

Clinical, bacteriological and immunological follow-up of household contacts of leprosy patients from a post-elimination area - Antioquia, Colombia

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Follow-up of the household contacts (HHC) of leprosy patients is still the best strategy for early detection of leprosy. HHC from a post-elimination region of Colombia studied in 2001-2002 were re-contacted in 2007. They were tested at both times by clinical examination, bacillary index (BI), PCR from a slit skin smear (SSS) and anti PGL-1 IgM titres. Thirty-two of 61 HHC (52%) were re-contacted. Nine HHC (28%) showed sero-conversion and one had a skin lesion (BI negative, nested PCR positive). Periodic evaluation of HHC can contribute to the detection of infected HHC as well as new and early leprosy cases.

Key words: household contacts - leprosy patients - follow-up - post-elimination region

Leprosy in Colombia is not a public health problem and control of leprosy is in the “post-elimination phase” (WHO 2006). The prevalence of leprosy in Colombia reported in 2008 was 0.87 per 100,000 inhabitants (SI-VIGILA 2008). Several regions of Colombia, however, show large differences in leprosy prevalence. For example, leprosy prevalence in state of Antioquia has fluctuated between 0.4-0.6 per 100,000 inhabitants, but there are regions in the states of Bolívar and Cesar where the prevalence ranges from 3.7 per 100,000 (SIVIGILA 2008). There were 345 new leprosy cases detected in Colombia in 2008 (SIVIGILA 2008); 3.52% of these were in children under 15 years of age and the percentage of grade II disability among new cases was 7.79% (WHO 2006). The number of new cases has remained around 350-500 since the multi-drug therapy (MDT) was introduced in 1985 (SIVIGILA 2008), indicating that the therapy has not been effective in preventing transmission (Meima et al. 2004) and that the number of new cases remains the same in a region that is considered to be in a post-elimination phase. Household contacts (HHC) are a high-risk population for developing leprosy (Goulart et al. 2008). At present, the Leprosy Control Programs do not routinely use to detect clinical leprosy follow-up in HHC since only one clinical examination is stipulated as a control measure at the time the index case is diagnosed. Nevertheless, clinical examination is not a good tool for detecting subclinical leprosy due to the fact that leprosy is a disease with a slow onset and the symptoms are difficult to detect in

the early stage of infection (Lockwood 2002). Therefore, diagnosis is often delayed, contributing to the onset of the disease and allowing transmission and sequelae (Lockwood & Kumar 2004). The use of other tests in addition to periodic evaluations by clinical exam to detect infected HHC, as well as detailing their immune response and bacteriological state, can contribute to the identification of infected HHC and new leprosy cases (Cardona-Castro et al. 2005).

The first study in 2001-2002 included 61 HHC and the follow-up in 2007 was able to re-contact 32 HHC (52.4%). During the first evaluation, these 32 HHC showed negative titres for anti PGL-1 IgM and neither clinical signs nor symptoms suspicious of leprosy were recorded. Twelve leprosy patients were the index cases of the 61 HHC; eight were male and four were female. These index cases included 11 patients with diagnosis of paucibacillary (PB) leprosy [bacillary index (BI) = 0] and one patient with multibacillary (MB) leprosy (BI = 2,4) at the time of the first evaluation. All of the index cases were re-contacted in 2007.

HHC and index cases were examined for signs or symptoms of skin and peripheral nervous leprosy. HHC and patients were tested for BI using the Ziehl Nielsen stain. Slit skin smear (SSS) from ear lobes, elbows and lesions were taken, along with nasal mucus samples (NS). The smears were examined for the presence of acid-fast bacilli (AFB). BI was recorded (Isenberg 1992). *M. leprae* DNA from SSS and NS of HHC was extracted using the DNeasy kit[®]. Nested PCR was carried out using the primers LP1-LP2 and LP3-LP4 (Donoghue et al. 2001). HHC serum samples were tested for anti PGL-1 IgM, which was applied using the native PGL-1 antigen provided by Dr. Patrick Brennan from Colorado State University, USA, following a previously described methodology (Cho et al. 1983). After explanation of the study and procedures, volunteers provided informed consent. In agreement with resolution 008430 of 1993 that regulates health studies in Colombia, this investigation was considered to involve minimal risk.

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The ages of the HHC ranged from 11-79 years old with an average age of 41.5 years. Nine of the HHC were males and 23 were females. Nine HHC who had negative titres at the time of the first study showed positive titres for anti PGL-1 IgM in 2007 (sero-conversion of 28%); one of them was an 11-year-old girl. One HHC had one light, hypo-pigmented skin lesion (2 x 3 cm), located on her left thigh with an anaesthetic area surrounding the lesion, which was BI negative and nested PCR positive from her SSS. This HHC was diagnosed as a PB patient and received the appropriate treatment, according to WHO recommendations. None of the HHC showed positive BI, including the new patient. For the nested PCR, only the new patient was positive. The 12 index cases of the HHC had a BI of zero and the clinical exam did not reveal active lesions of leprosy and/or clinical relapse in the second evaluation. Grade I and II disability was observed in 100% of patients.

Periodic evaluation of HHC by clinical exam, immune response and bacteriological state can contribute to the detection of infected HHC for new and early leprosy cases. Due to migration, not all of the participants could be followed, resulting in a loss of information. Only 32 (52.5%) of the study's first round participants were followed up. We are now recommending a yearly follow-up of HHC in an effort to reduce the risk of losing critical information. Nine of 32 HHC showed negative titres for PGL-1 during the first study, but after six years they now have positive titres (a 28% sero-conversion rate), which should signify either new exposition or infection or a slow immune response after contact with *M. leprae*. It is important to note that one of the HHC who sero-converted was an 11-year-old girl, which demonstrates the importance of follow-up of *M. leprae* infection in children for early disease detection and disability prevention in a young population. Other studies have shown frequencies of infected contacts that range from 13-93% (Meeker et al. 1986, Amezcua et al. 1987, Cardona-Castro et al. 2005, 2008). Early detection of PB leprosy was possible in one HHC who had a unique lesion and the diagnosis was confirmed by positive nested PCR. Treatment for PB leprosy was initiated in accordance with WHO recommendations. Results confirm that the use of multiple testing modalities and follow-up for HHC is important because the clinical exam done at the time of detection of the index case is not sufficient to know whether HHC are infected.

The 29 HHC that were not included in the follow-up were negative for anti PGL-1 IgM titres in the first study (2001-2002). The results of the evolution of these 29 HHC could change the results of this follow-up, a fact that represents a bias of this study.

Results reveal that leprosy transmission is occurring in post-elimination areas. The possible failure of treatment due to non-adherence or the appearance of antibiotic resistance need to be evaluated (Hernández et al. 2008). Classification as a post-elimination area contributes to the lack of financial resources for surveillance and leprosy public health control measures in a high-risk population.

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