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ORIGINAL ARTICLE

The yield and feasibility of integrated screening for TB, diabetes and HIV in four public hospitals in Ethiopia

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Background: Our objective was to demonstrate the feasibility of integrated care for TB, HIV and diabetes mellitus (DM) in a pilot project in Ethiopia.

Methods: Healthcare workers in four hospitals screened patients with TB for HIV and DM; patients with HIV for DM and TB; and patients with DM for TB. Fasting and random plasma glucose (RPG) tests were used to confirm the diagnosis of DM. We used screening checklists for TB and DM, and additional risk scoring criteria to identify patients at risk of DM.

Results: Of 3439 study participants, 888 were patients with DM, 439 patients with TB and 2112 from HIV clinics. Six of the patients with DM had TB of whom five were already on treatment; and 141 (32.4%) patients with TB had DM, of whom only five were previously diagnosed with DM. Symptomatic patients and those with a risk score of 5 or more were about three times more likely to have abnormal blood glucose level. Of 2075 HIV patients with RPG determined, only 31 (1.5%) had abnormal RPG.

Conclusions: Tri-directional screening was feasible for detecting and managing previously undiagnosed TB and DM. More work is needed to better understand the interaction between HIV and DM.

Keywords: Diabetes mellitus, Ethiopia, HIV, Integrated, Non-communicable diseases, Tuberculosis

Introduction

The burden of non-communicable diseases in low income countries is expected to rise from 47% in 1990 to 69% in 2030, and diabetes mellitus (DM) accounts for a significant proportion of this. Recent global estimates show that close to 300 million people were living with DM in 2010 of which about 7 million developed the disease during that year. The projected number for 2030 is over 400 million with about 30% of the prevalent cases expected to occur in low and middle income countries.[1] Both TB and HIV epidemics continue to be major public health problems in those same settings.[2,3] As DM and TB share similar risk factors, it is believed that the slightest interaction between the two diseases would result in devastating consequences.

Earlier studies revealed higher rates of TB among patients with DM compared to those without. In two districts in India, for example, nearly a half of TB patients had either diabetes or prediabetes. Moreover, patients with DM present with atypical clinical features of TB posing diagnostic challenges for clinicians. Also, TB treatment failure and relapse appear to be higher in patients with DM.[4,5] Similarly, there is a growing concern that people living with HIV (PLHIV) may be at increased risk of various non-communicable diseases including DM due to HIV per se or consequent to its treatment but the exact magnitude of the excess risk and associated risk factors continue to be priority agenda for future research.[6]

As part of the effort to address these challenges, WHO in collaboration with the International Union against Tuberculosis and Lung Disease (IUATLD) has developed a global framework for collaborative activities against TB and DM.[7] This guidance represents a major step in fostering collaboration between disease control programs for non-communicable and communicable diseases. There has also been considerable progress toward translating the global recommendations into action, with several pilot projects in the Asian continent documenting successful examples of bi-directional screening for TB and DM.[8–11]

However, there is limited experience from other continents, especially from sub-Saharan Africa where the dual burden of both communicable and non-communicable diseases is expected to rise.[12] In particular, the information on how to deliver integrated services using the existing TB/HIV integration platforms, without disrupting the existing services, is missing. Our objective was to demonstrate the feasibility of providing integrated clinical care for patients with DM, TB, and HIV in general public hospitals in Ethiopia.

Methods

Study setting

Ethiopia is one of the high TB and HIV burden countries.[13] Similarly, according to the estimates by the International Diabetes Federation (IDF) in 2013, about 1.8 million adult people within the age range of 20 to 79 years live with DM in Ethiopia, an estimated prevalence of 4.4%.[14] The country has well developed systems for coordinating the prevention and control of both TB and HIV, through a decentralized approach. More recently, the country developed a national strategy for prevention and control of non-communicable diseases including DM. However, the management of DM is often limited to hospitals where specialized medical services are available.

Design of the pilot implementation

Between February and June 2015, we piloted integrated screening for the three diseases in four secondary hospitals in Amhara and Oromia regions of Ethiopia. The hospitals were Bishoftu and Shashemene in Oromia and Debrebirhan and Debretabor hospitals in Amhara regions. We selected these hospitals purposively based on the actual case load and need for integrated services. At each hospital, we provided on-site orientation to a focal person (who was responsible for site level coordination) and to three clinicians working in TB, antiretroviral therapy (ART) and DM clinics. Clinicians in ART clinics screened patients both for TB and DM. Those in TB clinics screened patients for HIV and TB; and patients attending DM clinics were screened for TB. Screening for HIV among patients with DM was deferred because these patients were not among priority target groups for HIV in the Ethiopian setting and therefore test kits were not freely available unless specifically requested by the patient or provider. We provided minor supplies, mentoring support and monitored the progress during monthly visits to the hospitals using standardized checklists.

Procedures for disease screening

For TB screening in patients with DM, we adapted and used the screening checklist from the national guidelines.[15] Symptomatic patients were offered further diagnostic tests based on the symptoms and availability of diagnostic facilities. Sputum microscopy was the preferred method of diagnosis for patients with productive cough. The laboratory staff who performed the sputum examinations had college level training with additional on-the-job training on sputum microscopy. The TB laboratories in the four hospitals participated in a quarterly external quality assessment scheme on a regular basis. GeneXpert was the recommended primary test for PLHIV but not for patients with DM. Moreover, it was not widely available at the time of this pilot project. Chest radiography was available for patients upon clinician's recommendation.

Since there was no standardized screening tool for identifying patients at risk of DM, we used a combination of risk scoring, symptom checklist and blood test. The first step involved using risk scoring system adapted from the published literature.[16] The sensistivity and specifity of this tool in non-African populations was 81% and 54% respectively. Age, family history, hypertension, waist circumference, alcohol intake and smoking were used to build a scoring system. Scores for the individual variable ranged from 0–3 with the cut-off point of the total score being 5, i.e., patients with a score of 5 or more were considered 'high risk' groups. Irrespective of the risk scoring value, the clinic nurse administered a checklist of clinical symptoms developed by our team, and categorized the patients as being 'symptomatic' or 'asymptomatic'. Further, the clinic staff did either fasting or random plasma glucose (RPG) test using a glucometer. A fasting plasma glucose (FPG) of ≥126 mg/l or RPG of 200 mg/dl was considered suggestive of DM. Patients in TB clinics received FPG tests because they take their anti-TB medications before taking breakfast while those in ART clinics received RPG tests.

Data collection and management

We used the registers from TB units, outpatient TB screening registers and ART registers as main data sources. We also used laboratory logbooks and patient charts for additional sources of individual level information. Since there was no disease-specific register for DM, we designed a new temporary register to keep track of patients screened for TB in DM clinics. The screening checklists were used to capture the data. The clinicians in the TB, ART, and DM clinics completed the checklists as part of their routine clinical activity.

All completed checklists were filed and kept at each clinic. The site focal person then collected all completed checklists at the end of each work week, checked for completeness, and kept them in a master folder at the focal person's office. All completed and checked checklists were sent to the central data officer every 2 weeks, who then checked them for accuracy and completeness of the information.

Data entry and analysis

A centrally based data clerk entered data from checked and approved checklists into CSPro (Census and Survey Processing System, https://www.census.gov/population/international/software/cspro/) database, and then transferred to Statistical Package for Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA) for analysis. Analyses included descriptive statistics of the baseline characteristics; calculating proportion of patients with DM, TB or HIV among those screened; and bi-variate and multivariate analysis of factors associated with DM, TB or HIV diagnoses.

Ethics

The Ethics Committees of Regional Health Bureaus of Amhara and Oromia reviewed and approved the project as operational

research. Patients gave informed oral consent to undergo the screening tests as part of the routine care. Completed checklists were kept on a lockable shelf and only authorized project staff had access to the documents. Patient names were not recorded in the checklists. Other patient identifiers such as patient's medical record number was not included in the data file. The services were provided free of charge. Patients with additional conditions diagnosed through the project activity were referred to the available standard services.

Results

A total of 3439 patients participated in this study including 888 from DM clinics, 439 patients with TB, and 2112 PLHIV (Table 1).

TB in patients with DM

Of 888 patients screened for TB, 55.6% (494/888) were men, 60.4% (536/888) came from urban areas and 69.9% (621/888) were unemployed. Their median (IQR) age was 44 (28–55) years. Over a fifth (23.0%, 204/888) of them reported current history of hypertension. Six patients had TB, of whom five were already on treatment and one patient was newly diagnosed, making the overall TB prevalence estimate 676 per 100 000 population.

DM co-morbidity and HIV co-infection rates in patients with TB

Of 439 patients with TB screened for TB, 55.6% (244/439) were men and 62.0% (272/439) were from urban areas, and their median age was 30 years (IQR 22–45). FPG was determined in 435 of the 439 patients with TB. Of these 435 patients, 141 (32.4%) had FPG ≥126 mg/dl, of whom only five were known diabetic patients on follow up. Of the 89.3% (392/439) who knew their HIV status, 12.5% (49/392) were co-infected with HIV. On multivariate analysis, symptomatic patients and those with a risk score of 5 or more were about 2.8 times more likely to have higher blood glucose level. Also, being male was another risk factor for higher blood glucose level (Table 2).

Table 1. The yield of tri-directional screening for TB, diabetes, HIV, February–June 2015, Ethiopia

Screening parameters	Values
DM clinic	
Total screened for TB	888
Number (%) diagnosed with active TB	6 (0.7)
TB clinic	
Total screened for DM	439
Number (%) with FPG ≥126 mg/dl	141 (32.4)
Co-infected with HIV	49 (12.5)[a]
HIV clinic	
Total screened for DM	2112
Number (%) with RPG ≥200mg/dl	31 (1.5)[b]
Number (%) co-infected with TB	316 (15.8)[c]

DM: diabetes mellitus; FPG: fasting plasma glucose; RPG: random plasma glucose.
[a] Out of 392 who received HIV test.
[b] Data were missing for 37.
[c] Data were missing for 114.

Diabetes in persons living with HIV

We screened 2112 patients for DM, 39.2% (827/2112) were men, and 79.7% (1684/2112) lived in urban areas. Their median age was 35 (IQR 30–43) years. Of 2075 patients with RPG determined, 1.5% (31/2075) had RBS ≥200 mg/dl. At least one symptom of diabetes was reported in 2.1% (44/2112) of participants while 18.7% (394/2112) had diabetes risk score of ≥5. The proportion of patients with RBS ≥200 mg/dl was 18.2% (8/44) among those with symptoms of diabetes as compared to only 1.1% (23/2068) among asymptomatic ones (χ^2=85, p<0.0001). Also, 4.6% (18/394) of patients with diabetes risk score of ≥5 had an RPG ≥200 mg/dl as compared with only 0.8% (13/1681) among those with lower risk score (χ^2=32, p<0.0001). Similarly, male gender was associated with higher proportion of RPG ≥200 mg/dl (2.5% vs 0.9%, χ^2=8.2, p<0.01).

On multivariate analysis, having diabetes symptoms, risk score ≥5, and male gender were significantly associated with RBS ≥200 mg/dl (Table 3).

Discussion

This is the first experience of tri-directional screening for TB, DM and HIV in Ethiopia, and perhaps one of a few globally. The yield of TB among patients with DM was about three times the estimated prevalence in the general population, but over 83% of these were already detected and managed by the existing health system. On the other hand, about a third of TB patients had abnormal blood sugar suggestive of DM, but the existing health system had detected only 3.5% of these cases.

The findings have practical implications for integrating screening and diagnostic approaches for communicable and non-communicable diseases. If well-organized screening systems for DM were in place, the health system would have detected the >95% of previously unrecognized abnormal FPG among TB patients, leading to further improvements in treatment outcome. In contrast, because of its routine outpatient screening practice which is already in place for all outpatient clinic visitors, the TB program was able to detect and treat more than 83% of the TB cases among patients with DM even before the current screening was introduced. Programs for prevention and control of DM and other chronic diseases may benefit from the experiences of TB and HIV programs.

The yield of TB among DM patients in our study is lower than prevalence reports from earlier studies.[17] Feleke and Lester reported TB prevalence of 3.9% and 5.9%, respectively, among diabetic patients.[17,18] In another report, TB prevalence was found to be as high as 9.5% among diabetic patients admitted at a tertiary hospital in Addis Ababa.[19] A retrospective review of patients admitted at two tertiary hospitals in Addis Ababa showed cumulative TB prevalence of 5.5%.[20] Moreover, the prevalence of pulmonary TB was 6.2% among patients with diabetes with

Table 2. Logistic regression analyses of predictors of FBG ≥126 mg/dl in patients with TB in Ethiopia

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Symptom screen (symptomatic vs asymptomatic)	3.0 (1.5–5.9)	2.8 (1.4–5.6)
Risk score (≥5 vs <5)	2.8 (1.2–6.7)	2.8 (1.2–6.7)
Sex (male vs female)	1.7 (1.1–2.5)	1.6 (1.1–2.5)
Residence (urban vs rural)	1.3 (0.9–2.0)	1.2 (0.8–1.9)

Table 3. Predictors of abnormal plasma glucose among people living with HIV, February–June 2015, Ethiopia

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Symptom screen (symptomatic vs asymptomatic)	19.4 (8.1–46.2)	12.9 (5.1–32.4)
Risk score (≥5 vs <5)	6.2 (3.0–12.7)	4.9 (2.3–10.3)
Sex (male vs female)	2.8 (1.4–5.9)	2.5 (1.2–5.4)
Residence (urban vs rural)	3.5 (0.8–14.7)	3.4 (0.8–14.7)

symptoms suggestive of TB.[21] The lower TB prevalence among patients with DM in our study could be due to several reasons. First, the overall declining trend of TB incidence and prevalence in the Ethiopian population could be the main underlying reason.[13] Secondly, we carried out this project in hospitals which practice rigorous routine TB screening through which most of the TB cases might have already been detected. Thirdly, earlier studies were conducted in tertiary centers with more advanced DM which might have resulted in higher TB prevalence rates.

On the other hand, about 25% of patients with smear positive TB had DM and the rate was 6.7% among patients with smear negative TB in a TB specialized hospital in Addis Ababa.[22] The prevalence of DM in patients with TB in the current study is higher than earlier reports, and it is about three times the national prevalence estimate.[14] This further confirms the need to prioritize TB clinics as entry points for integrated management of non-communicable and communicable diseases. Routine screening for DM using a combination of symptom checklists and risk scoring followed by laboratory confirmation at the initiation of anti-TB treatment could be considered a feasible strategy.

The prevalence of DM among PLHIV was lower than the national prevalence estimate of 4.36 % in the general population of Ethiopia.[14] In a recent large cohort study in a developed setting, the risk of DM was not higher among PLHIV as compared with the rate in the general population but some antiretroviral drugs rarely used currently were associated with increased risk of DM.[23] Age of the patients was a significant risk factor for multiple comorbidities with non-communicable diseases.[24]

More data are needed to better understand the magnitude and risk factors for DM among PLHIV. The ongoing global collaborative research effort should be able to provide more insights into this interaction.[25]

Important lessons can be drawn from this pilot experience of integrating services for TB, HIV and DM. These results were achieved in a setting where nurses and non-specialist physicians were coordinating across three different clinics, suggesting the feasibility of the approach in settings with limited specialist and sub-specialist health workforces. The symptom-based screening and the use of clinical scoring criteria, with further standardization and validation, can be used as important tools to improve the yield of the screening approach. The higher TB-DM comorbidity rate clearly highlights the importance of targeting this patient population for bi-directional screening. On the other hand, the low proportion of patients with DM among PLHIV suggests that routine screening for DM may not be necessary in HIV clinics in Ethiopia unless further evidence proves excess risk in this patient group.

The study has some limitations as well. We used two different approaches to determine blood sugar levels in patients with TB and in patients with HIV; FPG for TB and RPG for HIV patients. This might have led to some differences in estimating the proportion of patients with DM. The diagnosis of TB was mainly done through symptom screening followed by sputum microscopy. Since most DM patients with TB are asymptomatic, we might have underestimated the TB rate among patients with DM.

Conclusions

The yield of TB among patients with DM was about three times the prevalence estimate in the general population, further confirming the higher risk of TB in this population. The existing routine TB screening system helped detect most of these TB patients. Systems and processes developed under HIV and TB programs served as useful entry points to detect and manage a significant proportion of previously unrecognized abnormal blood sugar levels in TB patients. Undetected DM, however, was common among patients with TB. This suggests the need to develop more effective screening systems for DM.

Future research should focus on identifying the best tools and algorithms for screening DM among patients with TB and HIV. Since routine blood test for all patients with TB and HIV may not be a cost-effective approach, simplified initial screening tools should be developed and tested. On the other hand, since most TB–DM co-infected patients may be asymptomatic for TB symptoms, improved diagnostic tools are needed for this group of patients. The feasibility and yield of newer molecular diagnostic tests such as GeneXpert among DM should be assessed in high burden settings.

Authors' contributions: DJ conceived and designed the study, coordinated implementation, supervised data collection, analyzed the data and wrote the first and subsequent drafts of the paper. NH contributed to designing data collection tools, supervised data entry and commented on the first and subsequent versions of the manuscript. TA supervised the clinical team and contributed to the revision of the manuscript. IJ and WK facilitated project implementation and reviewed and commented on the draft manuscript. DH, MM, PS and GS critically reviewed the manuscript for intellectual content and provided feedbacks on subsequent versions. All authors reviewed and approved the final version of the manuscript. DJ is the guarantor of the paper.

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