



Annual Report

**Minimizing HIV deaths
through rapid fungal diagnosis
and better care in Guatemala**

2017

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Executive summary

In 2016, Guatemala had 2,900 (1,400 – 5,200) new HIV infections and 1,600 (<1,000 – 2,800) AIDS-related deaths. There were 46,000 (31,000 – 65,000) people living with HIV in 2016, among whom only 36% (24% - 50%) were accessing antiretroviral therapy. Additionally, over 50% of the diagnosed patients are in advanced HIV stage which results in long periods of hospitalization and often death. From this perspective a project called “Minimizing HIV deaths through rapid fungal diagnosis and better care in Guatemala” was implemented by Global Action Fund for Fungal Infections (GAFFI) and Asociación de Salud Integral (ASI), in Guatemala. The objectives of this Program include: i) to implement rapid diagnosis for cryptococcal meningitis, disseminated histoplasmosis, *Pneumocystis* pneumonia and chronic pulmonary aspergillosis; ii) to develop a training program in fungal disease management for health workers in the HIV comprehensive care units of Guatemala and; iii) to develop a national registry for fungal infections. To develop this program, a network of laboratories connected with a central Mycology Laboratory was set-up, as well as trained clinicians in fungal diseases. The network has implemented the following actions: 1) Training activities; 2) Strategic alliances; 3) Development of a website; 4) Diagnostic guidelines and 5) Cohort study. Currently the network comprises 13 HIV units across Guatemala and one Reference Laboratory lead by ASI. Only two HIV units have declined the participation in the network so far, but conversations with them are still ongoing to get them in and cover the whole country.

This year, processes were implemented to improve the coordination of the network as well as to increase the training activities and the diagnostic portfolio in the Reference Laboratory. Activities included: (i) A better use of the website by the network to get all information about clinical samples analysis and patient’s data in the system; (ii) An in-depth analysis of the Reference Laboratory workflow to improve the turnaround time and the delivery of the results to the network; (iii) An increase in the number and modalities of the training activities for the network including virtual and face to face conferences. Topics covered included epidemiology, diagnosis and treatment of opportunistic infections, focused on fungal diseases and (iv) Incorporation of *Pneumocystis jirovecii* diagnosis to Reference Laboratory diagnostic portfolio.

Training activities included the following: (i) A II National workshop attended by 51 participants about opportunistic infections was held in February 2017 in Guatemala City; (ii) A workshop attended by 32 participants about opportunistic infections was held in May 2017 in Guatemala City; (iii) Four meetings in rural hospitals attended by 140 participants were also held; (iv) Three on line conferences to discuss clinical cases were done by means of ZOOM platform.

The diagnostic activities performed in the network during 2017 are as follows. Two thousand, three hundred and ninety-four patients were included in the study. Three hundred and seventy-one patients (15,5 %) had an opportunistic infection, 209 (56.3%) of which were fungal. *H. capsulatum* was diagnosed in 127 patients (34.2%), *C. neoformans* in 79 (21.3%) and other fungal infection in 3 (0.80%). One hundred and forty-seven (39.6%) cases of *M. tuberculosis* and other mycobacterial infections were also diagnosed. Ten cases (2.69%) of coinfection with *M. tuberculosis* and *Histoplasma capsulatum* were detected. Coinfections caused by other pathogens reached 1.34% (5 cases). In comparison with the same period of 2016, when the network was not still implemented, we observed a 110.8% increase in opportunistic infection diagnosis - from 176 to 371 cases. In addition, the network ruled out these infections in 2,023 HIV cases, allowing an earlier start of antiretroviral therapy and therefore the chance of a better outcome.

Training activities

Workshops

In February 7th and 8th, 2017 a II National Workshop: "*Management and treatment of Fungal Infections in HIV, a Country strategies*" was held on Guatemala City, with the goals of:

- Describe the advances in the proposal ""Minimizing HIV deaths through rapid fungal diagnosis and better care in Guatemala" implemented in 2016;
- Discuss the current guidelines for the management and treatment for fungal infections;
- Familiarize the participants with the different electronic tools, supported by GAFFI's project.

During this annual meeting, talks were provided by different experts such as Juan Luis Rodríguez Tudela (GAFFI), Ana Alastruey Izquierdo (Instituto de Salud Carlos III), Tom Chiller (CDC), Dalia Mei Ling Lau (ASI), Eduardo Arathoon (CFLAG), Diego Caceres (CDC) and Juan Carlos Pérez (CFLAG). This meeting was attended by 51 participants.

A workshop about opportunistic infections was held on May the 19th, 2017 in Guatemala City with the following goals:

- Provide a review of the components included in the proposal “Minimizing HIV deaths through rapid fungal diagnosis and better care in Guatemala”;
- Highlight the importance of opportunistic infections screening among HIV patients;
- Present the opportunistic infections electronic record card, which includes opportunistic infection management and follow-up;
- Present the e-Learning course “Opportunistic Infections Care in HIV patients”.

The workshop was attended by 32 participants, including medical doctors, microbiologists from the HIV units and personnel of the Ministry of Health/HIV program in Guatemala.

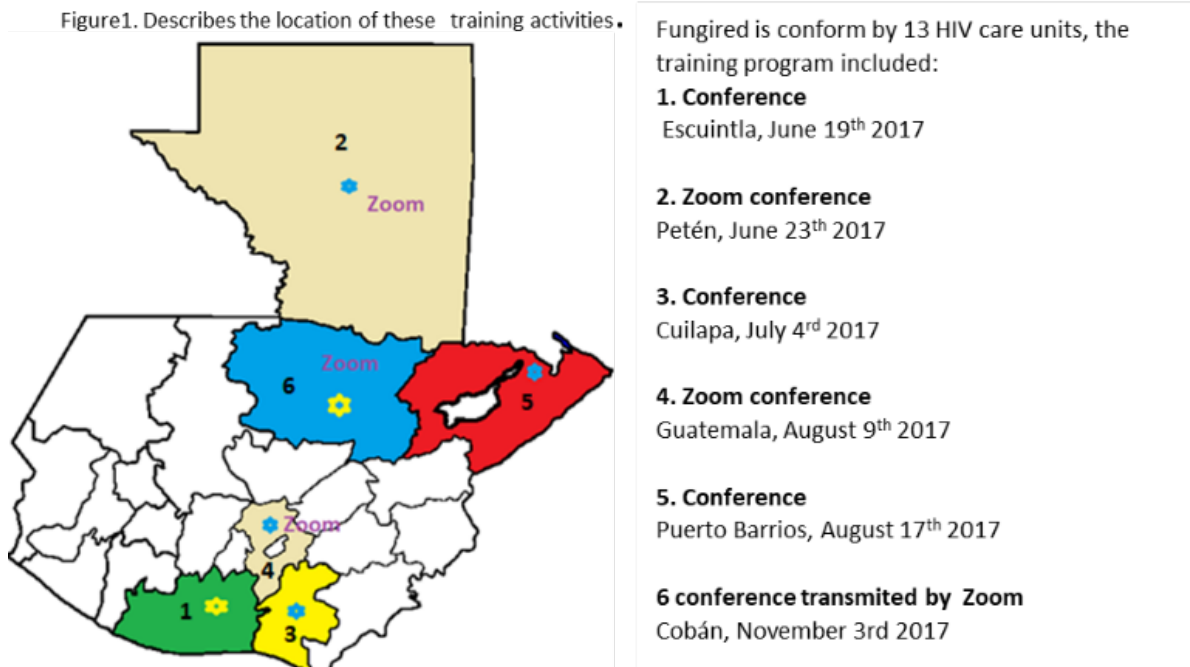
Face to Face meetings

Face to face meetings included discussions and oral presentations based on clinical cases. These are coordinated by an expert of the Clínica Familiar Luis Angel Garcia. Four activities were held in rural hospitals and attended personnel from the HIV unit, hospital authorities and internists, laboratory personnel and medical students. (i) Hospital Nacional de Escuintla, 40 participants; (ii) Hospital Regional de Cuilapa, 35; (iii) Hospital de La Amistad Japón Guatemala in Puerto Barrios, 41; (iv) Hospital Hellen Lossi de Laugerud de Cobán, 24;. Figure 1 shows the location of the conferences, including zoom conferences.

On Line meetings

Three virtual conferences were held by means of the ZOOM platform. These activities involved all HIV units, with rotating organizing roles. The first conference was coordinated by the HIV unit of Petén (June 23th), the second one by the Clínica Familiar Luis Angel García (August 9th). The

third one included a discussion of a clinical case at the HIV Unit and transmitted to other units.



This activity was coordinated by Coban's HIV Unit (November 3rd).

New diagnostic Portfolio at Reference Laboratory and technology transfer towards HIV units

In late 2017, diagnosis of *Pneumocystis jirovecii* pneumonia has been set up at the reference laboratory by means of a commercial PCR real time kit, FTD *Pneumocystis jirovecii*. For the first-time, patients in Guatemala have access to the diagnosis of this infection.

This year, ASI has finalized the program of training and transference of the LFA CrAg to all HIV units belonging to the network. Now, all HIV units can diagnose cryptococcosis locally.

Website

The website (www.fungired.gt) has been improved in 2017 and comprises three layers: i) General information; ii) Education and Training and; iii) Laboratory System.

1st Layer: General information

The first layer called “General information” describes FUNGIRed™ network, and the participants, HIV care units and the Reference Laboratory, as well as the clinical advisor for fungal infections. This section also provides information about its actions, workshops, results of the project and links to others web sites with related information.

2nd Layer: Educational and Training

The second layer, called “Education and training”, links to an e-Learning course entitled “Opportunistic Infections Care in HIV patients”. The on-line course is divided into four sections, each containing interactive lectures on various topics: (i) Initial clinical evaluation (review of systems); (ii) Mycobacterial infections; (iii) Mycotic infections and; (iv) other opportunistic infections. At the end of each section, participants must perform some homework and answer short quizzes. Newly implemented is a supervisor as well as a discussion forum to solve problems. The e-learning course was attended by 43 participants that received a certificate if they had completed at least 80% of the contents. Link: <http://elearning.asi.org.gt/login/index.php>

3rd Layer: Laboratory System

The third layer comprises the “Laboratory system” that has been developed on a web environment, which allows remote access through internet from computers, tablets or smartphones. Through this system, HIV units request on line individual diagnostic tests for opportunistic infections for their patients. It is not necessary to have an app or program installed or updated. An encrypted username and password is provided to selected people at each HIV care unit to access the system. All information is stored in a database based on SQL. All information in the system has 2 physical backups on 2 different servers for safety and confidentiality.

In addition, a quick delivery system for the clinical samples attending each HIV unit was setup to convey each one to the reference laboratory in collaboration with USAID | Capacity – PEPFAR. With this laboratory system, ASI knows in advance when the parcel will arrive and what samples it contains, which facilitates the organization of the workflow as well as a good use of the limited resources.

During 2017, the diagnostic portfolio included:

1. Diagnosis de cryptococcosis by means of smears, Indian ink, lateral flow LFA CrAg and culture of clinical samples;
2. *Histoplasma* diagnosis by means of smears, culture of clinical samples, PCR and urine antigen detection;
3. Detection of *Mycobacterium* spp by means of smears, culture, and PCR;
4. At the end of 2017, PCR detection of *Pneumocystis jirovecii* became available

As soon as the results of the requested tests are available, the system delivers them to the person in charge of the patient. Once the samples have arrived at the reference laboratory, the turnaround time has been established as follows: (i) Less than 24 hours for smears, LFA CrAg and *Histoplasma* antigen; (ii) 72 hours for *Mycobacterium* and *Histoplasma* PCRs; (iii) 6 to 8 weeks, or earlier if positive, results of fungal and *Mycobacterium* cultures.

The system allows a permanent communication between HIV units and ASI Reference Laboratory which means that those patients with a fungal infection get a quicker diagnosis and treatment than that provided before the implementation of the system.

The Electronic System also allows entering clinical data of each patient, including clinical signs and symptoms, results of local laboratory tests and radiological and clinical images as well as treatment given and follow up. This information can be exported to an Excel sheet to be analyzed. Each HIV care unit has access to their cases.

Global results can be found at www.fungired.gt as well as local information about the number of cases by region, HIV unit and opportunistic infection. This information is publicly accessible and updated monthly.

2017 Results

During 2017, all patients with recent HIV diagnosis and those who return to care were screened for opportunistic infections including test such as LFA for *Cryptococcus*; urine antigen for *Histoplasma*, stains and culture for fungi and *Mycobacterium*, PCR tests for diagnosis of *Histoplasma capsulatum* and *Mycobacterium tuberculosis*. Due to initiation of *Pneumocystis jirovecii* diagnosis late in the year, only cases with high clinical suspicion were tested. This

reference process included the 13 HIV units, all using the page www.fungired.gt to request the tests and delivery of the results. An in-depth evaluation of the results obtained this year will define the diagnostic approach for the following years.

Up until December 31st, 2017, 2,394 patients were tested which means 6,539 clinical samples processed by the network. Three hundred and seventy-one patients (15.5%) had an opportunistic infection, 209 (56.3%) of which were fungal. *H. capsulatum* was diagnosed in 127 patients (34.2%); *C. neoformans* in 79 (21.3%); and other fungal infection in 3 (0.8). One hundred and forty-seven (39.6%) cases of *M. tuberculosis* and other mycobacterial infections were also diagnosed. Ten cases (2.69%) of co-infection with *M. tuberculosis* and *Histoplasma capsulatum* were detected. Co-infections caused by other pathogens comprised 1.34% (5 cases). In comparison with the same period the previous year, when the network was not still implemented, we observed a 110.8% increase in the diagnosis of opportunistic infections, from 176 to 371 cases. In addition, the network ruled out these infections in 2,023 HIV cases, which facilitates the quick and safe start of antiretroviral therapy and therefore the chance of a better outcome.

Table 1. Etiologic results by microorganism

Cohort cases	Central and Reference Unit	HIV decentralized Unit	Total
<i>H. capsulatum</i> (HC)	23	104	127
<i>Cryptococcus neoformans</i>	46	33	79
<i>Cryptococcus albidus</i>		1	1
<i>Coccidioides posadasii</i>		1	1
<i>Sporothrix schenckii</i>		1	1
<i>M. tuberculosis</i> (MTB)	51	89	140
<i>M. avium</i>	2	0	2
<i>M. fortuitum</i>		2	2
<i>M. gordonae</i>		1	1
<i>M. abscessus</i>		2	2
Coinfections			
HC/MTB	2	8	10
<i>Cryptococcus</i> /MTB	1		1
<i>Cryptococcus</i> /HC	2	2	4
Total positive cases	127	244	371
Total negative cases	695	1328	2023
Total	822	1572	2394

Expenditure

Total payment for GAFFI contribution for year 2017 is £146,862.18. This budget covers personnel costs, training for the implementation of opportunistic infections diagnosis and treatment, follow up visits to HIV units, acquisition of equipment, reagents and diagnostic kits, shipping samples, maintaining and optimization of the website and laboratory online application and general costs.

Next Steps: Reference Laboratory model integration

OIs Surveillance

- To continue *in situ* visits for all units for data collection and quality control
- To reinforce and updated epidemiology data as part of the network surveillance system
- To validate project surveillance indicators

Logistic for better purchase system

- To collaborate with PAHO to optimize the purchase antifungals
- To reinforcement the local units procedures with the Ministry of Health for purchase of reagents and medicine

Publication of Results

- To announce the model results in a Workshop, at March 2018
- To continue data collection and analysis for publications
- To participate in the publication of abstracts and article

Communication and Training activities

- To continue improving of the website www.Fungired.gt
- To continue with case discussion among HIV units using Zoom platform
- To invite local and international external collaborators to discuss clinical cases
- To get more that 90% of diagnosis request use the lab system

Implementation of rapid diagnosis of OIs

- To get more than 90% of diagnosis requests trough the lab system.
- To implement the diagnosis of chronic pulmonary Aspergillosis
- To implement the test for PJP diagnosis for the HIV units.
- To improve the workflow at the reference laboratory and delivery system of the results.
- To continue *in situ* visits to the HIV units for Lab procedures and quality control reinforcement

Monitory & Evaluation

- To continue quality control reinforcement for lab System in CFLAG and HIV units
- To validate Project indicators
- To implement a Dashboard for M&E information in www.Fungired.gt