Author's response to reviews

Title: Higher Incidence of Perineal Community Acquired MRSA Infections among Toddlers

Authors:

Alexis Mccullough (Alexis.Mccullough@utoledo.edu)
Melissa Seifried (Melissa.Seifried@gmail.com)
Xiaochen Zhao (xzhao24@buffalo.edu)
Jeffrey Haase (jeffrey_haase@mhsnr.org)
William J Kabat (bkabat@childrensmemorial.org)
Ram Yogev (RYogev@childrensmemorial.org)
Robert M Blumenthal (Robert.Blumenthal@utoledo.edu)
Deepa Mukundan (Deepa.Mukundan@utoledo.edu)

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Author's response to reviews: see over
The Editor,  
BMC Pediatrics  

Dear Editor,

I thank all the reviewers for their thoughtful review of my manuscript and their recommendations to enhance the data presented. The revised manuscript has additional data with statistical analysis as recommended by all reviewers. Statistical analysis of the data has revealed significant association between site of the infection and age group. In order to reflect this, the title has been revised to “Higher Incidence of Perineal Community Acquired MRSA Infections among Toddlers”

A point by point response to the concerns of the reviewers is given below.

Sincerely,

Deepa Mukundan, M.D,
2222 Cherry Street, Suite 2300,
Toledo, OH 43608.
Phone: 419-251-8039, Fax: 419-251-7715
Email: Deepa.Mukundan@utoledo.edu
Reviewer 1

Major Compulsory Revisions

1. Material and Methods, first paragraph: More data, such as the catchment population of Mercy Children's Hospital, the total number of outpatients during the study period and the total number of S. aureus (MRSA and MSSA) infections, need to be provided in order to assess the significance of the findings of this manuscript.

Response: The data is presented in Figure 1 and page 4 last paragraph under the heading “Results”.

2. Various comparative statements are used throughout the manuscript: Abstract, first line "a six-fold increase...", background, third paragraph "a recent six-fold increase...", conclusion, first line "the incidence of CA-MRSA infection is increasing...", but data compared to current findings are not presented. Comparison of current findings with previous ones should be more clear.

Response: Comparison data from 2002 was added and shown in Figure 1. The title and appropriate changes have been made in the text - Paragraph 3 under the heading “Background” – Page 3.

3. Discussion, second and third paragraph: Possible risk factors are discussed, but corresponding results to support this discussion are lacking. In fact, this study does not seem to be designed to identify risk factors, and so relevant statements (background, third paragraph) should be probably removed.

Response: I agree. The statements alluding to risk factors were removed from the manuscript – Paragraph 3 Page 3 under the heading “Background”; and Paragraph 2&3 on Page 6 under the heading “Discussion”.

Minor Essential Revision

1. Figure 1 should be integrated in Table 1, as it presents baseline characteristics of CA-MRSA patients.

Response: Old table 1 and old figures 2 & 3 were combined under new Table 1 titled Patient characteristics– Page 15.
Reviewer 2

Specific comments:

The title of the article refers to the increasing incidence of perianal MRSA infections; however there is no corresponding data in the text; the authors only report a six fold increase of MRSA infections; what does that mean in numbers. Is it possible to demonstrate this increase based on increasing case numbers during the previous years or month?

Response: New data added with Figure 1 and in background to explain the increase in pediatric MRSA infections during the same time periods for the year 2002 and the study year 2007. The title has been changed to reflect the significance found after statistical analysis.

Abstract vs. Background:
“A six fold increase in caMRSA infections....” (abstract) vs. “a six fold increase in the number of MRSA infections...” (background). I guess, the information in the background section is correct.

Response: The wording in the abstract (Page 2) has been altered to reflect the correct information given in the background (Page 3).

Materials and methods:
There is no demographic detail on the hospital. E.g. how many patients are treated....?

Response: That information has been added under the “Results” section – Page 4 last paragraph. I found that the narrative flows better if this data is placed in the results section.

Discussion:
One aim of the study was to define risk factors for caMRSA infections in children. However, I did not find definite calculations about risk factors and probabilities. Most probably the case numbers are to low for more detailed calculations. However, this is not stated in the text. Thus, the discussion about putative risk factors remains speculative.

Response: I agree and therefore the statements alluding to risk factors were removed from the manuscript – Paragraph 3 Page 3 under the heading “Background”; and Paragraph 2&3 on Page 6 under the heading “Discussion”.
Reviewer 3

**Major Compulsory revisions:**

1. Background p 3 second paragraph: Several reports show the migration of USA300 into hospital settings, why the claim about molecular differences between CA and HA strains are not true (anymore). Rephrase.

Response: I agree that the line between the molecular differences of CA and HA strains are blurring. I have added that information and references under background –page 3, paragraph 2. However, for the purposes of this study we needed to have a frame of reference and so we used the clinical criteria used by the CDC to define them. The text has been rephrased to include the definition we used for CAMRSA – which was based on clinical criteria published by the CDC (reference below).


2. Material and methods: For what antibiotics were susceptibilities obtained? CLSI guidelines? Please provide more information.

Response: Added under “Materials and methods” – Page 3, last paragraph.

3. How many of the children had underlying conditions overall? Or, how many children had no underlying conditions?

Response: 33% had no pre-existing condition (Page 5, paragraph 3). None of the children in the study had pre-existing condition that was serious enough to require hospitalization. All their problems were being managed in the outpatient setting.

4. There are several studies referring to infections in children with underlying conditions using epidemiological definitions such as community onset health care associated (CO-HCA)or healthcare associated community onset (HACO) because children with underlying conditions are likely to be more frequently exposed to the healthcare system. Antibiotic resistance to, for example, clindamycin has been greater for isolates from these infections. (There is no clindamycin resistance in this present study. Is clindamycin used for the treatment of pediatric CA-MRSA infections at this hospital?) Authors could expand on this and should make sure to compare to studies where underlying conditions are reported.

Response: None of the children in our study were hospitalized. All their problems were being managed in the outpatient setting. Children who are previously or recently hospitalized children are more likely to have a healthcare associated MRSA infection that is resistant to clindamycin and other classes of antibiotics. This is why using the clinical criteria as established by the CDC was important as it does not include any patient with healthcare-related risk factors.
Yes, our center currently uses clindamycin to treat pediatric CAMRSA infections and thankfully the CAMRSA strains continue to be susceptible to clindamycin. Please see response to question 1 also.

5. There is no statistical analysis even to compare results between age groups. Thus, the conclusion is not supported. Authors should add statistical analysis.

Response: Statistical analysis has been included. Age group associations are presented in Table 2.

Minor essential revisions:

1. ACME, pvl should be spelled out in abstract. I could not find anywhere in the manuscript where pvl was completely described using the correct gene name (lukSF-PV) or referring to the protein made. What was the rationale to choose the specific set of genes analyzed by PCR? Why was not cap8 included, for example

Response: ACME and pvl spelled out in abstract also. pvl has been changed to lukSF-PV throughout the manuscript. Rationale for selecting the gene sets was alluded to in background Page 3 paragraph 2 and discussed in the last but one paragraph (Page 6) under the heading discussion.

2. A further discussion on Diversilab rep-PCR vs. PFGE could be added. Was there a greater discrimination between strains using the PFGE? Did the authors believe the USA500 designation to a few "USA300" isolates to be incorrect given the fact that these strains were also ACME positive? It is curious that 25% of isolates of a specific USA300 subtype were cap5 negative. Was this followed up using primers targeting other segments of cap5? Did they have another cap?

Response: Diversilab information has been clarified in the new manuscript – Page 6, last paragraph under the heading “Discussion”. As for the question on cap5 we are conducting further studies to answer those questions.

3. Table 2. Add percentages

Response: Added where appropriate.

4. Figure 3 can be deleted

Response: I have included figure 2 (the new figure 3) in the new manuscript as it enhances the data shown in Table 4. However, this figure can be excluded if there is space constraint.