Author's response to reviews

Title: Syndromic Oral Clefts with Associated Anomalies: Findings in the Hungarian Congenital Abnormality Registry

Authors:

Andrea Sarkozi (sarkoziandrea@mac.com)
Diego F. Wyszynski (dfw@bu.edu)
Andrew E. Czeizel (czeizel@interware.hu)

Version: 2 Date: 13 May 2005

Author's response to reviews: see over
We thank the BMC Oral Health and Dr. Peter Mossey for the very insightful critiques to our previous version of the article. We have addressed all the issues that were raised and revised the manuscript accordingly. We believe that these changes have improved substantially the overall quality of the paper and we hope that it will be now acceptable for publication.

Critique: “The first thing that struck me about the summary is the chronological mismatch between the two studies that are compared in this paper, which leads to some problems in a field where new syndromes are being discovered and classifications regularly updated. This needs to be acknowledged. On reading further in the summary it is apparent the criteria differ also and e.g. it is reported that in the HCAR 11.2% had “schisis association” whereas none of the north eastern France sample were reported to have this disorder. This reveals a bigger problem which is highlighted in the first paragraph of the introduction, the second sentence in the introduction should read “the reported prevalence” and the fact that there is so much variation reveals the subjectivity which is applied to the classification of oral clefts. The objectives of the paper seem fine but with the big question being the validity of comparison with another study where the chronology is later, and the methodology may have been different; and therefore the categorisation and percentages in each category need to be viewed with scepticism.”

Response: We agree 100%. Initially, we had thought that the comparison of our study with that of Stoll et al. (2000) could be of interest to the readership, particularly after describing the differences between the two studies in terms of ascertainment, classification, categorization, and inclusion/exclusion criteria. However, and reading Dr. Mossey’s critique it becomes completely apparent, this is extremely difficult to do, if not impossible, given the large chronological mismatch between the two studies. Therefore, in the revised manuscript we refrain from comparing the HCAR to the study of Stoll et al. (2000). We believe that this important modification to the manuscript makes it much tighter.

We also modified the summary to reflect the first point raised by Dr. Mossey. Now, the Conclusions read: “Surveillance systems, such as the HCAR, provide useful information about prevalence rates of congenital anomalies in a population. However, in a field where new syndromes are being discovered and classifications regularly updated, these rates should only be accepted as provisional.”

Critique: “Methods: the first paragraph deals with the method of ascertainment and leaves a few questions unanswered. Some explanation of the missing cases is required, e.g. in the HCAR 86% of cases with CP were reported to the Registry and the other 14% need to be accounted for in a little more detail.”

Response: We reviewed the manuscript that provided these percentages and realized that the actual participation rates were 95% for CL/P and 90% for CP. These high rates are likely to be unmatched by other whole-country, population-based studies (In the CDC-sponsored National Birth Defects Prevention Study, the response rate is approximately
We do not possess information as to why those few cases with orofacial clefts were not reported.

Critique: “Classification: I note that the classification used to categorise was (a) unspecified MCA, (b) unidentified (but specified MCA) and (c) identified syndromes or associations. In the methods section it would have been good to record the number and percentage in each of these three categories to give the reader a sense of perspective. This also raises the question of a classification system and despite others attempting to introduce such a system for congenital craniofacial anomalies (e.g. Tolarova and Cervenka (1998)). I think this paper should be mentioned, with a discussion of the relative merits of their system and that used by the authors of this paper.”

Response: Done.

We also added a sentence to the Discussion: “This might explain our finding of chromosomal anomalies in only 4.7% of the cases with MCAs, significantly less than other population-based studies (e.g. Tolarova and Cervenka: 8.8%, Stoll et al.: 7.8%).”

Critique: “Comparison of HCAR data to north eastern France study: While it is recorded here that the information in the Stoll et al (2000) study were collected in a similar fashion and I am not sure this was the case and a little more detail would be helpful particularly since the objectives of this study is to “compare and contrast” e.g. it would be good to know whether the Stoll et al study was hospital or population based, whether there was multiple source ascertainment, the diagnostic method e.g. clinical dysmorphologist or paediatrician etc and the classification system that was used. I realise that some of this can easily be obtained by obtaining the original publication but it would be much more reader friendly if this details was summarised in this paper.”

Response: As mentioned before, the comparison of the HCAR data to those of the north eastern France study was deleted from this revised version of the manuscript.

Critique: “Results: The third paragraph in the results section is somewhat confusing – in that it could be expressed more clearly, and the OFD syndrome appears to be classified as an “unidentified” syndrome ??

Response: Done. The OFD syndrome was incorrectly included in the paragraph and, therefore, it has now been deleted

Critique: “There is also an apparent problem in the diagnosis of subjects with chromosomal abnormalities as the Stoll study revealed that these were more frequent in the north eastern France study.”

Answer: This has now been addressed in the Discussion of chromosomal anomalies.

We also modified the last paragraph to read:
“The description of component anomalies in cases with multiple congenital anomalies may help identify recognizable entities and delineate new syndromes. This knowledge can be used to better understand the needs of the population (ie, diagnosis, prognosis, counseling) and to develop policies for health care. In order to be successful, birth defects surveillance systems must include experienced dysmorphologists up-to-date with the latest diagnostic tools and definitions. It behooves the readers to note that in the HCAR dataset, which contains almost 66,000 congenital anomalies (4% of the total live births), almost 10% of these had more than one anomaly and more than half of these could not be allocated to a particular syndrome or association. This in itself points to the need for a global effort to improve the sensitivity and specificity of diagnosis. It is our hope that the information displayed in this paper will contribute to increase that awareness.”