) | 2 (<1%) |
| Antibiotic use in the last 30 days (n=218*) | 109 (50%) |
| Prophylactic dose (n=215*) | 37 (17%) |
| Therapeutic dose (n=214*) | 86 (40%) |
| Pneumococcal vaccination (n=161*) | 49 (30%) |
| Years of HIV infection median (range) (n=187*) | 12 (1-30) |
| Regular usage of HAART | 42 (19%) |
| Viral load < 50 copies/ml (n=202*) | 32 (16%) |
| CD4 T cell count (/mm$^3$) median (range) (n=202*) | 57.5 (1-1108) |
| 1-49 | 98 (49%) |
| 50-199 | 48 (24%) |
| 200-349 | 20 (10%) |
| 350-499 | 17 (8%) |
| >499 | 19 (9%) |
| CURB-65 | |
| 0-1 | 161 (72%) |
| 2 | 47 (21%) |
| 3-5 | 16 (7%) |
| Pneumonia Severity Index | |
| I-II | 136 (61%) |
| III | 49 (22%) |
| IV-V | 39 (17%) |

* Data not available for all patients; SD: standard deviation; HAART: highly active antiretroviral therapy; results are shown as N (%) if not otherwise specified.

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SUPPLEMENTARY TABLE 2. Frequency of mixed etiology findings observed during routine plus extended microbiological investigation of community-acquired pulmonary infections in hospitalized patients living with HIV.

| **Etiology** | **N** |
|---|---|
| *Mycoplasma pneumoniae* + *Pneumocystis jirovecii* | 4 |
| *Pneumocystis jirovecii* + Rhinovirus | 3 |
| *Pneumocystis jirovecii* + *Mycobacterium tuberculosis* | 3 |
| *Streptococcus pneumoniae* + Rhinovirus | 3 |
| Adenovirus + *Pneumocystis jirovecii* | 2 |
| *Chlamydophila pneumoniae* + *Pneumocystis jirovecii* | 2 |
| *Histoplasma spp.* + *Pneumocystis jirovecii* + Rhinovirus | 2 |
| *Mycoplasma pneumoniae* + *Streptococcus pneumoniae* | 2 |
| Adenovirus + *M. avium* or *M. colombiensis* + *Pneumocystis jirovecii* | 1 |
| Adenovirus + *Pneumocystis jirovecii* + Pulmonary thromboembolism | 1 |
| *Bordetella pertussis* + *Streptococcus pneumoniae* + *Staphylococcus aureus* + Rhinovirus | 1 |
| *Chlamydophila pneumoniae* + *Streptococcus pneumoniae* | 1 |
| *Chlamydophila pneumoniae* + *Streptococcus pneumoniae* + *Mycobacterium tuberculosis* | 1 |
| Cytomegalovirus + Rhinovirus + Kaposi´s sarcoma | 1 |
| Coronavirus + *Pneumocystis jirovecii* + Rhinovirus | 1 |
| Coronavirus OC43 + Rhinovirus | 1 |
| *Histoplasma spp.* + *Mycobacterium tuberculosis* | 1 |
| Influenza A H1N1 + Pulmonary thromboembolism | 1 |
| Influenza A non H1N1 + Neoplastic disease | 1 |
| Influenza A non H1N1 + *Pneumocystis jirovecii* | 1 |
| Influenza B + *Mycoplasma pneumoniae* | 1 |
| Influenza B + Rhinovirus | 1 |
| *Mycobacterium avium* complex+ *Mycoplasma pneumoniae* | 1 |
| *Mycobacterium avium* complex + *Pneumocystis jirovecii* | 1 |
| *Mycobacterium avium* complex + *Mycobacterium tuberculosis* | 1 |
| Nonchromogenic slowly growing Mycobacteria + *Pneumocystis jirovecii* + Kaposi´s sarcoma | 1 |
| Mycobacteria + Rhinovirus | 1 |
| *Pneumocystis jirovecii* + Mycobacteria | 1 |
| *Pneumocystis jirovecii* + *Streptococcus pneumoniae* | 1 |
| *Pneumocystis jirovecii* + Rhinovirus + *Mycobacterium tuberculosis* | 1 |
| *Pneumocystis jirovecii* + Kaposi´s sarcoma | 1 |
| *Pneumocystis jirovecii* + Pulmonary thromboembolism | 1 |
| Kaposi´s sarcoma + *Mycobacterium tuberculosis* | 1 |
| *Staphylococcus aureus* + *Mycobacterium tuberculosis* | 1 |
| *Mycobacterium tuberculosis* + Rhinovirus | 1 |
| **Total** | **48** |

Supplemental Digital Content 2. Detailed results of sputum cultures for bacteria.

Prospective etiological investigation of community-acquired pneumonia in hospitalized people living with HIV.

Authors: Claudia Figueiredo-Mello, Pontus Naucler, Marinella D. Negra, Anna S. Levin.

Sputum cultures for bacteria were collected for 120 patients (54%) and resulted positive in 47 cases. Out of the 47 positive sputum cultures, only 15 cases had potential causative bacteria (1 case of *Escherichia coli*, 2 cases of *Klebsiella pneumoniae*, 3 cases of *Pseudomonas aeruginosa*, 1 case of *Rhodococcus* sp., 6 cases of *Staphylococcus aureus* and 2 cases of *S. pneumoniae*). An additional 10 patients would have had a possible etiology diagnosed using sputum cultures (1 case of *Escherichia coli*, 2 cases of *Klebsiella pneumoniae*, 3 cases of *Pseudomonas aeruginosa* and 4 cases of *Staphylococcus aureus*), most of which (8 cases) would have been associated with other etiology findings.

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SUPPLEMENTARY TABLE 3. Microbiological findings of community-acquired pulmonary infections in relation to season in hospitalized patients living with HIV.*

| **Etiology** | **Summer** | **Winter** | **P** |
|---|---|---|---|
| | **N = 51** | **N = 52** | |
| | **n (%)** | **n (%)** | |
| **Fungi** | **13 (25)** | **9 (17)** | 0.31 |
| *Pneumocystis jirovecii* | 13 (25) | 8 (15) | 0.20 |
| **Bacteria** | **13 (25)** | **9 (17)** | 0.31 |
| *Streptococcus pneumoniae* | 4 (8) | 4 (8) | 1† |
| *Mycoplasma pneumoniae* | 6 (12) | 0 | **0.01**† |
| *Clamydophila pneumoniae* | 0 | 4 (8) | 0.12† |
| **Virus** | **6 (12)** | **10 (19)** | 0.30 |
| Rhinovirus | 4 (8) | 8 (15) | 0.23 |
| Influenza | 1 (2) | 1 (2) | 1† |
| **Mycobacteria** | **9 (18)** | **9 (17)** | 0.96 |
| *Mycobacterium tuberculosis* | 7 (14) | 9 (17) | 0.62 |

* Only the seven most frequent pathogens are presented † Fisher´s exact test

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SUPPLEMENTARY TABLE 4. Microbiological findings of community-acquired pulmonary infections in relation to CD4+ T cell count in hospitalized patients living with HIV.*

| **Etiology** | **CD4+ < 200** **N = 146** **n (%)** | **CD4+ ≥ 200** **N = 56** **n (%)** | **P** |
|---|---|---|---|
| **Fungi** | **49 (34)** | **2 (4)** | **<0.01** |
| *Pneumocystis jirovecii* | 46 (31) | 2 (4) | **<0.01** |
| **Bacteria** | **25 (17)** | **15 (27)** | 0.12 |
| *Streptococcus pneumoniae* | 12 (8) | 8 (14) | 0.20 |
| *Mycoplasma pneumoniae* | 7 (5) | 5 (9) | 0.27 |
| *Clamydophila pneumoniae* | 6 (4) | 1 (2) | 0.68† |
| **Virus** | **25 (17)** | **10 (18)** | 0.90 |
| Rhinovirus | 15 (10) | 3 (5) | 0.27 |
| Influenza | 5 (3) | 5 (9) | 0.14† |
| **Mycobacteria** | **27 (18)** | **6 (11)** | 0.18 |
| *Mycobacterium tuberculosis* | 22 (15) | 6 (11) | 0.42 |

* Only the seven most frequent pathogens are presented † Fisher´s exact test