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Bundling HIV and TB Care at a District-Level Center in Sierra Leone: A high-yield method for diagnosing co-infection with TB and antiretroviral treatment failure among people living with HIV

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ABSTRACT

Background: Protocols for HIV care are widely accepted by all international organizations and are proven to reduce mortality and complications from living with HIV. Unfortunately, executing best practice recommendations in Sierra Leone is difficult due to shortages in staff, training, and medications.
Methods: From June 2016 to August 2016, we implemented both an HIV guideline-based clinical evaluation protocol and a patient-centered workflow for TB screening and CD4 testing in the HIV clinic at Koidu Government Hospital (KGH) in rural Sierra Leone. The primary outcome of interest was how often this service center resulted in a clinically significant change in the patients' HIV regimen. Reasons for changing regimen included diagnosis of co-infection with tuberculosis (TB), diagnosis of clinical or presumed immunologic treatment failure of antiretroviral (ART) medications and, need for adherence to weight-based dosing in pediatric patients.
Findings: A total of 188 patients with HIV were seen in the clinic; 49 (26%) of these patients had a clinically significant change in their HIV regimen. The most common reason for regimen change was TB co-infection diagnosis in 38 (20%) patients. The other reasons for HIV regimen changes included: eight children whose ART was adjusted to meet appropriate levels for weight-based guidelines, five patients diagnosed with presumed immunologic treatment failure (some also co-infected with tuberculosis), and two patients with a serious side effect to ART. Interpretation: A comprehensive, patient-centric HIV clinic can result in high rates of case detection for tuberculosis and recognition of immunological ART failure.

Introduction

In 2016, UNAIDS reported 67,000 Sierra Leoneans were living with HIV (UNAIDS, 2016). This accounts for a prevalence of approximately 1.7% of the general population, with 20% more females than males reported ((UNAIDS) UJPoHA, 2016). Sierra Leone has one of the worst care retention rates globally; only 30% of those living with HIV were accessing antiretroviral therapy in 2016 despite the worldwide 90-90-90 targets for HIV detection, treatment, and suppression (World Health Organization, 2016).

One strategy utilized by several other African countries to close gaps in the HIV care continuum is to foster patient empowerment and peer support. In Cape Town, South Africa, a population of 3,216 adults had a 97% rate of viral suppression (VL $\leq$ 400 copies/mL) after a scale-up initiative that involved frequent follow-up and adherence clubs (Tsondai et al., 2017). In Uganda, the rate of viral suppression improved from 42% in 2009 to 75% by 2016 after enacting a combination HIV prevention program including peer support. Uganda had a significant improvement in their overall HIV

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incidence rate as well, illustrating the concept of treatment as prevention (Grabowski et al., 2017).

Another strategy to close gaps in HIV care is to bundle services in a one-stop-shop that improves patient access. This strategy has been helpful in screening for co-infection with tuberculosis (TB) in people living with HIV. A study in rural South Africa found that offering both TB screening and HIV testing together was very acceptable to patients—91% agreed to both services—and high yield, they found a case notification rate of 730/100,000 for tuberculosis (Shenoi et al., 2017). Another study showed that standardized paper screening questionnaires used at the HIV clinic were an effective method to prompt initiation of isoniazid preventive therapy or TB treatment for people living with HIV in Papua New Guinea (Carmone et al., 2017).

Despite these and numerous other models showing that HIV care gaps can be closed, in Sierra Leone the huge shortages in staff, training, supplies, physical building limitations, and inadequate standardized protocols made it difficult to enact best practices. Overall, Box 1 summarizes the challenges in HIV and TB care delivery. To close these gaps and apply best practices for HIV care at KGH, we implemented the comprehensive clinic. We hypothesized that allowing patients to have TB screening and CD4 checked at the same place would increase uptake of both tests. Here, we describe the main targets of HIV care re-design and the clinical impact this had on participants.

Methods

Study population

Our target population for the intervention included all HIV infected patients (age 0–100 years) who were receiving HIV continuity care from the KGH HIV office and arrived for a clinic visit between June 1, 2016 and August 30, 2016. We excluded patients who were newly diagnosed with HIV infection during their first visit to the comprehensive clinic and those who were known to have HIV but had been registered and receiving continuity HIV care at one of the other ART centers in the district.

Outcome measures

The primary analysis focused on patients who were prescribed a change in their HIV regimen during the comprehensive clinic visit. The analysis assessed the total number of unique patients who accessed the clinic and whether they had a change in their HIV regimen due to: diagnosis of co-infection with tuberculosis, diagnosis of immunologic or clinical treatment failure, or change in ART regimen to meet weight-based dosing guidelines in pediatrics. Patients who met multiple criteria for changing their ART regimen were also included in the outcome analysis.

Box 1. Challenges in HIV Care Delivery at Baseline

- Insufficient staff numbers
- Inadequately trained staff (lack of clinicians)
- Absent vital sign, body mass index (BMI), or mid-upper arm circumference (MUAC) monitoring
- No accountability for checking and trending CD4 counts
- Gaps in screening for TB; not implemented in 100% of cases and difficult to monitor who was missed
- No viral load testing available
- Slim stock of HIV testing supplies and ART medications led to stock-outs and rationing
- Limited human resources and data resources to enable outreach to patients who were lost-to-follow-up
- TB services were provided in a different location with different staff (still no clinicians)

The World Health Organization (WHO) 2013 HIV Guidelines, WHO 2010 TB Guidelines, and Sierra Leone's 2006 National Antiretroviral Treatment Guidelines were used to classify the reason for regimen change (World Health Organization, 2013; National HIV/AIDS Secretariat and Health Sector Response Group, 2006; World Health Organization, 2010):

- Tuberculosis was diagnosed when a patient had a
  - sputum test positive for *either* acid-fast bacilli (AFB) via microscopy *or*
  - GeneXpert MTB/RIF test positive *or*
  - clinical history and physical exam findings that created a very high level of suspicion for smear-negative or extra-pulmonary TB.
- Presumed immunologic treatment failure was diagnosed in patients who failed to restore their CD4 count to more than 100 cells/mm^3 after 6 months of treatment. This modified definition was used because there were not baseline CD4 counts for comparison. Clinical treatment failure was diagnosed when a patient who had been taking ART for at least 6 months developed new WHO stage 3 or greater opportunistic infections, AIDS wasting syndrome, and/or dementia. The requirement of 6 months ART treatment prior to diagnosing clinical treatment failure is to differentiate it from immune reconstitution syndrome.
- Pediatric cases had their ART medication doses adjusted according to the weight-based guidelines from the MOHS.

Clinic design and setting prior to intervention

Prior to implementing this project, it was not standard of care for patients to have an evaluation by a clinician; including no vital signs, measurement of weight, or questions about side effects of ART medications. HIV clinic staff did monitor for signs of TB, but there was no standardized protocol for screening. Additionally, the TB office and HIV office were on opposite sides of the hospital grounds and operated on varying schedules. During the study period there was not consistent availability of chest X-ray radiography. Thus, the criteria for smear-negative TB diagnosis was clinical history and physical exam findings which supported TB as the most likely diagnosis, although chest X-ray was included in the clinical assessment when available.

Previously, there were no CD4 count records kept and it was not standard practice to measure CD4 with any set frequency; so, the definition of presumed immunologic treatment failure was adapted to "a single CD4 value below 100 cells/mm^3 if the patient had been on treatment for at least 6 months". Similarly, there was no viral load testing capacity so virologic failure of ART could not be used as a reason for switching HIV prescription. At the time of publication of this manuscript, chest radiography, CD4 counts, and viral load are in intermittent use at the KGH HIV office.

The clinic staff consisted of 2 HIV counselors who had the responsibilities to diagnose HIV via triple positive point-of-care rapid assays, prescribe antiretrovirals, counsel about and prescribe ART for prevention of mother-to-child-transmission of HIV, and monitor follow-up patients for side effects of their ART—there were no nurses or clinicians. Box 1 summarizes the challenges in the HIV care of patients before this project.

There were two available regimens for antiretrovirals, both fixed-dose: zidovudine 300 mg/lamivudine 150 mg/nevirapine 200 mg (ZLN) given twice daily or tenofovir disoproxil 300 mg/lamivudine 300 mg/efavirenz 600 mg (TLE) given once daily. A

pediatric formulation was only available for ZLN at fixed-dose 60 mg/30 mg/50 mg with daily number of pills adjusted by weight. Nevirapine-only syrup was available for exposed infant prophylaxis. The treatment for TB was fixed-dose combination tablets, each containing: rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg, and ethambutol 275 mg or only rifampicin and isoniazid for the continuation phase. The TB medications were dosed by weight, 1–5 tablets per day. Pediatric TB medications available were fixed-dose rifampin 60 mg/isoniazid 30 mg/pyrazinamide 150 mg for induction phase and rifampin 60 mg/isoniazid 30 mg for continuation phase.

Interventions

There were two arms of the intervention, summarized in Box 2. First, we equipped the clinic staff with a one-page comprehensive checklist at the point of care that incorporated all the recommended elements of HIV care. The template assesses weight, medication list, TB screening, lab tests, and adherence. Our office visit template can be found in Supplementary Figure 1, it was designed from the recommendations found in the HIV diagnosis and treatment guidelines published by the Sierra Leone National AIDS Secretariat in 2006 (most recent revision at that time) with adaptation of the WHO 2013 HIV guidelines in the case of defining and managing clinical and immunologic treatment failure.

Second, we embedded CD4 testing and screening for TB in the clinic. A comparison of the initial workflow for TB testing compared to the post-intervention workflow can be seen in Supplementary Figure 2. Venipuncture for collection of CD4 samples was performed in clinic and blood tubes were sent in batches daily to the hospital lab. Patients who screened positive for symptoms of, or exposure to, TB had sputum collection on site. Sputum was preferentially sent for AFB smear. GeneXpert MTB/RIF testing was used if the patient had prior treatment for TB and was suspected of recurrence or if the initial AFB smear was negative. This algorithm for MTB/RIF testing was used due to shortages in cartridge inventory limiting use for all HIV/TB suspects. Patients were asked to either return to clinic the following week for results or to give permission for a CHW to communicate results to them if transportation was prohibitive.

Results

A total of 188 patients with HIV were seen in the comprehensive clinic from June 1, 2016 to August 30, 2016. Of the 188 patients seen in clinic, 49 (26%) had a clinically significant change in their HIV regimen. Seven patients had two or more reasons to change their HIV regimen. Table 1 summarizes the reason for HIV regimen change.

The most common reason for changing HIV regimen was diagnosis of co-infection with tuberculosis (TB), which occurred for 38 (20%) patients. Twenty-three of these patients were tested for TB because they had a body mass index (BMI) below 18.5, which was the most common reason to suspect tuberculosis. Fifteen patients were identified because they had a CD4 count below 200 and history of exposure to a person with known TB. The average BMI for patients diagnosed with TB was 16.3 ± 1.8 and an average CD4 count of 268 cells/mm^3 $\pm$ 145 cells/mm^3. Of the 38 patients who were diagnosed with TB, 22 had a positive AFB smear, 8 had a positive MTB/RIF test, and 8 were diagnosed as smear-negative cases due to high clinical suspicion. One of the eight cases diagnosed on MTB/RIF testing had rifampin resistance (the patient had previously been treated for TB) and was referred to the National MDR Program.

The other reasons for change in HIV regimen were: five children whose ART medications were adjusted to achieve appropriate levels for weight-based guidelines, 11 patients who had been on ART at least 6 months were newly diagnosed with presumed immunologic treatment failure (seven who were also diagnosed with TB), and two patients who had a serious side effect to ART (one with psychosis on efavirenz and one with Steven's Johnson Syndrome on ZLN).

We also had eight patients diagnosed with solely clinical ART treatment failure due to AIDS wasting syndrome, but we engaged them in adherence monitoring programs instead of changing their ART regimen during this project period. If you include the intensified adherence monitoring as an intervention for these eight patients, then a full 30% of all patients who attended the clinic received an intervention in their HIV treatment because of our model of care.

We additionally report an unintended result from this project—stockouts of testing supplies for TB and HIV. This was temporized by Partners In Health who procured additional supplies in the short term; and later helping the Ministry of Health HIV staff design a better forecasting grid for HIV and TB tests and medications for the long term.

Box 2. Bundle of Services Implemented with the Comprehensive HIV Clinic

- Patient education and HIV health literacy
- Peer support amongst patients guided by community health workers
- Vital sign monitoring with body mass index (BMI) or mid-upper arm circumference (MUAC)
- On-the-spot collection of blood for CD4 testing
- On-the-spot collection of sputum for TB testing
- Office visit checklist (history questions, physical exam, TB screening, adherence)
- Improved access to multidisciplinary team including providers, nurses, social workers, and community health workers
- Human Resources to track sputum results
- Technical assistance with training, mentorship, and simulation of advanced HIV-medicine topics

Discussion

Our study shows that there is a significant burden of undiagnosed co-infection with tuberculosis in people living with HIV in Sierra Leone. Moreover, it is effective to promote clinic-based case finding for TB among this population by implementing standard checklists and reducing barriers in the workflow to screen all patients for TB. Beyond diagnosis of TB, we also showed that bundling CD4 testing can improve detection of presumed immunologic treatment failure.

The two main re-designs were an office visit template and embedding sputum collection and phlebotomy into the visit workflow. The office visit template functioned as a one page, point

Table 1
Reason for changing HIV regimen during the comprehensive HIV clinic and the number of patients who were impacted.

Reason to change HIV medication regimen	Number of patients impacted
Diagnosis of co-infection with tuberculosis	38
Diagnosis of immunologic failure of antiretrovirals	11
Pediatric weight-based dosing adjustments	5
Serious toxicity to antiretrovirals	2

of care, comprehensive timeline of the patient's HIV history and current treatment. The template standardized documention of weight, medication list, TB screening and lab tests, and assessing adherence counseling (see Supplementary Figure 1). This simple checklist empowered staff to implement the Sierra Leonean National HIV Guidelines with high precision and accuracy. Performing phlebotomy and sputum collection on site increased the number of patients with values recorded for TB testing and CD4 count and led to changing their HIV regimen.

Our results lend further support to the studies by Shenoi and Carmone that bundled services and checklists for HIV care are effective in closing gaps. Our results also support the body of literature showing that intensified case finding for TB within HIV clinics is acceptable to patients and improves case finding rates (Bigogo et al., 2018; Yoon et al., 2019; Owiti et al., 2019; Sawry et al., 2018; Gupta et al., 2014). Our experience is unique in that we describe an educational and programmatic way to build capacity in existing staff without added cost. The next frontier in standardization is mobile technology that allows the questionnaire to be accurately captured by community health workers on smartphone apps in the patients' homes. This technology automates data collection, further reduces patient access issues, and can have set electronic 'reminders' to staff.

Our main limitation was poor enrollment of the eligible HIV patients; the 188 patients who participated only represents 47% of the total eligible HIV population of KGH (number eligible = 394). The remaining HIV-infected patients did not arrive for a clinic visit during our three-month study period. This increases the possibility that our high rate of changing HIV regimen and case detection of TB were due to selection bias. In other words, patients who felt sick were more likely to present themselves and CHWs were more likely to bring patients with outward symptoms such as wasting syndrome, cough, or fever. This poor catchment was not anticipated when we designed the study because the HIV clinic has always had the expectation that patients return monthly for refills since the clinic does not have sufficient stock to give more than 30-day supplies of ART. Thus, patients who did not attend clinic during our study period are labeled as 'lost to follow-up' and are either: no longer taking or inappropriately taking ART, have transferred care to another center, or are deceased. This illustrates the magnitude of 'lost to follow up' in Kono District; another gap in the HIV care continuum that was not addressed with our intervention.

An important lesson to share with other program managers is our strategy for capacity building of technical medical expertise and quality improvement (QI) skills in low resource settings. These strategies are summarized in Box 3. One of the most pressing threats to QI projects is staff turnover, which necessitates empowering the next generation of managers to think critically. We encourage the use of the Institute for Healthcare Improvement's (IHI) Model for Improvement as a framework for building capacity in problem solving and quality improvement methodology among junior staff. This model emphasizes teamwork, downstream effect analysis, action, and monitoring so it balances a variety of leadership skills and attitudes which are important for success. Important next steps for this project would be capturing lost to follow up patients and engaging them in the bundled clinic.

Box 3. Key Recommendations for Successful Capacity Building in Quality Improvement in Low Resource Settings

- Specialist-level (ie fellowship-level) technical training in clinical content areas and motivational interviewing skills.
- Mentor all cadres during real-life clinical encounters on a recurring schedule
- Design pre- and post- tests for didactic topics
- Reiterate the most difficult didactic content areas with case studies and multimedia classes to ensure skilled application
- Use the Institute for Healthcare Improvement's Model for Improvement to train all staff in critical thinking and leadership skills and attitudes
- Consider designing objective structured clinical examinations (OSCE) to provide a forum for evaluating clinical skills and decision-making

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Declaration of interests

Conflicts of interest: The authors declare they have no conflicts of interest for this project. This project was approved by the IRB of University of South Florida Morsani College of Medicine and approved by the Sierra Leone Ethics and Scientific Review Committee as a quality improvement project.

Related publications: This project has not been submitted for publication in any other form.

Responsibility for publication: The corresponding author, Dr. Asa Oxner, had full access to the data included in the study and had the final responsibility for the decision to submit for publication.

Contributions of each author

All authors edited and approved the final draft of the manuscript in April 2018 and revisions in March 2019.

- AO: Substantial contribution to design of work, wrote the first draft of manuscript, adapted the HIV treatment protocol from WHO, and mentored the clinical staff on implementation.
- KK: Contributed to analysis of data, wrote the first draft of the introduction section of the manuscript and performed literature search.
- SH: Wrote the first draft of the introduction section of the manuscript and performed literature search.
- AM: Contributed to the conception of the project design, edited the final manuscript and formatted references section.
- JM: Contributed to the design of the project and daily implementation, assisted in writing the first draft of the conclusion section of manuscript and provided oversight of all clinical care in the KGH HIV office.
- JBT: Wrote the first draft of the methods section of manuscript, created patient educational materials, and redesigned the process flow for getting TB samples processed.
- FD: Wrote the first draft of the methods section of manuscript, and organized patients and their community health workers to arrive in clinic.
- AK: Assisted in writing the first draft of the methods section of manuscript, assisted in designing the workflow for pharmacy restocking and medication administration.
- AF: Wrote initial draft of methods section of manuscript, provided leadership for nurse training about collecting blood samples and sputum samples.
- ATK: Assisted with writing the initial draft of methods section of manuscript, created the schedule and workflow for the HIV clinic.
- TSA: Wrote the initial draft of the results section of the manuscript, collected de-identified data and validated the data.

- EE: Edited the initial draft of the results section, assisted with conceptualization of how to collect and validate the data from patient history forms.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2019.03.018.

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