Common mental disorders in TB/HIV co-infected patients in Ethiopia

Amare Deribew*1,2, Markos Tesfaye3, Yohannes Hailmichael4, Ludwig Apers5, Gemeda Abebe3,6, Luc Duchateau7 and Robert Colebunders2,5

Abstract
Background: The relationship between TB/HIV co-infection and common mental disorders (CMD) has been scarcely investigated. In this study, we compared the occurrence of CMD in TB/HIV co-infected and non-co-infected HIV patients in Ethiopia.

Methods: We conducted a cross sectional study in three hospitals in Ethiopia from February to April, 2009. The study population consisted of 155 TB/HIV co-infected and 465 non-co-infected HIV patients. CMD was assessed through face to face interviews by trained clinical nurses using the Kessler 10 scale. Several risk factors for CMD were assessed using a structured questionnaire.

Results: TB/HIV co-infected patients had significantly (p = 0.001) greater risk of CMD (63.7%) than the non-co-infected patients (46.7%). When adjusted for the effect of potential confounding variables, the odds of having CMD for TB/HIV co-infected individuals was 1.7 times the odds for non-co-infected patients [OR = 1.7, (95%CI: 1.0, 2.9)]. Individuals who had no source of income [OR = 1.7, (95%CI: 1.1, 2.8)] and day labourers [OR = 2.4, 95%CI: 1.2, 5.1) were more likely to have CMD as compared to individuals who had a source of income and government employees respectively. Patients who perceived stigma [OR = 2.2, 95%CI: 1.5, 3.2]) and who rate their general health as "poor" [OR = 10.0, 95%CI: 2.8, 35.1]) had significantly greater risk of CMD than individual who did not perceive stigma or who perceived their general health to be "good".

Conclusion: TB/HIV control programs should develop guidelines to screen and treat CMD among TB/HIV co-infected patients. Screening programs should focus on individuals with no source of income, jobless people and day labourers.

Background
The global burden of disease report revealed that neuropsychiatric conditions accounted for up to a quarter of all the disability-adjusted life years lost[1]. In low and middle income countries (LAMIC), neuropsychiatric disorders such as depression, anxiety and somatoform disorders account for 9.8% of the global burden of diseases[2].

The risk factors for mental health problems are complex [3]. Poverty, low education, social exclusion, gender disadvantage, conflict and disasters are the major social determinants of mental disorders[2]. Presence of medical illnesses [4] stigma and discrimination [5] also play a role in the development of depression.

The recent Lancet series on global mental health highlighted the lack of research on the interactions between mental disorders and communicable diseases such as tuberculosis (TB) and HIV/AIDS in low income settings [4]. A high rate of depressive disorders has been reported among patients with HIV in high income countries. In the United States, a higher rate of depressive disorders was observed in HIV seropositive women (19%) than in HIV seronegative women (4.8%)[6]. Bing and colleagues [7] also reported that the 12-month prevalence of major depression was 36% in HIV infected adults compared to 7.6% in the general population in the United States. Some studies in LAMIC (Kenya, Democratic Republic of Congo and Thailand) also revealed that the rate of depression was higher in HIV seropositive patients than in HIV negative individuals [8].
The neurtropism of the HIV, opportunistic infections of the central nervous system and side effects of antiretroviral therapy (ART), especially the Efavirenz, may cause mental health problems[4]. There is evidence that individuals with mental health problems are at higher risk of contracting HIV due to their higher risk behaviours[9].

Adherence to ART is adversely affected by depression[10-12]. Moreover, depression may reduce the CD4 lymphocyte count, increase viral load and mortality in patients with AIDS[13-15]. On the other hand, treatment of depression has been found to improve health outcomes in patients with HIV[14,15].

Some studies have investigated the relationship between common mental disorders (CMD) and TB. A study conducted in Turkey showed that the prevalence of depression and anxiety was 19% for recently diagnosed patients with TB, 22% for defaulted TB patients, and 26% for patients with multidrug-resistant TB[16]. The prevalence of CMD in 53 Nigerian TB patients recruited in a chest clinic was 30%, compared to 5% in healthy controls[17]. A study done in Pakistan showed that the prevalence of depression and anxiety among TB patients was 43% and 47% respectively[18]. TB patients have poor mental health and quality of life compared to the general population in United Kingdom[19].

TB/HIV co-infection poses immense diagnostic and economic challenges for developing countries[20]. HIV is the strongest risk factor for the development of active pulmonary and extra pulmonary TB. TB also accelerates the deterioration of the immune status of patients with HIV[21-24] and it is one of the leading causes of mortality in people living with HIV/AIDS (PLHA)[25]. In Ethiopia, the rate of TB/HIV co-infection ranges from 45% in Addis Ababa[26] to 52% in North Ethiopia[27].

Although several studies have been done concerning the interaction between either HIV/AIDS or TB with mental health problems, little is known about the effect of TB/HIV co-infection on common mental disorders. CMD, characterized by a significant level of depressive, anxiety and/or somatic symptoms are common among women in Ethiopia[28,29]. So far the magnitude of CMD among men and the interaction between CMD and communicable diseases has not been investigated in Ethiopia. The objective of this study was to compare the occurrence of CMD in TB/HIV co-infected and non-co-infected HIV patients in Ethiopia.

Methods
Study Settings and Population
From February to March, 2009, we conducted a cross sectional study in three hospitals in Oromiya regional state of Ethiopia. Based on the availability of patients, we selected Adama, Nekemet and Jimma specialized hospitals in the east, west and southwest part of Ethiopia respectively. The methodology of this study is described elsewhere[30]. In brief, the study population consisted of 155 TB/HIV co-infected and 465 non-co-infected HIV patients. All TB patients in the first two months of TB treatment were asked to participate in the study. For each TB/HIV co-infected patient, 3 non-co-infected HIV patients were also asked to participate. The latter were selected using a simple random sampling technique using the patients’ unique identification number in the HIV clinics. TB was diagnosed using national TB guidelines[31]. The non-co-infected patients were also screened for the presence of any signs and symptoms of TB. Non-co-infected HIV patients with a prior history of TB were excluded from the study. Patients who were less than 15 years old, had TB meningitis or another opportunistic infection, had a chronic illness like diabetes, cardiovascular disease or hypertension were excluded from the study.

Data collection procedures
CMD was assessed through face to face interviews by trained clinical nurses using the Kessler 10 scale[32] which consisted of 10 five-point Likert scale (0 = never, 1 = rarely, 2 = some of the time, 3 = most of the time, 4 = all of the time) questions. For the diagnosis of CMD, the Kessler 10 scale was validated in Ethiopia against a gold standard of psychiatrists’ diagnosis[28]. In a previous study, two psychiatrists used the validated Comprehensive Psychopathology Rating Scale (CPRS) to diagnose CMD[29]. The CPRS has 66 items; 40 symptoms based on the subjective report of the interviewee, 25 signs rated on the basis of observation during the interview and a global rating indicating presence of significant mental disorder. The presence of clearly defined symptoms or signs of mental disorder was rated on a 4-point scale (0-3). The definitions of each scale point were standardized as follows: 0 = not present; 1 = doubtful whether present, and not interfering with life; 2 = definitely present and of moderate severity; 3 = severe or incapacitating. The psychiatrists were asked to conduct a full psychiatric interview and then complete the CPRS ratings using all available information[28,29]. Caseness of CMD was determined on the basis of any of the combination of depressive, anxiety and/or somatic symptoms present at clinically significant level. At the cut-off point of 6/7, the Kessler 10 scale had a sensitivity and specificity of 84.2% and 77.8% respectively to diagnose CMD[28].

Perceived stigma was measured using a questionnaire adopted from Berger et al[33]. The instrument was highly reliable in a pre-test (Cronbach’s a = 0.93). The stigma scale consisted of four-point Likert scale (strongly disagree, disagree, agree, strongly agree) questions concerning perceived isolation, shame, guilt and disclosure of the HIV status. Item scores of the stigma questions were
summed to construct a single stigma variable. Participants were classified as having or not having perceived stigma using the mean of the stigma variable as cut-off point. Perceived general health of the participants (good, medium and poor) was assessed by asking the question ‘How would you rate your health?’

Medical charts were reviewed to collect clinical information and level of adherence to antiretroviral and TB treatment. Individuals who took more than 95% of the prescribed doses were labelled as adherent to antiretroviral therapy.

**Data Analysis**
Data were analyzed using SPSS version 16.0 software. Item scores of the Kessler scale were summed and individuals who scored above the cut-off point of 6/7 [28]were labelled as having CMD. The Pearson’s chi-square test was used to evaluate the association between exposure variables (TB/HIV co-infection, socio-demographic and clinical characteristics of the patients) and CMD. A stepwise logistic regression model was used to adjust for the effect of confounding variables. Variables significantly associated (P < 0.05) with CMD or TB/HIV co-infection in the Pearson’s chi-square test were included in the logistic regression model.

**Ethical consideration**
Ethical clearance was obtained from the Jimma University ethical review board. Written informed consent was obtained from the study participants. To ensure confidentiality, we used codes to analyze the data.

**Results**
All of the 465 non-co-infected HIV patients and 124 (80%) of the co-infected HIV patients participated in the study; 31 TB/HIV co-infected patients were lost to follow up before interview. Of the co-infected patients, smear negative, smear positive and extra pulmonary TB accounted for 61 (49.2%), 42 (33.9%), 21 (16.9%) respectively. From the total TB/HIV co-infected patients, 4 (3.2%) interrupted their TB treatment once.

The age distribution of TB/HIV co-infected and non-co-infected patients was similar. Fifty percent of the co-infected and 60.2% of the non-co-infected HIV patients were females (P < 0.05). Higher proportion of co-infected patients (43.5%) had no source of income compared to the non-co-infected patients (26.7%) [OR = 1.9, (95%CI: 1.0, 3.8)]. After adjusting for confounding variables, co-infected patients (57.5%) were more likely to have a lower CD4 lymphocyte count than non-co-infected patients (27.4%) [OR = 3.6; (95%CI: 2.1, 6.1)]. Before the diagnosis of TB, significantly larger proportions (78.0%) of the co-infected patients were in stage III of the WHO classification compared to the non-co-infected HIV patients (56.0%). All of the non-co-infected and 75.6% of the co-infected patients were taking antiretroviral treatment during the survey (Table-1).

The internal consistency of the Kessler 10 scale was high (Cronbach’s α = 0.93) and correlation between items in the Kessler scale ranged from 0.50 to 0.79.

A lower CD4 lymphocyte count, a WHO stage of III and IV, taking antiretroviral treatment, types of antiretroviral therapy, adherence to antiretroviral therapy, age, sex, literacy and marital status were not significantly associated with CMD in the bivariate analysis. On the other hand, occupation, source of income, TB/HIV co-infection, perceived stigma and perceived general health were significantly associated with CMD in the bivariate analysis and were therefore further evaluated in the multivariable model. Individuals who had no source of income [OR = 1.7, (95%CI: 1.1, 2.8)], and day laborers [OR = 2.4, (95%CI: 1.2, 5.1)] were more likely to have CMD as compared to individuals who had a source of income and government employees respectively. CMD was present in 63.7% of the TB/HIV co-infected patients and in 46.7% of the non-co-infected patients. TB/HIV co-infected patients were 1.7 times more likely to experience CMD than the non-co-infected patients [OR = 1.7, (95%CI: 1.1, 2.9)]. Patients who perceived stigma [OR = 2.2, 95%CI: 1.5, 3.2)] and who rate their general health as “poor” [OR = 10.0, 95%CI: 2.8, 35.1)] had significantly greater risk of CMD than individual who did not perceive stigma or who perceived their general health to be ‘good’ (Table-2).

**Discussion**
We assessed the occurrence of CMD in TB/HIV co-infected and non-co-infected patients using the Kessler scale (K10)[28]. Caseness of CMD was assessed using a cut-off point of 6/7 of the K10 which had a sensitivity and specificity of 84.2% and 77.8% against the psychiatrists’ assessment using CPRS. Several studies showed that the K10 had strong psychometric properties[32,34-36] and can discriminate between cases and non-cases reported in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[32,36]. In this study, 79 (64%) of the TB/HIV co-infected patients had CMD which is higher than the findings of Hanlon et al (33%) [28] and Tesfaye et al (40%)[28] among women in Ethiopia. The prevalence of depression among HIV seropositive women (19%) in the United States was also lower as compared to our study[6]. The differences in prevalence of mental disorders could be attributable to several factors including the population being studied, the study periods and the diagnostic tools[29]. TB/HIV co-infected patients were 1.7 times more likely to have CMD than non-co-infected HIV patients. However, we did not find a significant association between CD4 lymphocyte count and CMD, which is consistent with several previous stud-
Table 1: Socio-demographic and clinical characteristics of the study population in three hospitals of, Ethiopia, April, 2009

| Variables                  | TB/HIV coinfected patients | HIV patients | Crude OR (95%CI) | Adjusted OR (95%CI) |
|----------------------------|-----------------------------|--------------|------------------|---------------------|
|                            | Number (%)                  | Number (%)   |                  |                     |
| Age in Years               |                             |              |                  |                     |
| 15-24                      | 12(9.7)                     | 42(9.1)      | 1                | -                   |
| 25-34                      | 53(42.7)                    | 221(47.5)    | 0.8(0.4,1.7)     |                     |
| > = 35                     | 59(47.6)                    | 202(43.4)    | 1.0(0.5,2.1)     |                     |
| Sex                        |                             |              |                  |                     |
| Male                       | 62(50)                      | 185(39.8)    | 1.5(1.0,2.2)*    | 1.9(1.0,3.7)*       |
| Female                     | 62(50)                      | 280(60.2)    | 1                | 1                   |
| Educational status         |                             |              |                  |                     |
| Illiterate                 | 30(24.2)                    | 74(15.9)     | 1                | 1                   |
| Literate                   | 94(75.8)                    | 391(84.1)    | 0.6(0.4,0.9)*    | 0.8(0.4,1.6)        |
| Marital status             |                             |              |                  |                     |
| Single                     | 24(19.3)                    | 75(16.1)     | 1.3(0.7,2.5)     | -                   |
| Married                    | 42(33.9)                    | 191(41.1)    | 0.9(0.5,1.6)     |                     |
| Divorced                   | 33(26.6)                    | 93(20.0)     | 1.5(0.8,2.7)     |                     |
| Widowed                    | 25(20.2)                    | 106(22.8)    | 1                |                     |
| Occupation (n = 580)       |                             |              |                  |                     |
| Government worker          | 17(14.8)                    | 51(11.0)     | 1                | 1                   |
| Private employee           | 15(13.1)                    | 83(17.8)     | 0.5(0.2,1.1)     | 0.9(0.3,2.7)        |
| Merchant                   | 1(0.9)                      | 69(14.8)     | 0.4(0.2,1.0)     | 0.6(0.2,2.3)        |
| Farmer                     | 13(11.3)                    | 32(6.9)      | 1.2(0.5,2.8)     | 2.0(0.6,6.6)        |
| Housewives                 | 15(13.0)                    | 79(17.0)     | 0.6(0.3,1.3)     | 1.4(0.4,4.7)        |
| Day laborers               | 22(19.1)                    | 93(20.0)     | 0.7(0.4,1.5)     | 1.6(0.6,4.8)        |
| No Job                     | 32(27.8)                    | 58(12.5)     | 1.6(1.1,3.4)*    | 1.7(0.5,5.1)        |
| Have source of income      |                             |              |                  |                     |
| Yes                        | 70(56.5)                    | 341(73.3)    | 1                | 1                   |
| No                         | 54(43.5)                    | 124(26.7)    | 2.2(1.4,3.2)*    | 1.9(1.0,3.8)*       |
| WHO staging (n = 582)      |                             |              |                  |                     |
| Stage II                   | 13(10.6)                    | 136(29.6)    | 1                | 1                   |
| Stage III                  | 96(78.0)                    | 257(56.0)    | 1.6(1.3,1.9)*    | 2.3(1.1,4.6)*       |
| Stage IV                   | 14(11.4)                    | 66(14.4)     | 1.2(0.9,1.5)     | 1.3(0.5,3.5)        |
| CD4 lymphocyte count (n = 489) |                     |              |                  |                     |
| < 200                      | 46(57.5)                    | 112(27.4)    | 1.9(1.2,2.8)*    | 3.6(2.1,6.1)*       |
| > = 200                    | 34(42.5)                    | 297(72.6)    | 1                | 1                   |
| Antiretroviral therapy     |                             |              |                  |                     |
| Yes                        | 93(75.6)                    | 462(100)     | 0.02(0.001, 0.04) | 0.01(0.001, 0.003)* |
| No                         | 31(24.4)                    | 3            | 1                |                     |

*statistically significant (P < 0.05)
Table 2: Association of socio-demographic and clinical characteristics and CMD in three hospitals of Ethiopia

| Variables                  | Common Mental Disorders | Crude OR | Adjusted OR |
|----------------------------|-------------------------|----------|-------------|
|                            | Yes (%) | No (%) | (95%CI) | (95%CI) |
| Sex                        |          |        |         |         |
| Male                       | 132(53.4) | 115(46.6) | 1 | |
| Female                     | 164(48.0) | 178(52.0) | 0.8(0.5,1.1) | - |
| Literacy status            |          |        |         |         |
| Literate                   | 236(48.7) | 249(51.3) | 1 | - |
| Non-literate               | 60(57.7)  | 44(42.3)  | 1.4(0.9,2.2) | |
| Age                        |          |        |         |         |
| 15-24                      | 21(38.9)  | 33(61.1)  | 1 | - |
| 25-35                      | 145(52.9) | 129(47.1) | 1.7(0.9,3.2) | |
| > = 35                     | 130(49.8) | 131(50.2) | 1.5(0.8,2.8) | |
| Marital status             |          |        |         |         |
| Single                     | 48(48.5)  | 51(51.5)  | 0.6(0.4,1.0) | - |
| Married                    | 106(45.5) | 127(54.5) | 0.5(0.4,0.9) | |
| Divorced                   | 65(51.6)  | 61(48.4)  | 0.8(0.5,1.2) | |
| Widowed                    | 77(58.8)  | 54(41.2)  | 1 | |
| Occupation                 |          |        |         |         |
| Government employee        | 23(33.8)  | 45(66.2)  | 1 | 1 |
| Private employee           | 49(50.0)  | 49(50.0)  | 1.9(1.0,3.7) * | 2.2 (1.1,4.6)* |
| Merchant                   | 35(44.3)  | 44(55.7)  | 1.5(0.8,3.0) | 2.1 (1.0,4.4)* |
| Farmers                    | 24(53.3)  | 21(46.7)  | 2.2(1.0,4.8) | 1.8 (0.8,4.2) |
| Housewives                 | 40(42.6)  | 54(57.4)  | 1.4(0.7,2.7) | 1.2 (0.5,2.8) |
| Day Laborers               | 66(57.9)  | 48(42.1)  | 2.7(1.4,5.0) | 2.4 (1.2,5.1) |
| Jobless                    | 59(64.8)  | 32(35.2)  | 3.6(1.8,6.9) | 2.5 (1.1,5.6) |
| Have source of income      |          |        |         |         |
| Yes                        | 190(46.2) | 221(53.8) | 1 | 1 |
| No                         | 106(59.3) | 72(40.7)  | 1.6(1.2,2.4) | 1.7(1.1,2.8) |
| HIV/TB co-infection        |          |        |         |         |
| No                         | 217(46.7) | 248(53.3) | 1 | 1 |
| Yes                        | 79(63.7)  | 45(36.3)  | 2.0(1.3,3.0) | 1.7 (1.1,2.9) |
| WHO staging(n = 582)       |          |        |         |         |
| Stage II                   | 73(49)    | 76(51)    | 1 | |
| Stage III                  | 194(55.0) | 159(45.0) | 1.1(0.5,1.2) | - |
| Stage IV                   | 24(30)    | 56(70)    | 0.8(0.7,1.5) | |
| CD4 lymphocyte count(n = 489) |      |        |         |         |
| < 200                      | 74(46.8)  | 84(53.2)  | 1.2(0.8,1.7) | - |
| > = 200                    | 171(51.7) | 160(48.3) | 1 | |
| Taking antiretroviral therapy |          |        |         |         |
| Yes                        | 274(49.4) | 281(50.6) | 1 | - |
| No                         | 22(64.7)  | 12(35.3)  | 1.8(0.9,3.8) | |
| Adherence to antiretroviral therapy(ART) | | | | |
| Yes                        | 285(49.7) | 288(50.3) | 1 | - |
ies[37-39]. TB/HIV co-infected patients can be at higher risk of CMD as a result of stigma and discrimination by the society[5]. We also found out that perceived stigma was one of the independent predictors of CMD. People with perceived stigma may have a low self image and be socially isolated which may predispose them to CMD[40].

Poverty is known to be a major risk factor for mental health problems [3]. Many individuals in developing countries suffer from CMD as a result of stress caused by poverty[3,41]. In this study, daily labourers and jobless individuals, both economically disadvantaged groups, were at a higher risk of CMD. Use of the locally made alcohol called "Katikala", which is common among daily labourers in Ethiopia [42], can also predispose to CMD. In contrast with other studies[3,40,43], we did not observe a significant association between marital status, gender and CMD.

In our study, the perception of poor general health was strongly associated with CMD. However, there could be a bi-directional relationship between perceived general health and depression. Poor perceived general health could have resulted from the presence of CMD.

Although antiretroviral drugs, particularly Efavirenz, can cause CMD[4], our result did not show an association between this drug and CMD. Adherence to antiretroviral therapy has been reported to be affected by depression[4]. However, in our study we did not observe an association between adherence and CMD.

Some methodological limitations need to be noted in interpreting the findings of this study. First, the Kessler 10 scale is not 100% sensitive and specific and we might have misdiagnosed or missed some cases of CMD. Second, no detailed validation study was done for the stigma scale. Third, 20% of the TB/HIV co-infected patients were lost to follow-up which might introduce information bias. Important risk factors of CMD such as substance and alcohol use were not assessed.

### Table 2: Association of socio-demographic and clinical characteristics and CMD in three hospitals of Ethiopia (Continued)

|                     | No     | Yes    | OR (95% CI)  | P-Value |
|---------------------|--------|--------|--------------|---------|
| **ART regimen (n = 555)** |        |        |              |         |
| Nevirapine based    | 179(48.5) | 190(51.5) | 1            |         |
| Efavirenz based     | 95(51.1)   | 91(48.9)   | 1.10(0.7,1.5) |         |
| **Perceived Stigma** |        |        |              |         |
| No                  | 132(41.9)  | 183(58.1)  | 1            | 1       |
| Yes                 | 164(59.9)  | 110(40.1)  | 2.0(1.4,2.8)* | 2.2(1.5,3.2)* |
| **Perceived General Health** |        |        |              |         |
| Good                | 168(39.4)  | 258(60.6)  | 1            | 1       |
| Medium              | 102(76.1)  | 32(23.9)   | 4.8(3.1,7.6)* | 4.7 (2.9,7.6) * |
| Poor                | 26(89.7)   | 3(10.3)    | 13.3(9.4,44.5)* | 10.0 (2.8,35.1)* |

*P-Value < 0.05

### Conclusions

TB/HIV co-infected patients were at higher risk of developing CMD than non-co-infected patients. Occupation, perceived stigma and perceived general health were other risk factors for CMD. TB/HIV control programs should develop guidelines to screen and treat CMD among TB/ HIV co-infected patients. Screening programs should focus on individuals with no source of income, jobless people and day labourers. We recommend prospective cohort study to investigate the cause effect relationship of risk factors and CMD.

### Competing interests

The authors declare that they have no competing interests.

### Authors’ contributions

AD conceived and designed the study, analyzed the data and drafted the manuscript. MT participated in the design, conception and reviewed the article. YH, GA and LA were involved in report writing and reviewing. LD and RC were involved in analysis and critically reviewed the article. All authors read and approved the final manuscript.

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### Author Details

1. Department of Epidemiology, Jimma University, Jimma, Ethiopia
2. Department of Epidemiology and Social Sciences, Antwerp University, Antwerp, Belgium
3. Department of Psychiatry, Jimma University, Jimma, Ethiopia
4. Department of Health Service Management, Jimma University, Jimma, Ethiopia
5. Institute of Tropical Medicine, Antwerp, Belgium
6. Department of Medical Laboratory Sciences and Pathology, Jimma University, Jimma, Ethiopia
7. Department of Physiology and Biometrics, Ghent University, Ghent, Belgium

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