Electronic data capture: share your experience!

Many research projects developed and conducted by GABRIEL laboratories have a clinical dimension that requires the collection of personal patient data, as well as patient meta-data to perform analysis of the results. For example, the HINTT-TB, PEARL, and Typhoid projects depend on personal information gathered from patients regarding their age, their comorbidities, their vaccination status, etc. However, the sharing of this data can be problematic for multisite projects. Until now, data that has been recorded on paper can’t be shared among partners, and this restricts the amount of interchange during analysis, and retards the analytical process itself, especially when the source of the data must be investigated. Adopting an electronic data capturing system can improve partner collaboration on GABRIEL’s multisite projects. Of course, this type of methodology must comply with clinical research regulations on the privacy and traceability of the access of the database. There are many of such electronic systems. LabBook, Redcap, and Castor are some examples. As we would like to acquire one of these systems to deploy within the GABRIEL network, your experience with this type of system (advantages, disadvantages, costs, etc.,) is of great interest to us. Please send an e-mail to: jean-luc.berland@fondation-merieux.org
An update on the Pneumonias’ Etiology Among Refugee and the Lebanese populations (PEARL) study

The harsh circumstances regularly affecting refugees in Lebanon influence the transmission of respiratory pathogens, the natural history, and the severity of community-acquired pneumonia (CAP). The etiologies of CAP are consequently subject to vary and this, in turn, impacts the case management of the disease. The Pneumonias’ Etiology Among Refugee and Lebanese populations (PEARL) study was set up during the Syrian crisis in Lebanon in order to evaluate the causal contribution of pathogenic microorganisms found in the respiratory tract of children and adults presenting signs of CAP.

PEARL is a prospective multi-center case-control study conducted in Lebanese primary healthcare facilities that serve a predominantly Syrian refugee population. The inclusion of patients was launched in November 2016 and was completed in March 2018. Nasopharyngeal swabs, and urine and blood samples from more than 1,400 cases and controls were analyzed to identify the bacterial and viral etiological agents of CAP. Testing was run in four laboratories, two of which are GABRIEL members: the Rodolphe Mérieux Laboratory in Beirut and the Microbiology, Health and Environment Laboratory in Tripoli.

Preliminary results were presented at the GABRIEL meeting at Les Pensières Center for Global Health in France, as well as at the 28th European Congress of Clinical Microbiology and Infectious Diseases in Madrid, Spain, and at the 7th International Congress of the Faculty of Pharmacy of the Université Saint-Joseph in Beirut. The protocol was published on the platform, Gates Open Research. The results showed that CAP cases were mild to moderate in the study population, and that the incidence was lower during the second winter season. Viruses apparently played a predominant role in the etiology of overall CAP, but more so during the first winter season. *Streptococcus pneumoniae* had a low or null role in the first winter season but was the leading cause of CAP in the second. The 5 most frequently observed serotypes of *Streptococcus pneumoniae* have been incorporated into the PCV13 vaccine.

The transcriptomic profile of the host will soon be performed at Nationwide Children’s Hospital (Ohio, USA). This supplemental analysis should help to better identify the contribution of these various pathogens to CAP.

Thomas Kesteman, Mérieux Foundation, Beirut (Lebanon)
HIV-Infected pregnant adolescent outcomes in Haiti: a most vulnerable population

Mother-to-child transmission of HIV (MTCT) is the main contributor to the pediatric HIV epidemic. Although early diagnosis and adherence to care are critical to eliminating vertical transmission, post-partum loss to follow-up is common and is an important barrier to optimizing HIV outcomes in women and children. The World Health Organization’s (WHO) Prevention of MTCT (PMTCT) option B+ is a policy that provides antiretroviral therapy (ART) to all HIV+ pregnant women regardless of their health status. This option has been the standard of care in Haiti since 2009. This is the largest PMTCT program in the Caribbean.

The objective of our analysis was to evaluate HIV+ pregnant adolescent outcomes, as compared to those of pregnant young women and adults. We analyzed retrospective data from HIV+ pregnant women and their infants enrolled in the GHESKIO PMTCT program from January 1999 through July 2014. At PMTCT program entry, HIV+ pregnant women undergo a medical history and physical examination, as well as routine laboratory tests that include a CD4 count, in addition to an antenatal assessment, WHO staging, syphilis testing, and rapid treatment for those who test positive.

We evaluated retrospectively the outcomes of HIV+ pregnant women in three of the following age groups: adolescents aged 15-19 years; young women aged 20-24 years; adult women aged > 24 years. Results are exhibited in the Table. Among all 4,665 pregnant women, 65% (235/364) of adolescents received antiretroviral medications prior to delivery, as compared to 74% (547/739) of young women, and 76% (2,719/3,562) of adults. Adolescents also were less likely to be retained in PMTCT care through delivery, as compared to other age groups, 64% vs 74% and 76%, respectively. A total of 3,218 infants were reported born alive among 3,414 women retained through delivery (94%), a result that did not differ by age group (92-95%). Among infants enrolled in PMTCT, 84% (183/217) of them born to adolescent mothers were tested for HIV, as compared to 89% (438/494) and 93% (2,334/2,507) of infants born respectively to young women and adults. The HIV transmission rate ranged from 7.7% in adolescents (14/183), to 5.3% in young women (23/438) and 93% (2,334/2,507) of infants born respectively to young women and adults.

Retention of HIV+ women at 12 months after PMTCT enrollment was significantly lower in adolescents, as compared to that in young women and adults: 72.7% (95% CI 67.6-77.2%), 80.4% (95% CI 77.2-83.2%), and 83.8% (95% CI 82.5-85.0%), respectively (log rank p=0.0003).
Adolescent HIV+ pregnant women have poorer outcomes across the PMTCT care continuum, as compared to young women and adults. This is an extremely vulnerable population that needs tailored interventions to improve uptake of ART and retention in care and to eradicate transmission.

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Evaluation of a new immunological diagnostic tool (QFT-P+HBHA) and identification of candidate biomarkers useful for monitoring the efficacy of tuberculosis treatment

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), is a treatable and curable disease, yet it remains a major public health concern across the world. Side effects associated with long-term antibiotic therapy may lead patients to abandon the treatment regimen, entailing subsequent treatment failure, development of drug-resistant TB, and fueling of the spread of this disease throughout the community. According to the World Health Organization, all patients being treated should be monitored to assess their response to treatment (success or failure). However, currently, there are no highly accurate, sensitive and rapid tools able to efficiently monitor the efficacy of treatment. The detection of blood-based biomarkers may form a promising potential tool that answers this need.

In this context, the GABRIEL network has initiated a pilot multi-center study aimed at identifying new prognostic biomarkers of TB. The study’s objectives include, among others, the identification, evaluation and validation of new supportive tools and reliable biomarkers for monitoring the effectiveness of anti-TB therapy. This will be investigated by:

- evaluating, *in vitro*, whether the host Interferon-response detected with a combination of one commercial IGRA (Interferon-release assay) blood test, called QuantiFERON-TB Gold Plus (QFT-Plus), together with a non-commercial assay based on the response to a mycobacterial antigen called “Heparin-binding hemagglutinin” (HBHA), can be an effective tool for monitoring the efficacy of treatment against tuberculosis,

- identifying new biomarkers to monitor the efficacy of TB treatment with the use of high-throughput single-cell analysis methods (e.g. mass cytometry), as well as of host transcriptomic analysis.

Ultimately, such tools should improve the management of patients undergoing treatment, increase the cure rate, and reduce the emergence and circulation of resistant *Mtb* strains. These tools may also serve to develop new therapeutic strategies that are more rapid and more effective.

Together with other members of the GABRIEL network, the Health and Environment Microbiology Laboratory at the Lebanese University is collaborating on this project and acting as an implementing site to enroll local TB patients. This is an important opportunity to further enhance our active collaboration.
on an international scale, and to expand our research network with other GABRIEL members by working cooperatively for the improved care of TB patients.

Monzer Hamze, Health and Environment Microbiology Laboratory, Tripoli (Lebanon)

Implementation of a loop-mediated isothermal amplification test for pulmonary tuberculosis diagnosis in four pilot microscopy centers in Cameroon

Background

Microscopy remains the main diagnostic tool for identifying tuberculosis (TB) in developing countries. However, since 2016, WHO has recommended WRDs (WHO-recommended rapid diagnostics) for accurate and rapid detection of TB. Loop-mediated isothermal amplification (LAMP) is the new WRD for initial diagnosis of TB for individuals with signs and symptoms of TB. Our challenge was to implement the TB-LAMP technique in Cameroon as replacement of microscopy and to assess its clinical and operational performances.

Intervention

Four microscopy centers in two regions of Cameroon (Center and South) have used the technique for their routine diagnosis of pulmonary tuberculosis in adults. These sites were selected according to their workload. No specific adjustments were made in those laboratories. Data was collected from June 2017 to March 2018. During this period, all suspected TB patients (adults) arriving at these microscopy centers were diagnosed using TB-LAMP.

Results

From June 2017 to March 2018, a total of 7,503 suspected TB patients were diagnosed using TB-LAMP. Regarding clinical performance, in the first quarter of 2017, TB-LAMP improved the overall positivity by 21.53% at all four sites when compared with data obtained by microscopy. Medical doctors found an approximately 80% correlation between results from TB-LAMP and radiography. Concerning operational performance, technicians have been very satisfied with the test. TB-LAMP is easier to use, and a preliminary background in molecular biology is unnecessary. The technique is robust. There is no need for maintenance and no equipment failure has yet been identified.

Conclusion

TB-LAMP has been easily implemented in the four microscopy centers in Cameroon. In addition to operational and clinical performances, its ease of use and its robustness are valid criteria to warrant TB-LAMP as a WRD for the initial diagnosis of pulmonary TB in adults in low-income countries with high TB prevalence. However, obtaining all materials through Global Drug Facility (GDF) remains problematic.

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Diagnosis of extrapulmonary TB in developing countries: a promising tool

Although tuberculosis affects the lungs in about 85% of TB patients, the infection may cause lesions in nearly any part of the body. Extrapulmonary TB (EPTB) accounts for 15 to 20% of TB cases. Several methods are available to diagnose pulmonary TB (PTB) conclusively. However, the diagnosis of EPTB has been very problematic until now, especially in resource-limited settings. Although EPTB is not transmissible, the delay in diagnosing the infection has been a significant cause of increased morbidity and mortality. We conducted a study to ascertain the performance of the GeneXpert® technique as a diagnostic tool for EPTB.

A total of 78 clinical samples were collected from suspected EPTB cases over a period of 17 months from January 2017 to May 2018, of which 48 came from the cerebrospinal fluid (CSF) of suspected meningitis patients, four from pus from infected wounds, two from lymph node biopsy specimens, sixteen from plural fluid, four from ascitic fluid, one from synovial fluid, and two from urine. Specimens were examined at the Rodolphe Merieux Laboratory of Chittagong, Bangladesh, using the GeneXpert MTB/Rif assay, conventional culture (LJ media), and microscopy (ZN stain) to check for the presence of MTB.

Among the samples from suspected cases, seven from CSF, one from pus, and one from lymph node specimens were tested positive by the GeneXpert MTB/Rif assay. Only one CSF specimen was found to be culture- and microscopy-positive and was GeneXpert-positive as well.

Aside from one pus specimen that was both GeneXpert- and microscopy-positive, but culture negative, no other specimens from EPTB cases were culture- and microscopy-positive.

Across the world, the diagnosis of EPTB is a challenging task. As MTB is paucibacillary, routine diagnostic testing for its detection is difficult. GeneXpert has shown to be a promising tool for the early detection of life-threatening cases of EPTB, such as tubercular meningitis that is prevalent in developing countries.

Jabin Akhter and Prof. MA Hassan Chowdhury, Bangladesh Institute of Tropical and Infectious Diseases, Chittagong (Bangladesh)

“MDR-TB in Georgia” project

The National Center for Tuberculosis and Lung Diseases (NCTLD) in Georgia, the Emerging Pathogens Laboratory (EPL) in France, and the French National TB Reference Center have rolled out the «MDR-TB in Georgia» project. This project is funded by Expertise France, as part of the 5% Initiative call for proposals, launched in 2017. The 5% Initiative on HIV/AIDS, Tuberculosis, Malaria, France’s indirect contribution to the Global Fund to Fight AIDS, Tuberculosis and Malaria, placed under the oversight of the Ministry of Foreign Affairs and International Development (“MAEDI”) and implemented by Expertise France. The «MDR-TB in Georgia» project aims to reduce the acquisition and primary transmission of TB drug
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resistance through 3 specific objectives: i) to train NCTLD laboratory staff in the newly introduced susceptibility testing to drugs, such as bedaquiline and delamanid, ii) to train clinicians in patient support through the management of TB drug side effects, and iii) to identify transmission «hot spots» throughout Georgia. To achieve the latter objective, patient contact tracing surveys will be challenged by comparing the genomes of the strains of M. tuberculosis isolated from patients. With massively parallel sequencing, similarities between strains can be analyzed much more accurately than with conventional genotyping methods, such as spoligotyping and MIRU-typing, and thus transmissions among patients can be better monitored. The results will be used to complete these contact tracing surveys. During the 36-month duration of the project, approximately 600 MDR-TB cases are expected to be included in the study.

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Publications by GABRIEL members since October 2017

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