Epidemiology and control of tuberculosis and sexually transmitted infections in Thyolo District, Malawi

Zachariah, R.

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SUMMARY

This thesis describes operational research conducted in Thyolo district in rural southern Malawi. The studies were carried out within the framework of a district HIV/AIDS and sexually transmitted infection control program of an Non Governmental Organization (Medecins sans Frontieres-Luxembourg). All the studies were all conducted during the tenure of the author in Malawi.

Chapter 1 gives an overview of HIV/AIDS, Tuberculosis and sexually transmitted infections in terms of; burden of disease, interactions between TB and HIV and between sexually transmitted infections and HIV, the consequences of these diseases, the framework for control and some of the main operational research questions linked to these diseases in sub-Saharan Africa.

This chapter also provides background information on Malawi and the extent of the TB-HIV and sexually transmitted infection epidemics. This is followed by a short description of Thyolo district, which was the main site of the studies included in this thesis.

Chapter 2 describes the feasibility and effectiveness of offering voluntary counseling, HIV testing and adjunctive cotrimoxazole prophylaxis in reducing mortality among TB patients registered under routine programme conditions in the rural district of Thyolo. The study was designed as a “before” and “after” cohort study using historical controls. A total of 1986 patients was registered in the study; 1061 in the intervention group (which received voluntary counseling, HIV testing and cotrimoxazole) and 925 in the historical control cohort (which received no such interventions). In the intervention group, 1019(96%) patients were pre-test counselled, 964 (91%) underwent HIV testing and 938(88%) were post-test counselled. The overall HIV-seroprevalence rate was 77%. A total of 693 patients were given cotrimoxazole of whom 14(2%) manifested minor dermatological reactions. The adjusted relative risk of death in the intervention group compared with the control group was 0.81(p<0.001). The number needed to treat with a package of voluntary counseling, HIV testing and adjunctive cotrimoxazole to prevent one death during anti-TB treatment was 12.5. This study shows that voluntary counseling, HIV testing and adjunctive cotrimoxazole is feasible, safe and reduces mortality rates in TB patients under routine programme conditions.

Chapter 3 describes compliance to cotrimoxazole prophylaxis in HIV infected TB patients during the continuation phase of anti-TB treatment. The study also describes the sensitivity, specificity and positive predictive values of verbal verification and pill counts as methods of checking compliance.

Cotrimoxazole compliance was assessed in a cohort of TB patients who were attending follow-up centres during the continuation phase of anti-TB treatment between months 4 to 6. Verbal verification of drug intake, physical verification of pill count balance, and urine trimethoprim detection by gas chromatography and mass spectrometry were used for assessing compliance.

Using urine trimethoprim detection as the gold standard for compliance, trimethoprim was detected in 82 (94%) of 87 patients in the cohort. “Verbal verification” of cotrimoxazole intake and objective “pill count balances” showed high sensitivity and positive predictive values compared with the gold standard of urine trimethoprim detection.

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The study shows that compliance to cotrimoxazole as an adjunct to anti-TB treatment in HIV-infected TB patients was good, and can be assessed simply and practically by verbal verification and pill counts.

Chapter 4 is a cross-sectional study that verified compliance to cotrimoxazole among HIV infected individuals who completed anti-TB treatment 3-6 months earlier. The study determined the proportion of individuals who continued with cotrimoxazole prophylaxis for the prevention of opportunistic infections, and the reasons for continuing or stopping prophylaxis.

76(93%) of 82 HIV infected individuals who were alive at the time of interview were continuing with cotrimoxazole and wished to do so indefinitely. The most common reason for continuing the drug was to prevent illness associated with HIV while the most common reason for stopping was long distances to the health facility. 96% of patients received cotrimoxazole free of charge from a health center. Of those who wished to continue indefinitely, the majority(63%) could not afford to pay for the drug.

The study shows that in the rural setting of study, the great majority of HIV-infected individuals continued with cotrimoxazole after completing anti-TB treatment and that making the drug available and providing it free of charge is essential if it is to remain accessible for longer term prevention of HIV related opportunistic infections.

Chapter 5 presents the findings of a series of cross-sectional studies that were carried out to determine whether faecal *Escherichia coli* (E.coli) resistance to co-trimoxazole in TB patients changed with time and whether the resistance pattern was different in HIV positive TB patients who were taking co-trimoxazole prophylaxis.

Co-trimoxazole resistance among *E.coli* isolates in TB patients at the time of registration was 60% in 1999 and 77% in 2001 (p<0.01). Resistance was 89% among HIV infected TB patients (receiving co-trimoxazole), while in HIV negative patients (receiving anti-TB therapy alone) it was 62% (p<0.001).

The study shows a significant increase of *E.coli* resistance to co-trimoxazole in TB patients which is particularly prominent in HIV infected patients on co-trimoxazole prophylaxis. Since a high degree of plasmid mediated transfer of resistance exists between E.coli and the Salmonella species, these findings could herald limitations on the short and long term benefits to be anticipated from the use of co-trimoxazole prophylaxis in preventing *non typhoid salmonella* bacteraemia and enteritis in HIV infected TB patients in Malawi.

Chapter 6 is a study conducted in new patients registered with TB to determine the prevalence of malnutrition on admission and the association between malnutrition and early mortality (defined as death within the first four weeks of treatment).

There were 1181 patients with TB, (576 men and 605 women), whose overall HIV-infection rate was 80%. 673 (57%) TB patients were malnourished on admission (body mass index < 18.5 kg/m²). There were 259 (22%) patients with mild malnutrition (body mass index 17.0-18.4 kg/m²), 168 (14%) with moderate malnutrition (body mass index 16.0-16.9 kg/m²) and 246 (21%) with severe malnutrition (body mass index < 15.9 kg/m²).

95 (8%) patients died during the first four weeks. Significant risk factors for early mortality included increasing degrees of malnutrition, age > 35 years, and being HIV-positive. In all patients (n-1181), 10.9% of 414 patients with moderate to severe malnutrition died in the first
four weeks compared with 6.5% of 767 patients with normal to mild malnutrition (OR 1.8, 95% CI; 1.1-2.7).
The study shows that in patients with TB, a body mass index < 17.0 kg/m² is associated with an increased risk of early death. This group of patients should receive nutritional rehabilitation and should be prioritised for other care related interventions.

Chapter 7 presents the findings of a study conducted among men presenting with urethral discharge to Thyolo district hospital. The study looked at health seeking and sexual behavior, the prevalence of Neisseria gonorrhoeae (N.gonorrhoeae) and Chlamydia trachomatis (C.trachomatis), and antibiotic susceptibility
Out of a total of 114 patients, 61% of reported having taken some form of medication before coming to the sexually transmitted infection clinic. The most frequent alternative source of care was the traditional healer. 68 (60%) patients reported sex during the symptomatic period the majority (84%) not using condoms. Using ligase chain reaction on urine, N.gonorrhoeae was detected in 91 (80%) and C.trachomatis in 2 (2%) of urine specimens. 45 of 47 N.gonorrhoeae isolates produced penicillinase, 89% showing multi-anti-microbial resistance.
This study emphasis the need to integrate alternative care providers and particularly traditional healers in control activities, and to encourage their role in promoting safer sexual behaviour.
In patients presenting with urethral discharge in our rural setting, C.trachomatis was not found to be a major pathogen. The high resistance of N.gonorrhoeae reiterates the importance of anti-microbial susceptibility surveillance of in order to prevent treatment failures and control the spread of resistant strains in Malawi.

Chapter 8 describes a study conducted among commercial sex workers. The study was carried out in order to; determine the prevalence and pattern of sexually transmitted infections, describe sexual behaviour among those who have a sexually transmitted infection and identify socio-demographic and behavioural risk factors associated with “no condom use”.
Consecutive new commercial sex workers presenting to a mobile clinic underwent detailed examination for sexually transmitted infections and those found with an infection were interviewed after obtaining informed consent.
There were 1817 female commercial sex workers of whom 448 (25%) were diagnosed with a sexually transmitted infection. Of these, there were 237 (53%) cases of abnormal vaginal discharge with or without dysuria, 116(26%) cases of pelvic inflammatory disease and 94 (21%) cases of genital ulcer disease.
The great majority (87%) engaged in sex while symptomatic with 17% engaging in unprotected sex. Having unprotected sex was associated with being married, being involved with commercial sex outside a known rest-house or bar, having an ulcerative genital disease, having less than 2 clients per day, indulgence in alcohol and having had no prior medication for sexually transmitted infections.
The high levels of sexually transmitted infections particularly genital ulcer disease and unprotected sex among commercial sex workers underlines the importance of targeted interventions for them and their clients. The findings could help to re-orient or even develop strategies on promoting safer sex in high-risk populations.

Chapter 9 presents findings on the prevalence, incidence and patterns of sexually transmitted infections among male inmates of two prisons in Thyolo. Out of a total of 4229 inmates that were studied during a 2 year period, 178(4.2%) were diagnosed with a sexually transmitted
infection. This included 83(46%) inmates with urethral discharge, 60(34%) with genital ulcer disease and 35(20%) inmates with epididymo-orchitis. 50(28%) infections were considered incident cases acquired within the prisons (Incidence risk=12 cases/1000 inmates/year). Genital ulcer disease was the most common infection in this group comprising 52% of all sexually transmitted infections.

This study shows that a considerable proportion of sexually transmitted infections among inmates are acquired within prison walls. In a setting of same sex inmates, this suggests inter-prisoner same-sex sexual activity. Prisons in Malawi do not allow access to condoms as it is felt that this would encourage homosexuality which is illegal. The findings have implications on HIV transmission and might help in developing more rational policies on the control of sexually transmitted infections and condom access within Malawi prisons.

Chapter 10 presents data on HIV prevalence in various blood donor population and socio-demographic risk factors associated with prevalent HIV. The study also assesses the feasibility of offering routine voluntary counselling services to blood donors.

Crude HIV prevalence was found to be 22% while the age standardized prevalence (>15 years) was 17%. Prevalence was lowest among rural donors, students and in males of the age group 15-19. There is a highly significant positive association of HIV prevalence with increasing urbanization. Significant risk factors associated with prevalence for both male and female donors included having a business-related occupation, living in a semi-urban or urban area, and being in the age group 25-29 for females and 30-34 for males. All blood donors were pre-test counselled and 90% were post-test counselled in 2000.

HIV prevalence in blood donors is alarmingly high, raising important concerns on the potential dangers of HIV transmission through blood transfusions. Limiting blood transfusions, use of a highly sensitive screening test, and pre-donation selection of donors is important. The experience also shows that it is feasible to offer pre and post test counselling services for blood donors as an entry point for early diagnosis of asymptomatic HIV infection and broader preventive and care strategies.

Chapter 11, which is the final chapter of this thesis, covers a general discussion on some of the principal findings, implications of these studies on policy and practice in Malawi, and areas for further research.