

PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Leprosy in children- a Cuban experience on leprosy control
AUTHORS	Ruiz-Fuentes, Jenny Laura; Rumbaut Castillo, Raisa; Hurtado Gascón, Laura; Pastrana, Fernanda

VERSION 1 – REVIEW

REVIEWER	Reviewer name: Peter Rohloff Institution and Country: Maya Health Alliance, Guatemala Brigham and Women's Hospital, Boston USA Competing interests: None
REVIEW RETURNED	06-Jun-2019

GENERAL COMMENTS	<p>This is an interesting and important topic and I recommend that it be included in the journal. However the article has problems with structure and focus and it will require a very extensive rewrite in order to be suitable for publication.</p> <p>Most importantly, it is unclear what the overall intent of the article is - is this primarily a (1) synthesis of unpublished case data and epidemiological data from Cuba on pediatric leprosy (an original research article), or (2) is it a review article summarizing the historical experience and relevant available literature from Cuba, or (3) is it a clinical review article of pediatric leprosy more generally? The article tries to do all three things and this is not very effective.</p> <p>I would recommend that the authors choose one of these approaches and then rewrite the article accordingly. I suspect the authors are leaning more toward strategy (1) or (2). If so, then much of the current content of the article should be eliminated entirely (operational definitions, clinical manifestations, much under diagnosis) as this content would be more appropriate in a general clinical review article.</p> <p>If this is primarily a research article, then it needs to be structured to provide a more formal methods section, where the authors provide a great deal more information on the search and chart review strategies they used to collect the case and epidemiological data. Given the robustness of the Cuban public health response to leprosy, the readership of the journal will be very interested in better understand these different data streams and how the authors synthesize them. This will also be important for reviewers to ascertain bias or representativeness of the available data sources.</p> <p>Similarly, if a research article, tables providing detailed sociodemographic and clinical descriptors of patients will be very important. It will especially be important to have information on how diagnosis was established (number biopsied, pathological procedures used, number diagnosed just clinically, etc) and available treatment and outcomes data as well.</p>
-------------------------	---

	<p>A small amount of this data is present (the case series from 2014) but it is unclear where this data comes from and what data there is on the other ~100 cases).</p> <p>If the goal is more a review of the Cuban public health response to leprosy—also very interesting— then some of the above details will be less important, but a more timeline oriented description of trends in leprosy more generally in Cuba (including adult leprosy), the various public health mechanisms involved, etc will be needed.</p> <p>Regardless of which approach is taken, it will also be helpful to separate out the engagement with literature and studies from other settings. As the article is written now, citations and references to leprosy outside of Cuba are admixed throughout the entire manuscript, and these references should be part of the introduction, or engaged with in the discussion, but otherwise removed from the middle part (methods and results) part of the manuscript.</p>
REVIEWER	<p>Reviewer name: Dr.Aparna Palit Institution and Country: All India Institute of Medical Sciences, Bhubaneswar, India Competing interests: I declare no competing interest</p>
REVIEW RETURNED	06-Jun-2019
GENERAL COMMENTS	<p>The authors have presented the data on childhood leprosy in Cuba, where the defined leprosy elimination was achieved long time back (1993). They have nicely shown the current status of childhood leprosy and the relevance of the country's strategy of leprosy control. So, there are two areas of focus of discussion in the article.</p> <p>In this regard, the title of the article may be modified with inclusion of a phrase which states the country's strategy on leprosy control.</p> <p>Authors have not followed the Ridley Jopling's clinico-immunological classification for categorizing the disease in their study subjects. Like classification of leprosy at any age group, childhood leprosy should also be classified according to this system, to have uniformity in understanding.</p> <p>Page 5: Lines 4-5: Descriptions of tuberculoid leprosy as 'papulo-lichenoid lesions, characterized by micronodules with acute plaques, single and small' is not classical. the term 'lichenoid' is not acceptable in the context of leprosy. These descriptions are best to quote from a standard text book on leprosy.</p> <p>Page 6: lines 49-50; one child presented with arthralgia and myalgia. Was the child in reaction? This has to be clarified as these are not the symptoms of leprosy per se, but indicate associated type 1 or type 2 reaction . The authors have mentioned that there was no patient with reaction in their series.</p> <p>Page 7: lines 17-22; Meaning not clear. The sentences need re-structuring to ensure comprehensibility.</p> <p>Page 8: lines 37-50; These two paragraphs on slit skin smear may be omitted.</p> <p>Intra-familial contacts were not found in 23% of the childhood leprosy cases; neighborhood or social contacts might have played a role in disease transmission in these cases.</p>

	<p>The details of the cases may be omitted or placed in a table.</p> <p>Overall, though the contents are good, readability and comprehensibility of the article is poor because of linguistic shortcomings and grammatical mistakes. This aspect must be taken care of as priority.</p>
--	---

VERSION 1 – AUTHOR RESPONSE

The authors acknowledge the reviewer's comments to improve the quality of manuscript. We modified from the title and big part of the rest of the manuscript taking into account the recommendations of the reviewers. We believe that changes substantially improve the manuscript and we hope it can be considered positively for publication in the journal.

In this revised version, we focused mainly on the Cuban experience in the control of childhood leprosy.

VERSION 2 – REVIEW

REVIEWER	<p>Reviewer name: Dr.Aparna Palit</p> <p>Institution and Country: All India Institute of Medical Sciences, Bhubaneswar, Odisha, India</p> <p>Competing interests: None</p>
REVIEW RETURNED	05-Aug-2019

GENERAL COMMENTS	<p>The manuscript is better than earlier; however, following changes are recommended:</p> <ol style="list-style-type: none"> 1.Abstract: Objective: We summarize the historical experience on childhood leprosy control in Cuba: The word historical should be replaced with past 2.Introduction section, 3rd paragraph: 8th line The diagnosis of a new case in children and adolescents shows the active circulation of bacillus: circulation should be replaced by transmission 3. Clinical manifestations, first paragraph, 1st line: The diagnosis of leprosy is essentially clinical ; Diagnosis of leprosy should be based on 'cardinal features of leprosy' 4.Clinical manifestations, 5th paragraph, 1st line: Indeterminate Leprosy (IL according to Ridley and Jopling classification)(18): Indeterminate leprosy is not a type in Ridley and Jopling classification system, it is part of Indian classification system <p>The various sections of the manuscript are not well linked and the reader has to search for information, making it unpleasant to read. It can be improved further with little more effort.</p> <p>Few grammatical and spelling mistakes are still there and need correction.</p>
-------------------------	--

REVIEWER	<p>Reviewer name: Peter Rohloff</p> <p>Institution and Country: Maya Health Alliance - Guatemala</p> <p>Brigham and Women's Hospital - USA</p> <p>Competing interests: None</p>
REVIEW RETURNED	10-Aug-2019

<p>GENERAL COMMENTS</p>	<p>The article has been well edited, and the focus on the review of the Cuban experience with pediatric leprosy is very interesting and appreciated.</p> <p>I have a few fairly minor comments:</p> <p>Abstract (and elsewhere) -recommend replacing “last 18 years” with the year range - I feel these discussion of national strategy and the conclusions here don’t follow from the rest of the abstract - I think this is because (see below) the sections of the paper on “strategy” and “cuba in context with the Americas” still need a bit of work to bring out the health system responses to leprosy</p> <p>Introduction Sentence on “leprosy not being a natinal health problem since 1994” - would be helpful for readers to cite if the 1/10,000 case threshold is that used in eradication programs or why that threshhold particularly is epidemiologically important</p> <p>“Reaction complications are rare” - maybe just clarify these are immune mediated reactions for people who aren’t familiar with leprosy pathology</p> <p>Clinical Manifestations In the section on clinical manifestation, I would suggest adding a Table about leprosy classification schemes and helping the readers out by more explicitly linking the different clinical entitites described (e.g TL IL LL) to the paucibacillary and multibacillary classification. Many readers will not be very familiar with classification schemes for leprosy, and they are a bit confusing. Also, I think the authors are using the 1996 WHO scheme for PB vs MB (just counting number of skin lesions rather than microscopic criteria) but it would be helpful to clarify this.</p> <p>I think the paragraph on children with leprosy in Cuba at the end of the clinical manifestations section might need to move into the epidemiology for flow, but perhaps not if the classification system can be better explained- A table of clinical manifestations in Cuba might also be an easier way to present this paragraph (number of children with PB vs MB distribution based on skin lesions, number with disabilities, “other manifestations” (myalgias), etc</p> <p>Epidemiology Data presented o 2000-2017, but abstract and intro talk about 2000-2018</p> <p>I think the statement about MB forms indicating active circulation in patients without treatment could be expanded - a good place to educate readers briefly about the dynamics of leprosy transmission and help to explain what the factors underlying this ongoing higher-intensity transmission in Cuba could be.</p> <p>Strategy for control I think timeline here could be helpful. It is unclear how these initiatives relate to the drop in leprosy in the 1990s vs ongoing maintenance surveillance. It would be nice for the authors to trace how the public health system responses correlate to epidemiological changes in the country and what—if any—changes are newly in place given the recent recognition of a shift to more MB forms.</p>
--------------------------------	---

	<p>In context with the Americas I think this section still needs some clarification. Cuban's overall incidence of leprosy is very low compared to, say, Brazil - what is working in Cuba and how could these strategies be used elsewhere? This question is posed in this section but not explicitly answered, rather the different comparative studies cites from Columbia, Brazil, etc seem to show similar patterns e.g. of intrafamilial disease transmission for example which is expected - I think what is missing is comparison of the public health systems responses.</p> <p>For example, is there something about the Cuban experience using IgM anti PGL1 screening that is novel and could be applied elsewhere? Is the major point here that Cuban system was using this assay to case find vs just being used in seroprevalence studies elsewhere?</p> <p>The conclusion has this - even when prevalence is low, helath education campaigns, regular and complete treatment, and contact tracing are important. But the details of how these strategies are operationalized in Cuba (under "strategy" and "in context with the Americas") could be better realized.</p>
--	--

VERSION 2 – AUTHOR RESPONSE

Reviewer 1. We have reviewed the grammar and tried to expand the explanations and improve the connections between the different sections in the final text

Reviewer 2. We have decided not to include a table that collects the clinical manifestations of the children diagnosed because we consider that the information presented would not be much more illustrative and could coincide, at least in one part, with the one collected in Figure 2. However, we decide to move that paragraph to the next section in order to improve the flow of information.

VERSION 3 – REVIEW

REVIEWER	<p>Reviewer name: Peter Rohloff Institution and Country: Maya Health Alliance/Guatemala Brigham and Women's Hospital/Boston Competing interests: None</p>
REVIEW RETURNED	02-Oct-2019
GENERAL COMMENTS	I have really enjoyed reading the successive versions of this paper and I think it is much improved. I recommend publication.

VERSION 3 – AUTHOR RESPONSE

The authors appreciate your comments and the hard work done in revising the manuscript. We believe that each of your comments and suggestions has allowed us to improve the quality of this work. We have considered your suggestions as time and we have made the necessary corrections.