Adherence to and outcome of isoniazid chemoprophylaxis among household contact children of adults having pulmonary tuberculosis in Alexandria, Egypt
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Background
Current international guidelines recommend 6–9 months of isoniazid (INH) preventive chemotherapy to prevent the development of active tuberculosis (TB) in susceptible children exposed to Mycobacterium tuberculosis. However, this is dependent on good adherence, as shown by previous studies.

Objectives
This study was conducted to describe the outcome of screening of contact children aged 5 years or less with household exposure to an adult pulmonary TB index case to determine the prevalence and possible risk factors of infection among contact children and to determine the extent and outcome of adherence of contact children to unsupervised INH chemoprophylaxis for 6 months.

Methods
A descriptive facility-based cross-sectional study was conducted from March 2009 to August 2010. Research settings were three of the National TB control program chest dispensaries (primary care facilities) in Alexandria, Egypt. Facility-based TB treatment registers of the previous 3 months were used to identify all new adult pulmonary TB cases. All children aged 5 years or less living in the same house as the index cases were identified and screened for TB. The contact children were given unsupervised INH preventive chemotherapy once active TB was excluded. Adherence to and outcome of preventive chemotherapy were followed up. Preventive chemotherapy consisted of unsupervised INH monotherapy for 6 months with monthly collection of tablets from the clinic. Adherence was documented after completion of the 6-month preventive treatment period. Adherence was considered reasonable if tablets were collected for more than 4 months, poor if collected for 2–4 months, and very poor if collected for less than 2 months.

Outcome measures
(a) Prevalence of infection and disease and the possible risk factors among contacts. (b) The extent and outcome of adherence to unsupervised INH chemoprophylaxis among contact children. (c) Factors behind poor adherence.

Results
In total, 197 adult TB index cases from 187 households were identified. In all, 297 children aged 5 years or less experienced household exposure, of whom 252 (84.9%) were fully evaluated. Tuberculin test was positive in 136 of the 252 child contacts (54.0%), of whom 130 were contacts of sputum-positive patients and six were contacts of sputum-negative patients. The important risk factors for transmission of TB infection were younger age, male sex, severe malnutrition, absence of BCG vaccination, contact with a sputum-positive adult who was a source case, household overcrowding, and exposure to environmental tobacco smoke. Thirty-three children were diagnosed and treated for TB at the baseline screening and 217 received preventive INH chemotherapy. Of the children who received preventive chemotherapy, only 36 (16.6%) completed at least 4 months of unsupervised INH monotherapy. During the subsequent follow-up period, eight children developed TB (secondary attack rate for TB disease was 3.7%), of whom four received no preventive chemotherapy and four were poorly adherent.

Conclusion
The prevalence of TB infection and clinical disease among children in household contact with adult patients is high, and risk is significantly increased because of child contact, index patients and environmental factors. Adherence to 6 months of unsupervised INH chemoprophylaxis was very poor.

Keywords:
adherence, child contact, isoniazid, preventive chemotherapy, tuberculosis screening
Introduction
A large percentage of children with household exposure to a sputum smear-positive adult tuberculosis (TB) index case become infected with *Mycobacterium tuberculosis* [1–3]. Following infection, the risk of developing disease is highest (20–50%) in very young (<3 years of age) and/or immunocompromised children [4]. These high-risk children may experience rapid disease progression, which identifies them as the priority group to receive preventive chemotherapy [5].

Currently, the WHO and the International Union against Tuberculosis and Lung Disease recommend that all children younger than 5 years of age who are in household contact with a sputum smear-positive index case should be actively traced and screened for TB [5,6]. Six months ofisoniazid (INH) is recommended as preventive chemotherapy once active TB has been excluded, because, with good adherence, 6–9 months of INH monotherapy has proven effective for preventing TB in children infected with *M. tuberculosis* [7–10].

Screening of children is difficult in resource-limited settings [11–13], and several reports have shown that even when screening is performed adherence to 6–9 months of unsupervised INH preventive chemotherapy is often very poor [14–18]. These studies have been criticized, mainly for their retrospective methodology, and international guidelines have remained unchanged. However, adherence is a crucial component of any preventive chemotherapeutic regimen. The present study was conducted to study the effects of adherence to unsupervised INH monotherapy for 6 months and its outcome among children with household exposure to an adult pulmonary TB case.

Specific objectives

1. To describe the outcome of screening children aged 5 years or less having a household exposure to an adult pulmonary TB index case.
2. To determine the prevalence and possible risk factors of infection among contact children.
3. To determine the extent and outcome of adherence of contact children to unsupervised INH chemoprophylaxis for 6 months.

Subjects and methods

Study design
A descriptive facility-based cross-sectional epidemiological approach was used to estimate the prevalence of infection and disease and to investigate the effects and outcomes of adherence of contact children to chemoprophylaxis.

Study setting and population
The study was conducted between March 2009 and August 2010 in Alexandria, Egypt. Three National TB control program chest dispensaries (primary care facilities, El Maamoura, Moharum Beih and Kom El Shokafa) were randomly selected as study settings. Facility-based TB treatment registers were used to identify all new adult pulmonary TB cases in the previous 3 months. Cases were diagnosed in these chest dispensaries on the basis of suggestive symptoms and signs and were confirmed either by the presence of acid fast bacilli on direct smear microscopy using Ziehl–Neelsen staining of sputum (referred to as smear-positive pulmonary TB patients) or by diagnostic chest radiograph in the absence of TB bacilli in sputum specimens (referred to as smear-negative pulmonary TB patients).

For the purpose of this study, household contact children are defined as those children aged up to 5 years who were living in the same house as the adult index case at the time of diagnosis. The exclusion criteria were: being previously treated for TB infection; presence of concurrent conditions identified as risk factors for TB (hematological, or reticuloendothelial system malignancies); and being previously or currently on immunosuppressive drugs including corticosteroids. Three trained social workers visited the homes of new adult index cases and recorded the names and ages of all children resident at that address and collected the required data. According to Egypt National Tuberculosis control Programme guidelines, all children younger than 5 years of age were invited for interviewing and screening at the local primary healthcare clinic.

Screening and treatment
Every child under 5 years was screened using tuberculin skin testing (TST), which was performed by the intradermal injection of 1 Tuberculin Unit of Purified Protein Derivative PPD-RT23/Tween 80 into the volar surface of the left forearm using a 26-G needle and disposable syringe. This was read 72 h later in good light with the forearm slightly flexed. Induration was measured by the pen method [17]. A transverse induration greater than 10 mm was defined as a positive tuberculin test suggestive of TB infection (to minimize false-positive misclassification of the TST results due to BCG vaccination, the present study used 10 mm as a criterion for a positive TST). A single technician at each facility trained in the administration and interpretation of the tuberculin test performed the procedure in all children.

All children under 5 years were then subjected to a posteroanterior erect chest radiography, which was interpreted by a single experienced radiologist (unaware of the results of tuberculin testing) and labeled as consistent or not consistent with TB to identify children who will require anti-TB treatment. The rest of the contact children under 5 years were given unsupervised INH monotherapy as chemoprophylaxis for 6 months. INH was recommended as a daily dose of 10–15 mg/kg/day with a maximal dose of 300 mg. Tablets were collected monthly from the clinics. Adherence was documented at the end of 6 months.

Adherence was considered reasonable if tablets were collected for more than 4 months, poor if collected for
2–4 months, and very poor if collected for less than 2 months. The contact children were followed up during the study period and for an additional 2 months after the end of the study to identify those who were subsequently diagnosed as secondary cases of TB. The same methods of diagnosis as used on the cases were employed. The child contact was considered a secondary case if active TB was absent at the time of the baseline screening but developed during the follow-up period.

Data collection methods and tools

Interviewing
Three trained qualified nurses, one at each facility, used a structured interview questionnaire to collect the following data from parents or guardians of the contact children:

(1) Characteristics of the index adult case (age, sex, relation to the child contact, sputum results, and symptom duration).

(2) Characteristics of the contact child:
(a) Demographic data of the contact child (age, sex).
(b) History of other diseases such as diabetes mellitus and bronchial asthma.
(c) History of BCG vaccination and examination of scars.
(d) Detailed clinical data, including history of fever, cough for more than 2 weeks, failure to gain weight, loss of appetite, decline in weight, fatigue, and symptoms of extrapulmonary TB such as lymphadenopathy.

(e) Weight measurements using a single precalibrated beam balance. Malnutrition was classified as follows: grade 1 – weight 71–80% of expected; grade 2 – weight 61–70% of expected; grade 3 – weight 51–60% of expected; and grade 4 – weight less than 50% of expected. Grades 1 and 2 were categorized as mild malnutrition and grades 3 and 4 as severe malnutrition [19].

(3) Environmental factors, including the number of individuals per household and exposure to tobacco smoke.

The study tool was pilot tested on a randomly selected group of children (n = 15).

Record keeping
For each child participant who was screened, nursing staff used a treatment sheet to document the outcome variables, such as the results of the induration in millimeters, the results of the chest radiograph if taken, whether the participant received chemoprophylaxis or whether the treatment was started, the number of clinic visits for collecting the chemoprophylaxis, and whether the chemoprophylaxis was completed and its outcome. Also any reported side effects of INH monotherapy and any possible reasons for poor adherence were also recorded.

Ethical considerations
Written informed consent was obtained from parents or guardians of children in the household, and approval was obtained from the Research Ethics Committee of the Faculty of Medicine, Alexandria University. The proposed research was also approved by Directorate of Health Affairs in Alexandria. Complete confidentiality was ensured and was maintained throughout the study.

Statistical analysis
Data entry, analysis, and tabulation were carried out using an SPSS software package (version 18.0; SPSS Inc., Chicago, Illinois, USA). Frequencies were computed for index and contact variables, TB screening results, adherence to chemoprophylaxis, outcome of adherence to chemoprophylaxis, and reported reasons for poor adherence. Proportions were compared simultaneously by the χ²-test. The Fisher exact test was used when the χ²-test was not valid. Bivariate analysis of the risk factors for contracting a latent TB infection was performed using the odds ratio (OR) and its 95% confidence interval (CI). A multivariate logistic regression model was constructed to control the confounders. The factors included in the multivariate model were based on the association of the risk factor with TB infection in bivariate analysis. The independent variables used in the logistic models were all dichotomous. The level of significance was set at P value less than 0.05.

Results
Background characteristics of the index patients and child contact
During the study period, 197 adult TB index cases [185 were sputum smear-positive (93.9%) and 12 (6.1%) were sputum smear-negative culture-positive source cases; 121 were male (61.4%); 129 were 15–40 years of age (65.5%) were identified. Of the 197 adult TB cases, 147 (74.6%) were current smokers. Mothers were the source cases in 76% of instances. Symptom duration was more than 3 months in 172 adult index cases. The number of individuals per household was more than six in 110 households.

From 187 households, 297 child contacts aged up to 5 years were identified (on average 1.59 children aged 5 years or less per household). Complete information (symptoms, TST, and chest radiograph) was available for 252 (84.9%) of 297 children included in the analysis. Boys constituted 56.0% of the children. Sex ratio (M:F) was 1.3:1. The mean age of the children was 30 months (range: 1–60 months) (Table 1). Of the 252 child TB contacts included in the analysis, 240 (95.2%) were contacts of sputum smear-positive cases and 12 (4.8%) were contacts of sputum smear-negative culture-positive cases.

Table 1 also shows that a total of 236 child contacts had a BCG scar, and the remaining 16 did not, although their parents reported that they had been administered the BCG vaccine. However, this could not be confirmed in the absence of a written record on vaccination. No child showed a history of diabetes or bronchial asthma. With regard to malnutrition, a total of 157 child contacts (62.3%) showed no evidence of malnutrition, whereas 54 (21.4%) were mildly malnourished and 41 (16.3%) had...
With regard to adherence to INH unsupervised monotherapy, the adherence was very poor for more than half of the children (51.6%) and it was poor in 6.0% of children.

Adherence to unsupervised INH chemoprophylaxis is shown in Fig. 2 and Table 4. Adverse effects (hypersensitivity and gastrointestinal manifestations) were reported in 12 children using INH monotherapy. Five percent of contact children who received chemoprophylaxis reported unexplained fever and 4.6% reported fatigue. Other symptoms were weight loss and failure to thrive.

Viruses and other respiratory pathogens are now thought to be the most significant cause of cough in children. Cough was reported as being present in 48 (21.9%) of 219 screened (141; 56.0%) were completely asymptomatic. More than half of the children (51.6%) and it was poor in 6.0% of children. Reasonable adherence was identified for only 16.6% of children.

Other factors associated with TB infection were exposure of the child to environmental tobacco smoke (OR 6.7, 95% CI = 1.5–9.7) and household overcrowding (number of individuals per household >6) (OR 5.9, 95% CI = 1.9–7.6), and household overcrowding.

A multivariate model was constructed to control for confounders. The effect of child age less than 3 years (OR = 5.2, 95% CI = 2.6–11.7) and child contact to smear-positive source cases (adjusted OR = 3.9, 95% CI = 1.8–8.4) remained. Other variables, including child sex, malnutrition, BCG scar, source case proximity, exposure to environmental tobacco smoke, and household overcrowding were no longer significant. These variables explained 82.8% of the variability in infection risk (R² = 82.8%).

**Tuberculosis manifestations in contact children**

Symptoms reported at the time of screening are illustrated in Table 3. More than half of the children screened (141; 56.0%) were completely asymptomatic. Cough was reported as being present in 48 (21.9%) of 219 contact children. Five percent of contact children who received chemoprophylaxis reported unexplained fever and 4.6% reported fatigue. Other symptoms were weight loss and failure to thrive.

**Adherence to and outcome of chemoprophylaxis**

Adherence to unsupervised INH chemoprophylaxis is shown in Fig. 2 and Table 4. Adverse effects (hypersensitivity and gastrointestinal manifestations) were reported in 12 children using INH monotherapy.

With regard to adherence to INH unsupervised monotherapy, the adherence was very poor for more than half of the children (51.6%) and it was poor in 6.0% of children. Reasonable adherence was identified for only 16.6% of children.
At the end of 6 months of chemotherapy, the secondary attack rate (SAR) for TB was 3.7% (8/217) (95% CI: 2.2, 4.1). Figure 3 illustrates the number of incident secondary cases of TB among child contacts per follow-up. The median time for diagnosis of secondary cases was 4.7 months. Of the eight secondary cases who subsequently developed TB 4/56 (7.1%) received no chemoprophylaxis (because of drug unavailability) and 4/112 (3.6%) were poorly adherent to treatment.

Factors behind poor adherence to chemoprophylaxis
Reasons for poor adherence of contact children (n = 125) to INH chemoprophylaxis have been illustrated in Fig. 4. The most common reason for poor adherence as mentioned by caregivers was unavailability of the drug because of high cost (67.2%). Other factors were the inconvenience of daily medication over the 6-month period for a completely healthy child (60%), followed by the need to attend regular clinic visits for follow-up (47.2%). Unsupervised nature of the prophylaxis course was ranked as another reason (42.6%). The least-mentioned reasons were lack of resources for screening and follow-up (12.0%) and occurrence of adverse events including hypersensitivity reactions and gastrointestinal distress (9.6%).

Discussion
Contact screening and management has the potential to reduce the burden of TB disease in children. A study has shown that INH preventive therapy can reduce the

Table 2. Possible risk factors for tuberculosis infection among household contact children of adult pulmonary tuberculosis patients in primary care facilities during the year 2009

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Total</th>
<th>TST-positive children (n = 136)</th>
<th>TST-negative children (n = 116)</th>
<th>P valuea</th>
<th>Crude odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child age, &lt;3 years</td>
<td>160</td>
<td>113 (83.1)</td>
<td>47 (40.5)</td>
<td>0.000</td>
<td>6.7 (2.2–13.8)*</td>
</tr>
<tr>
<td>Child sex, boy</td>
<td>141</td>
<td>120 (88.2)</td>
<td>21 (18.1)</td>
<td>0.000</td>
<td>7.3 (2.5–12.9)*</td>
</tr>
<tr>
<td>Severe malnutrition</td>
<td>41</td>
<td>33 (24.3)</td>
<td>8 (6.9)</td>
<td>0.000</td>
<td>4.0 (2.2–7.2)*</td>
</tr>
<tr>
<td>Absence of BCG scar</td>
<td>18</td>
<td>14 (10.3)</td>
<td>2 (1.7)</td>
<td>0.014</td>
<td>2.1 (1.2–3.7)*</td>
</tr>
<tr>
<td>Contact with sputum positive adult</td>
<td>185</td>
<td>130 (95.6)</td>
<td>53 (45.7)</td>
<td>0.000</td>
<td>5.2 (1.8–8.6)*</td>
</tr>
<tr>
<td>Source case age, (15–40 years)</td>
<td>129</td>
<td>67 (49.3)</td>
<td>62 (53.4)</td>
<td>0.381</td>
<td>0.7 (0.3–2.7)</td>
</tr>
<tr>
<td>Source case relation to the child, mother</td>
<td>76</td>
<td>64 (47.1)</td>
<td>12 (10.3)</td>
<td>0.028</td>
<td>3.8 (1.7–6.5)*</td>
</tr>
<tr>
<td>Source case symptom duration &gt;3 months</td>
<td>172</td>
<td>101 (74.3)</td>
<td>71 (61.2)</td>
<td>0.062</td>
<td>1.2 (0.8–4.8)</td>
</tr>
<tr>
<td>The number of individuals per household &gt;6</td>
<td>110</td>
<td>89 (65.4)</td>
<td>21 (8.1)</td>
<td>0.000</td>
<td>5.9 (1.9–19.6)*</td>
</tr>
<tr>
<td>Exposure to environmental tobacco smoke</td>
<td>147</td>
<td>118 (86.8)</td>
<td>29 (25.0)</td>
<td>0.000</td>
<td>6.7 (1.5–29.7)*</td>
</tr>
</tbody>
</table>

CI, confidence interval; TST, tuberculin skin test.
*P value was calculated from the \( \chi^2 \)-test or the Fisher Exact test; significance was set at \( P \) values less than 0.05.
*If the confidence interval does not overlap zero, the effect is said to be statistically significant.

Table 3. Symptoms reported in contact children less than 5 years of age who were exposed to pulmonary tuberculosis cases in primary care facilities during the year 2009

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Total number (n = 252) (%)</th>
<th>Treated for tuberculosis (n = 33) (%)</th>
<th>Not treated for tuberculosis (n = 219) (%)</th>
<th>Crude odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>141 (56.0%)</td>
<td>0 (0.0%)</td>
<td>141</td>
<td>–</td>
</tr>
<tr>
<td>Cough (&gt; 2 weeks duration)</td>
<td>62 (24.6)</td>
<td>14 (42.4)</td>
<td>48 (21.9)</td>
<td>5.9 (2.1–10.9)*</td>
</tr>
<tr>
<td>Fever</td>
<td>14 (5.6)</td>
<td>3 (21.4)</td>
<td>11 (5.0)</td>
<td>3.6 (1.7–6.5)*</td>
</tr>
<tr>
<td>Weight loss*</td>
<td>19 (7.5)</td>
<td>10 (30.3)</td>
<td>9 (4.1)</td>
<td>10.1 (4.6–9.5)*</td>
</tr>
<tr>
<td>Fatigue</td>
<td>16 (6.3)</td>
<td>6 (38.2)</td>
<td>10 (6.0)</td>
<td>4.8 (1.4–15.4)*</td>
</tr>
</tbody>
</table>

CI, confidence interval.
*Weight loss is weight loss or flattening or faltering of growth curve documented on the growth chart.
*If the confidence interval does not overlap zero, the effect is said to be statistically significant.

Table 4. Adherence to antituberculosis treatment and preventive chemotherapy, and outcome according to preventive chemotherapy adherence among contact children less than 5 years of age who received chemoprophylaxis (n = 252) in primary care facilities during the year 2009

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>Not given</th>
<th>Very poor</th>
<th>Poor</th>
<th>Reasonable</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB treatment (n = 32)</td>
<td>0</td>
<td>1 (3.1)</td>
<td>3 (9.4)</td>
<td>29 (90.6)</td>
</tr>
<tr>
<td>Preventive chemotherapy INH (n = 217)</td>
<td>56 (25.8)</td>
<td>112 (51.6)</td>
<td>13 (6.0)</td>
<td>36 (16.6)</td>
</tr>
<tr>
<td>Outcome</td>
<td>4/56 (7.1)</td>
<td>4/112 (3.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

INH, isoniazid; TB, tuberculosis.
The present study identified lack of resources in the national TB control program as an important obstacle to chemoprophylaxis. Unavailability of the drug was the main reason stated for poor adherence to chemoprophylaxis. Therefore, it would be very useful to identify children at greatest risk for infection – for example, children less than 3 years of age. Literature review revealed the vulnerability of this age group, and recent reports from India also indicate that children younger than 3 years are at highest risk of developing severe disease manifestations [23]. In addition, in children aged 3 years or more, the majority of transmission in endemic areas occurs outside the household [24]. Therefore, in resource-limited settings in which TB services are overstretched, it seems warranted to focus the provision of preventive chemotherapy on those children who are at highest risk to progress to disease following household exposure (<3 years and/or immunocompromised) [25]. This seems like the most realistic way to improve access to preventive chemotherapy for those children who are most likely to benefit.

Poor nutritional status has been reported to decrease TST reactivity in children. Severe malnutrition was shown to reduce immune responsiveness to BCG [26]. Multivariate analysis of the present study, however, did not find an association between TST positivity and nutritional status, similar to what was reported previously in Botswana [27]. In this study the proportion of severely malnourished children may have been small to some extent among child contacts, which resulted in low power to detect an effect.

Sputum smear-positive TB patients infect more of their child contacts than do smear-negative patients, with numbers varying between studies [28]. This was confirmed in the obtained results, in which contacts of smear-positive index cases had a significantly high risk of infection (95.6%). Strategies to control TB in high-burden countries are directed to adult smear-positive cases and to their early detection and treatment to substantially reduce transmission and prevent infection in contact children [28].

As TB is an airborne disease, the risk of an uninfected person becoming infected is strongly associated with the likelihood of an infected child developing disease by as much as 80% [20]. Furthermore, contact tracing will identify children who require TB treatment at an earlier stage [21]. Findings of the present work confirm the importance of contact investigation in identifying new TB cases and providing chemoprophylaxis to young children based on the high risk of infection.

The prevalence of TB infection among contact children less than 5 years of age who received chemoprophylaxis (n=252) in primary care facilities during the year 2009, One child was lost to follow-up. Very poor adherence: received therapy for less than 2 months. Poor adherence: received therapy for 2–4 months. Reasonable adherence: received therapy for more than 4 months. INH, isoniazid; TB, tuberculosis.

Reported reasons for poor adherence of contact children to INH chemoprophylaxis (n=125) in primary care facilities during the year 2009. Categories are not mutually exclusive. INH, isoniazid.

The need to attend regular clinic visits
Unsuervised nature of the course
Inconvenience of daily medication over a six months period
Unavailability of the drug due to the cost on the program

Adherence to chemoprophylaxis among contact children less than 5 years of age who received chemoprophylaxis (n=252) in primary care facilities during the year 2009. One child was lost to follow-up. Very poor adherence: received therapy for less than 2 months. Poor adherence: received therapy for 2–4 months. Reasonable adherence: received therapy for more than 4 months. INH, isoniazid; TB, tuberculosis.

Number of incident secondary cases of tuberculosis (n=8) among child contacts per time of follow-up in primary care facilities during the year 2009.
probability of coming into contact with an individual with active pulmonary TB and the intimacy of that contact. A recent study reported that contact with a female household member, especially the mother, carries a significantly greater risk of infection and disease for the child than does contact with a male household member [29]. The bivariate analysis of the present work revealed a similar pattern. This is most likely explained by the fact that in Alexandria, as in many parts of the world, children under 5 years are in closer physical contact with their mothers.

Higher exposure is likely to occur among people who live in the same house or who spend long periods of time in the same room [30]. This known risk factor for TB is confirmed by the significant association between household crowding and TB infection among the child contacts as seen in the bivariate analysis. Similarly, exposure to tobacco smoke is a well-known risk factor for TB infection, which was confirmed in the present study as well. In accordance, previous contact studies have found that exposure to passive smoking and household overcrowding are significant risk factors for TB infection in children [31]. However, these relations were not confirmed in the multivariate analysis of the present study, as the sample size was probably not sufficiently large to detect a difference.

The ultimate effectiveness of a chemotherapeutic intervention is determined through actual adherence in ‘real life’ conditions [32]. Available data on adherence to chemoprophylaxis in children are limited. The most striking observation in the current study was the poor adherence to unsupervised INH chemoprophylaxis.

Poor adherence to unsupervised INH monotherapy was also reported in previous studies [33,34]. The current study allowed accurate documentation of the total number of contact children and administering INH chemoprophylaxis to all children under 5 years of age. This was not the case in previous studies, which documented adherence of only those children who turned up for screening after preventive chemotherapy was initiated, which imposes a significant selection bias.

The finding that 25.8% of children up to 5 years of age with household exposure to a TB index case were not even offered preventive chemotherapy is almost certainly a gross underestimation of the situation in most endemic areas. The study areas had limited resources and lacked accessibility to TST and chest X-ray screening tests, and also lacked availability of preventive drugs. Effort was made during the study period to ensure that all contact children were traced and screened. A survey conducted in Malawian hospitals showed that child contacts were screened for TB in only 12% of hospitalized adult TB cases [35].

In the present study, reasons for poor adherence were documented. Inconvenience of daily medication over a 6-month period for an asymptomatic child was one of the commonly stated reasons for poor adherence. This negative risk perception could be explained by the fact that children who receive preventive chemotherapy are completely healthy. Therefore, healthcare personnel need to pay particular attention to ensure that the concept of risk reduction is effectively conveyed, which may strengthen the argument to focus preventive chemotherapy in endemic areas, primarily on high-risk children.

In the present study, the SAR was used as a measure to estimate the risk of acquiring the disease in the household contact children less than 5 years of age. Although the SAR is most often applied to infectious diseases with short incubation periods in well-defined social networks, it can also be used for chronic infectious diseases, such as TB, to estimate the risk of developing the disease following household exposure [1]. The present work estimated SAR to be 3.7%. This rate was higher than that reported from Japan (1%), USA (1%), and Finland (0.7%) but lower than that reported from Haiti (16.1%) [36]. All of the new TB cases were household contacts of an active pulmonary TB case. This uncovers a major gap in the contact-tracing mechanisms and treatment of TB infection among the household contacts of active TB cases, or at least nonadherence to treatment and its completion. Achieving high rates of completion of therapy in recently infected contacts of active cases of pulmonary TB is essential to maximize public health prevention efforts aiming at elimination of the disease.

The main limitation of this study was the fact that it was conducted in facility-based settings and represents contacts of only a very small proportion of pulmonary TB cases that were registered and treated in the study settings over the same period. Moreover, no intervention was performed to improve adherence of children who defaulted, as the study aimed to document adherence in ‘real life’. Chemoprophylaxis was provided in the same way as in the studied clinics, and adherence was documented only after completion of the 6-month treatment period.

Conclusion
Prevention and early detection of pediatric cases are essential tasks in TB control. Adherence to unsupervised INH chemoprophylaxis for 6 months is poor, mainly because of unavailability, which is why the drug has to be available all the time. There is also a need for improving adherence through strategies like the use of short-duration multidrug supervised regimens, particularly in children who are at high risk for infection and disease progression following exposure.

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Conflicts of interest
There are no conflicts of interest.

References


