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Evaluation of collaborative tuberculosis and human immunodeficiency virus activities in Phnom Penh, Cambodia

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SUMMARY

SETTING: Phnom Penh, Cambodia.

OBJECTIVES: 1) To monitor the number of tuberculosis (TB) patients undergoing human immunodeficiency (HIV) testing during TB treatment and trends of referral of TB-HIV patients to HIV services following the appointment of TB-HIV coordinators in TB wards, and 2) to investigate factors that influence undesirable TB treatment outcomes.

DESIGN: Retrospective descriptive study based on a review of patient records and interviews with programme staff.

RESULTS: Eighty-six per cent of newly registered TB patients underwent HIV testing. Most of the TB-HIV patients were referred to HIV services. Using logistic regression analysis, the risk of an undesirable treatment outcome in extra-pulmonary TB was significantly lower than in smear-positive pulmonary TB. Interviews revealed that patients in poor clinical condition at the start of TB treatment or who faced social problems, such as homelessness or foreign nationality, were at considerable risk for undesirable TB treatment outcomes.

CONCLUSION: The appointment of TB-HIV coordinators to TB wards resulted in better HIV testing uptake and referral to HIV care and treatment services. To save TB-HIV patients' lives, it is important to continue this kind of study over a longer term to monitor these activities and to identify high-risk patients.

KEY WORDS: TB-HIV; human immunodeficiency virus; tuberculosis; Cambodia

IT IS ESTIMATED that one third of people living with the human immunodeficiency virus (HIV) worldwide are co-infected with tuberculosis (TB).[1] To reduce the burden of HIV-related TB, the World Health Organization (WHO) developed an expanded strategy, built on the existing DOTS strategy and comprehensive HIV/AIDS (acquired immunodeficiency syndrome) prevention and care.[2] However, examples of the actual implementation of the TB-HIV programmes in the field[3–10] are limited, and it is therefore pertinent that we share our experience of implementing TB-HIV collaborative activities in Cambodia.

In 2006, TB-HIV coordinators were appointed to facilitate HIV testing in TB wards and referral to HIV services in Phnom Penh, Cambodia. We monitored and evaluated our newly implemented TB-HIV activities by analysing TB-HIV data obtained from TB register books and interview surveys.

The study objectives were to investigate 1) whether the number of TB patients undergoing HIV counselling and testing increased after the implementation of the new programme; 2) whether TB patients diagnosed as HIV-positive were certain to receive HIV services such as cotrimoxazole preventive treatment (CPT), home-based care and/or antiretroviral treatment (ART); and 3) whether TB treatment for patients with both HIV and TB disease (TB-HIV patients) was successful and if not, the reasons for failure.

METHODS

Study design

This was a retrospective descriptive study based on review of patient records and interviews with programme staff.

Study setting

Cambodia has a high burden of both TB and HIV. Under the National TB Control Programme (NTP), one of the country's pilot TB-HIV collaborative programmes has been implemented in Phnom Penh, which has the country's highest prevalence of HIV among TB patients (26.0% in 2005 and 21.7% in 2007).[11] The programme was started in 2005 to improve access to HIV counselling and testing (HCT) services for TB patients, whereby HCT was provided

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by mobile counsellors at the operational district referral hospitals, a service known as 'mobile counsellor activity'. The number of TB patients who made use of this service was reported on a monthly basis by the operational district TB medical supervisors.

Although TB patients were provided with funds to cover the transport costs from their nearest health centre to the operational district referral hospital where HCT was being offered, few patients made use of this service in 2005. The programme strategy was therefore changed in 2006: four TB ward staff members, one from each of the operational district referral hospitals, were appointed as TB-HIV coordinators. Their role was to conduct HIV testing and offer TB patients counselling services in the TB wards—both in-patient and out-patient—of each health facility, while supervising all TB-HIV activities carried out in the operational district for which they were responsible. Furthermore, to improve communication among stakeholders and establish the flow of referral between TB and HIV services, regular TB-HIV stakeholder meetings were started whereby both TB and HIV staff met to discuss problems.

Study population

The study population consisted of TB patients registered between 2006 and 2008 at the 21 health centres and referral hospitals in Phnom Penh.

Data collection

Data were obtained from TB registers and treatment cards between 2006 and 2008. Annual data were collected when all TB treatment had been completed. Data collected included sex, age, TB type, treatment outcome, whether or not TB patients underwent HCT during TB treatment, and HIV test results. For confirmed TB-HIV patients, we also collected data on the first diagnosis (TB or HIV), administration of CPT during TB treatment, receipt of services from the home-based care team or in the opportunistic infection (OI)/ART ward while undergoing TB treatment, and administration of ART during TB treatment.

Interviews conducted by TB staff at each health centre inquired about TB-HIV patients who had undergone TB treatment and had either defaulted or died in 2007 and 2008 (there were no cases of treatment failure). We decided to stop inquiring about TB-HIV patients treated in 2006; as a long time had passed between treatment and the interviews in 2009, TB staff members did not remember the patients well.

Analysis and statistics

The number of TB patients (excluding those already confirmed to be HIV-positive) who underwent HCT during TB treatment was counted annually and compared with the data collected during the mobile counsellor activity in 2005. A dedicated database of TB-HIV patients was created using SPSS Version

Table 1 HIV screening for registered TB patients (excluding patients already diagnosed HIV-positive at the time of TB diagnosis) and referral of TB-HIV co-infected patients to HIV services, by calendar year*

	2006		2007		2008		Total	
	Registered TB patients, excluding HIV-positive patients at time of TB diagnosis *n/N* (%)	Patients already diagnosed HIV-positive at time of TB diagnosis† *n/N* (%)	Registered TB patients, excluding HIV-positive patients at time of TB diagnosis *n/N* (%)	Patients already diagnosed HIV-positive at time of TB diagnosis† *n/N* (%)	Registered TB patients, excluding HIV-positive patients at time of TB diagnosis *n/N* (%)	Patients already diagnosed HIV-positive at time of TB diagnosis† *n/N* (%)	Registered TB patients, excluding HIV-positive patients at time of TB diagnosis *n/N* (%)	Patients already diagnosed HIV positive at time of TB diagnosis† *n/N* (%)
TB patients registered	1443		1550		1375		4368	
	1254/1443 (87)	189/1443 (13)	1387/1550 (90)	163/1550 (11)	1231/1375 (90)	144/1375 (11)	3872/4368 (89)	496/4368 (11)
HIV testing during TB treatment	894/1254 (71)	—	1353/1387 (98)	—	1095/1231 (89)	—	3342/3872 (86)	—
HIV-positive patients among registered TB patients, excluding those already diagnosed HIV-positive at time of TB diagnosis who underwent HIV testing	50/894(6)	—	52/1353 (4)	—	34/1095 (3)	—	136/3342 (4)	—
HIV-positive patients who received CPT	49/50 (98)	121/189 (64)†	48/52 (92)	163/163 (100)	32/34 (94)	129/144 (90)	129/136 (95)	413/496 (83)
HIV-positive patients who received OI/ART or home-based care service	45/50 (90)	45/189 (24)†	41/52 (79)	152/163 (93)	29/34 (85)	133/144 (92)	115/136 (85)	330/496 (67)
HIV-positive patients who received ART	21/50 (42)	21/189 (11)†	24/52 (46)	111/163 (68)	11/34 (32)	74/144 (51)	56/136 (41)	206/496 (42)

* As percentages are rounded off to the closest whole number, total percentage is not always 100.
† CPT, OI/ART or home-based care were not adequately recorded for patients already known to be HIV-positive at the time of TB diagnosis in 2006: 67 (35%) cases of CPT, 79 (42%) cases of OI/ART or home-based care, and 102 (54%) cases of ART were not recorded.
HIV = human immunodeficiency virus; TB = tuberculosis; CPT = cotrimoxazole preventive treatment; OI = opportunistic infection; ART = antiretroviral treatment.

17.0 (Statistical Package for Social Sciences, Chicago, IL, USA).

TB treatment outcomes categorised as undesirable were defaulted, failure or died. Two cases with missing data on treatment outcome were excluded, and we did not consider transferred out cases as undesirable, as these patients were referred to another health facility for further treatment. To investigate the presence or absence of factors related to undesirable treatment outcomes among TB-HIV patients, a multivariate logistic regression analysis was conducted.

Data obtained from interviews were qualitatively analysed by the Kawakita Jiro method (affinity diagram),[12] whereby each sentence from the interview was recorded and grouped by content with a specific code.

Study approval

The study protocol was approved by the Ethics Committee of the Research Institute of Tuberculosis, Tokyo, Japan. Approval was also obtained from the Cambodian NTP. As the NTP determined the study to be part of routine programme monitoring, review by an ethics committee in Cambodia was deemed unnecessary.

RESULTS

HCT during TB treatment

Of the total 4368 TB patients reported, 496 (11%) were known to be HIV-positive at the time of TB diagnosis, whereas 3872 (89%) did not know their HIV status. Among the newly registered TB patients with unknown HIV status, 3342 (86%) underwent HCT during anti-tuberculosis treatment (Table 1).

In 2005, in all four operational districts an average of 10 (range 0–21) TB patients per month attended HCT provided by the mobile counsellor. This number increased in 2006 to an average of 66 (range 52–83) TB patients per month attending the service provided by the TB-HIV coordinators.

Referral of TB-HIV patients to HIV services

A total of 632 TB-HIV patients were registered with the TB wards from 2006 to 2008: 496 (78%) were TB patients already known to be HIV-positive at the time of TB diagnosis, and the remaining 136 (22%) were TB patients who tested HIV-positive after TB diagnosis. Of the 632 TB-HIV patients, 291 (46%) were women and 341 (54%) were men (age range 5–78 years, mean 35 years; Table 1).

Among newly registered TB patients with unknown HIV status who subsequently underwent HCT during TB treatment, 136 (4%) were found to be HIV-positive, of whom 129 (95%) received CPT, 115 (85%) received services offered by home-based care teams or an OI/ART ward and 56 (41%) received ART.

Among the 496 patients already diagnosed as HIV-positive at the time of TB diagnosis, 413 (83%) received CPT, 330 (67%) received services from a home-based care team or an OI/ART ward, and 206 (42%) received ART during TB treatment. However, information concerning HIV services received was inadequately recorded, particularly in 2006.

TB treatment outcomes and risk factors for undesirable treatment outcomes

Regardless of type of TB or of first diagnosis (TB or HIV), TB treatment was successful in more than 80% of the TB-HIV patients (Table 2). Undesirable outcomes were not significantly different in TB-HIV patients when analysed using logistic regression for age, sex, first diagnosis (TB or HIV), and referral for HIV services (CPT, home-based care or OI/ART ward and/or ART). However, using logistic regression analysis, the risk of an undesirable treatment outcome for extra-pulmonary TB was significantly lower than for smear-positive pulmonary TB (odds ratio 0.23, 95% confidence interval 0.09–0.57, $P < 0.05$).

Of 393 TB-HIV patients registered in 2007 and 2008, 18 (5%) died and 16 (4%) defaulted from TB treatment. Some common characteristics were found

Table 2 Type of TB and treatment outcome of TB-HIV patients*

	TB patients who tested HIV-positive after TB diagnosis				TB patients already diagnosed HIV-positive at time of TB diagnosis†			
	Sputum smear+ pulmonary TB *n* (%)	Sputum smear− pulmonary TB *n* (%)	Extra-pulmonary TB *n* (%)	Total *n* (%)	Sputum smear+ pulmonary TB *n* (%)	Sputum smear− pulmonary TB *n* (%)	Extra-pulmonary TB *n* (%)	Total *n* (%)
Number evaluated	51 (100)	40 (100)	45 (100)	136 (100)	121 (100)	143 (100)	230 (100)	494 (100)
Treatment outcome								
Successful	43 (84)	35 (88)	40 (87)	118 (89)	103 (85)	127 (89)	218 (95)	448 (91)
Failure	0	0	0	0	1 (1)	1 (1)	2 (1)	4 (1)
Defaulted	4 (8)	0	3 (7)	7 (5)	3 (3)	5 (4)	2 (1)	10 (2)
Transferred out	1 (2)	4 (10)	2 (4)	7 (5)	2 (2)	1 (1)	4 (2)	7 (1)
Died	3 (6)	1 (3)	0	4 (3)	12 (10)	9 (6)	4 (2)	25 (5)

*As percentages are rounded off to the closest whole number, total percentage is not always 100.
†Treatment outcomes of 2 TB patients already known to be HIV-positive at the time of TB diagnosis were unknown in 2006 (no record).
TB = tuberculosis; HIV = human immunodeficiency virus; + = positive; − = negative.

among these TB-HIV patients during their interviews with the staff. The first involved clinical problems, such as poor health before attending the TB ward, which might have caused treatment delay. The second involved social issues, such as homelessness, foreign nationality or fear of disclosure of HIV status, leading to refusal of home-based care, or low educational level and mental disorders.

DISCUSSION

The number of TB patients who underwent HCT during TB treatment increased after the TB-HIV coordinator activity was implemented. Moreover, most of the TB patients found to be HIV-positive were referred to the HIV services and received CPT, which was in no way inferior to the referral rate for patients with known HIV-positive status at the time of TB diagnosis. Approximately 40% of the TB-HIV patients received ART, and TB treatment was successful in around 80% of the TB-HIV patients in this study. Logistic regression analysis of the survey results found that only the risk of an undesirable treatment outcome for extra-pulmonary TB was significantly lower than for smear-positive pulmonary TB; no other obvious risk factors were observed for those patients who died or defaulted. However, some risk factors emerged from data from interviews. Patients who died or defaulted were often clinically ill before initiating TB treatment, and homeless individuals, foreigners who did not understand the Cambodian language and patients who refused to sign up for home-based care may constitute groups at higher risk for death or default.

The WHO and the Joint United Nations Programme on HIV/AIDS recommend a provider-initiated HCT approach[13] and that HIV testing be made available to TB patients on site to increase access and uptake.[14] In accordance with these recommendations, HIV testing administered by TB staff in TB wards was implemented. Before the establishment of our project's 'TB-HIV coordinator activity', TB patients needed to attend voluntary HCT centres outside the health facilities where they were receiving TB treatment. At that time, few TB patients attended HIV testing even when transportation costs were covered. However, as shown in Table 1, after HCT was made available at the same site where TB treatment was given, around 90% of patients underwent HIV testing. It is reported that the stigma associated with HIV/AIDS may be one reason for refusing HIV testing.[15] However, this may not always be the main barrier; indeed, the distance TB patients must travel to HCT centres seems to be a greater obstacle to undergoing testing.[16–18] To identify TB patients who are HIV-positive and refer them to HIV services as soon as possible, it is thus important for HCT to be available on the TB ward.

Although most of the TB patients who tested positive for HIV after TB diagnosis were referred to HIV services and received CPT, only 30–40% of these received ART, a lower proportion than among those TB patients who were already known to be HIV-positive at the time of TB diagnosis in 2007 and 2008. However, we cannot comment on the appropriateness of this number, as the initiation of ART in TB-HIV patients depended on CD4 cell count at that time, and these data were not available in the TB registers. According to the new WHO guidelines, ART should be initiated in all HIV-infected individuals with active TB.[19] The CAMELIA (Cambodian Early versus Late Introduction of Antiretroviral Drugs) clinical trial in Cambodia reported that the introduction of ART 2 weeks after the initiation of TB treatment significantly reduced mortality in TB-HIV co-infected patients.[20] On the basis of these latest recommendations and findings, guidelines on the initiation of ART for TB-HIV patients were changed in Cambodia in 2010, and all TB-HIV patients are now eligible for ART.[21] We now need to monitor whether the administration of ART is improving under the new recommendations.

It should also be noted that a greater proportion of patients who were already diagnosed as HIV-positive at TB diagnosis were registered among TB-HIV patients. Appropriate commencement of ART and the implementation of isoniazid preventive treatment (IPT) are needed to prevent HIV-positive patients from developing TB. In Cambodia, IPT has been implemented only in limited areas.[22] It is necessary therefore to extend IPT to other areas to reduce the number of TB-HIV patients; standard operating procedures for this have already been developed.[23]

Around 80% of patients in the present study had a successful TB treatment outcome. However, compared to the treatment outcomes for all new patients with smear-positive TB in Phnom Penh (1% died and 2% defaulted in 2007[24]), a higher proportion of TB-HIV patients defaulted or died. Common risk factors for mortality among TB-HIV co-infected patients include a lack of access to CPT or ART, extra-pulmonary TB and a low CD4 count.[25–30] Logistic regression analysis of the survey results from our study found that only the risk of an undesirable treatment outcome for extra-pulmonary TB was significantly lower than for smear-positive pulmonary TB. This result contrasts with data from another study.[28] This discrepancy might be due to the limitations of diagnostic methods for extra-pulmonary TB in Cambodia, such as inaccurate diagnoses or the detection of only mild cases of extra-pulmonary TB.

Our logistic analysis study has one limitation in that the sample size may not have been sufficiently large to determine associations. The results of interviews suggest the existence of more risk factors for undesirable treatment outcomes. Consequently, it is important to continue this kind of study over a longer period of time to more precisely identify the actual risk factors. If possible, this kind of study should be included as part of routine activities.

CONCLUSION

After implementing HIV testing in TB wards by TB-HIV coordinators and holding regular stakeholder meetings, the number of TB patients undergoing HIV testing increased and most TB-HIV patients received HIV services. The results of the logistic regression analysis showed that only the risk of an undesirable treatment outcome for extra-pulmonary TB was significantly lower than for smear-positive pulmonary TB. From patient interviews, high-risk groups seem to be patients who were clinically ill before the initiation of TB treatment and those who were socially vulnerable. To save the lives of a greater number of TB-HIV co-infected patients, similar studies aimed at determining the actual risk factors for undesirable TB treatment outcome are required.

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RÉSUMÉ

CONTEXTE : Phnom Penh, Cambodge.
OBJECTIFS : 1) Suivre le nombre de patients tuberculeux (TB) subissant un test pour le virus de l'immunodéficience humaine (VIH) au cours du traitement de la TB ainsi que les tendances au transfert des patients TB-VIH vers les services VIH après l'engagement de coordinateurs TB-VIH pour travailler dans les salles de TB, et 2) investiguer les facteurs influençant les résultats défavorables du traitement TB.
SCHÉMA : Etude descriptive rétrospective se basant sur la révision de dossiers des patients et sur des interviews avec le personnel du programme.
RÉSULTATS : Les tests VIH ont été pratiqués chez 86% des patients récemment enregistrés comme TB. La plupart des patients TB-VIH ont été référés vers les services VIH. Lors de l'analyse par régression logistique, le risque de résultats indésirables du traitement dans la TB extrapulmonaire est le seul qui soit significativement moindre que dans la TB pulmonaire à bacilloscopie positive. Les interviews ont révélé que le risque d'un résultat indésirable du traitement TB était considérablement plus élevé chez les patients dont l'état clinique était médiocre au début du traitement TB et chez ceux qui devaient faire face à des problèmes sociaux, comme le fait d'être sans abri ou d'être un sujet étranger.
CONCLUSION : L'engagement de coordinateurs TB-VIH pour travailler dans les salles TB a entraîné une meilleure prise en charge des tests VIH et un meilleur transfert vers les services de soins et de traitement VIH. Si l'on veut sauver les patients TB-VIH, il est important de poursuivre ce type d'étude à plus long terme afin de surveiller ces activités et d'identifier les patients à haut risque.

RESUMEN

MARCO DE REFERENCIA: La ciudad de Phnom Penh en Camboya.
OBJETIVOS: 1) Vigilar el número de pacientes tuberculosos en quienes se practica la prueba diagnóstica del virus de la inmunodeficiencia humana (VIH) durante el tratamiento antituberculoso y la tendencia de las remisiones de los pacientes que presentan una coinfección a los centros de atención del VIH después de haber asignado coordinadores de la atención de la tuberculosis (TB) y el VIH a trabajar en los servicios de TB, e 2) investigar además los factores pronósticos de un desenlace indeseable del tratamiento de la TB.
MÉTODO: Fue este un estudio descriptivo retrospectivo basado en el análisis de los expedientes clínicos de los pacientes y en entrevistas con el personal del programa.
RESULTADOS: Se practicó la prueba diagnóstica del VIH a 86% de los pacientes recién notificados al registro de TB. La mayoría de los pacientes TB-VIH fue remitida a los servicios VIH. Según el análisis de regresión logística, solo el riesgo de un desenlace terapéutico indeseable en los casos de TB extrapulmonar fue significativamente inferior al riesgo de los casos de TB pulmonar con baciloscopia positiva. Las entrevistas revelaron que los en condiciones clínicas deficientes al comienzo del tratamiento, los que afrontan problemas sociales como la falta de domicilio o los pacientes de origen extranjero se encontraban en alto riesgo de presentar un desenlace indeseable del tratamiento antituberculoso.
CONCLUSIÓN: La asignación de los coordinadores de la atención de la TB-VIH en los servicios de TB conduce a una mayor aceptación de la prueba diagnóstica del VIH y a un mayor índice de remisiones a los centros de atención y tratamiento del VIH. Con el propósito de salvar a los pacientes TB-VIH es importante continuar este tipo de estudios durante periodos más prolongados, a fin de supervisar estas actividades y detectar a los pacientes de alto riesgo.