Tuberculosis burden in Bangladesh: epidemiological estimates and people’s perspectives
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Summary

Tuberculosis (TB) is one of the major causes of sickness and deaths among adults worldwide. The disease caused millions of sufferings and deaths in the last two decades, and a global emergency was declared by the World Health Organization (WHO) in 1993 to control its expansion. Directly Observed Treatment, Short course (DOTS) is a package of curative and preventive strategies advocated by WHO to diagnose and treat TB cases in an effort to attain TB control globally. Bangladesh, one of the 22 high TB burden countries in the world, adopted and started implementing DOTS since 1993. The true burden of disease in the country is not exactly known. National notification data have the limitation of being vulnerable to underreporting of TB cases, while reliable data from national surveys are absent in the country. In this thesis, we presented studies on the TB burden in Bangladesh in terms of prevalence of the TB disease, and the prevalence of the TB infection. In addition we described the social aspects of TB, care seeking behaviour of TB cases and persons with symptoms suggestive for TB, knowledge on TB-related issues in the community, and the quality of field level sputum collection procedures in the prevalence survey.

The burden of disease

In chapter 2 we reported the national TB disease prevalence among adults (15 years and above). This prevalence estimate was obtained through a nationwide cross sectional household survey which was carried out during 2007-2009. The aim of the survey was to determine the prevalence of sputum smear-positive TB in Bangladesh. We collected two sputum samples from each of the 52,098 participants who consented to participate. Sputum samples were examined at field laboratories with fluorescence microscopy. A total of 33 smear-positive TB cases were diagnosed among the person examined and were put under treatment. The overall prevalence in the population aged 15 years and above after adjustment for study design and attrition was 79.4 per 100,000 (95% CI 47.1-133.8). The prevalence was higher in males (121.7 per 100,000 [95% CI 69.6-212.8]) compared to females (40.3 per 100,000 [95% CI 13.4-121.4]), in rural areas (86.0 per 100,000 [95% CI 47.9-154.3]) compared to urban areas (51.1 per 100,000 [95% CI 27.7-94.1]) and among person with a lower level of education. The survey did not include persons below 15 years, and did not identify sputum smear-negative or extra pulmonary TB cases.

In chapter 3 we reported the prevalence of tuberculous infection and its associated Annual Risk of Tuberculous Infection (ARTI). The estimate was obtained by including a tuberculin survey in the national TB prevalence survey. The prevalence of TB infection is traditionally measured among children (5-14 years) with the assumption that it is reflecting the magnitude of recent transmission. The risk of
infection in the general population is deducted from this prevalence of infection in children and expressed as ARTI. The tuberculin survey was the first one after the only other tuberculin survey conducted in 1964-66. This was a multi-staged community-based, cross-sectional survey including 17,718 children below 15 years. The prevalence of infection was estimated by using the mixture method and the cut-off method (with a cut off point of ≥ 8 mm). The mixture method was used because it is the best methodology to dissect skin reactions due to exposure to Mycobacterium tuberculosis or reactions due exposure to other mycobacteria or BCG vaccination. The cut-off method was used to mimic the approach used in the 1964-66 tuberculin survey. The prevalence of infection was 10.0 % and 17.9 % in 5-9 years and 10-14 years respectively with corresponding ARTI was 1.5% and 1.7% according to mixture analysis. This was 12.4 % and 22.6 % in 5-9 years and 10-14 years respectively using a cut off point ≥8 mm. The associated ARTI for 5-9 and 10-14 years was 1.9% and 2.1%, respectively. The study showed a relation between the prevalence of infection and TB exposure (belonging to a household with a TB case identified in the survey), with an odds ratio [OR] for exposure of 4.5 (95%CI 1.7–11.9). Comparing the data from the current tuberculin survey with those from the 1964-66 survey showed only a moderate reduction the prevalence of infection for the two decades in which TB control activities were implemented, although the interval of 45 years between the two surveys is too large for a reliable estimate of the trend in the prevalence of infection.

The data on the burden of TB in Bangladesh remains difficult to interpret. While there is a clear decline in the prevalence of active disease, which fits the notification data, the burden of infection seems to have changed very little over the past 20 years. Despite this, the two surveys provided valuable information for the management of TB control by the NTP of Bangladesh.

**Outreach of the National Tuberculosis Programme**

In chapter 4 we assessed whether access to TB control activities of the NTP, including free DOTS service, is equitable with respect to socio economic position (SEP). This analysis addressed the lack of information on TB notification or TB prevalence data segregated by SEP. The prevalence survey from 2007-09 had the unique feature of collecting assets information from all the participating 21,427 households. Similar data were collected from a sample of TB case detected routinely under the DOTS programme of the NTP from the same cluster where the survey was carried out. We compared the SEP of the case detected under survey (active case detection) and that of the cases under DOTS (passive case detection). The prevalence of tuberculosis was five times higher in the lowest SEP quartiles of population (95.4 per 100,000, [95% CI: 48.0-189.7]) to highest SEP quartile population (19.5 per 100,000, [95% CI: 6.9-55.0]). The SEP distribution for the two types of TB cases
differed markedly. Among the survey cases, 75.8% were from lower two quartiles; while among cases under NTP, 57.1% were from uppermost two quartiles of the population. These findings indicate that TB prevalence is highest among the poor, while at the same time the poor are accessing the free DOTS services available through the country less often than individuals with the highest SEP. Despite a large emphasis of pro-poor development strategies, the NTP seems to miss those populations that need its service most.

**Care utilization**

In chapter 5 we described the care seeking behaviour of both actively identified TB cases in the survey and passively identified cases by the NTP. In total 273 TB cases were interviewed using structured questionnaires. The main aim was to assess trajectories of care-seeking, and services received at specific points of care. Of the included cases, 33 were actively detected under survey and 240 were sampled randomly from the passively detected cases under NTP by its routine DOTS programme from registers in the same clusters as where the survey took place. All the 33 actively detected case initially sought non specific care, or self-care (home remedies or traditional treatment). The majority of them (82%) remained with no care or self-care up to fourth subsequent point of care. From the passively detected cases, 118 (49%) initiated care seeking by visiting an informal provider. Of those 52 (44.0%), 17 (14.4%) and 5 (4.2%) remained in that informal care sector at second, third and fourth subsequent points of care. Prescription of medication was the principal care provided by any of the providers. Patients were very seldom referred for advice or investigations. These findings highlight the important role of informal providers in the pathway of diagnosis and treatment of persons with TB symptoms in Bangladesh, and the need to involve all types of care providers in TB-control activities for improved case detection by the NTP.

Knowledge of TB could be an important factor in not only care seeking decisions, but also in decisions on the initiation of treatment, and treatment compliance. In chapter 6 we described the knowledge on TB among a sample of newly diagnosed TB cases and controls from the general population. This study included 240 TB cases from the TB registers from the 40 clusters where the national prevalence survey was implemented and 240 adult individuals randomly selected from the households under survey. All participants were interviewed using a structured, pre tested questionnaire. Although the results showed overall a large knowledge on major aspects of TB (symptoms, transmission, prevention, treatment), the community controls showed poorer knowledge in some areas compared to TB cases, including TB transmission (80% vs.88%), mode of transmission (67% vs. 82%), knowing other symptoms than cough (78% vs. 89%), curability of TB (90% vs. 98%) and free availability of treatment (75% vs. 95%). Overall knowledge was explored by creating
a “knowledge score”. After controlling for other factors in a multivariable model, community controls had more than three times (OR 3.46, [95% CI: 2.00-6.09]) more often poor knowledge compared to the TB cases. This shows a potential opportunity of use of TB cases as peer educators by the NTP in its efforts to communicate more effectively TB-control strategies and messages to improve care seeking of TB suspects in the community.

In chapter 7 we described the results of a laboratory add-on study to the national TB prevalence survey. It evaluated the validity of judging the quality of submitted specimens by macroscopic assessment. Such evaluation is often done in the clinical setting to identify specimens to be sputum and suitable for culture. The accuracy of measuring the prevalence of smear-positive TB in a field situation depends on the quality of specimens submitted by the participants (who in the large majority do not have any symptoms). This study examined randomly selected specimens from 901 participants with a cough for more than 2 weeks in the prevalence survey. The field staff was asked to classify the specimens as sputum or saliva based on macroscopic features. The samples were transported to the central laboratory where they were assessed against four known algorithms for classification of specimens based on microscopic features (Gram stain). All submitted specimens were cultured for TB. The results showed a very poor correlation between the macroscopic classification and the microscopic characteristics of the specimens. Specimens categorised as saliva in the field were actually sputum in 30% to 60% of the times, depending on algorithm used. This implies that in a field setting of a prevalence survey, macroscopic assessment is of no value for judging the quality of specimens provided. All specimens should therefore be submitted for examination. In the survey setting there is a need for stringent quality assurance procedures for specimen collection and handling instead. Such procedures were present throughout the survey in Bangladesh.

In chapter 8 we combined the findings from the previous chapters and discussed their implications for future TB-control in Bangladesh. We identified research needs and priority areas for strengthening activities from the NTP.