Author's response to reviews

**Title:** Prevalence of anemia and deficiency of iron, folic acid, and zinc in children under 2 years of age and beneficiaries of the Mexican Social Security Institute.

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**Version:** 2  **Date:** 23 August 2007

**Author's response to reviews:** see over
Reviewer's report-1
Title: Prevalence of anemia and deficiency of iron, folic acid, and zinc in children under 2 years of age and beneficiaries of the Mexican Social Security Institute.
Version: 1 Date: 25 June 2007
Reviewer: Steven S Abrams
Reviewer's report:
General

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
Please discuss in more detail the use of a ferritin of 10 as a cut-off. Most recent work has used a value of 12. It would be best to provide the incidence of iron deficiency using both cut-offs in the paper.

The reviewer is right in pointing out that there is controversy around the best cut-off to use, particularly given the age group; some authors recommend a cut-off between 8-12 µg/l, looking for an equivalent of the 5th percentile according to age. The problem is that the variations in this age group may be as wide as 5-11. So, following the reviewer’s suggestion, we ran the analyses using both 10 and 12 µg/l, and observed a difference of around 4 percentual points. The major change that we would observe with a cut-off of 12 µg/l would be in the larger prevalence of anemia not associated with iron deficiency; however, these results did not show a significant change. Therefore, we decided to stick to the cutoff of <10 µg/l. We are including a table showing these contrasts, for the reviewer to look at (but not in the paper). We include these results in page 10, and discuss these findings on pages 17 and 18.

The inclusion of infants who are 1-5 months of age changes the analysis considerably. It would be best to analyze this group separately.
Infants < 2.5 kg at birth would also be best analyzed separately.

We agree on the importance of taking birth weigh (often used as a proxy for gestational age) into consideration when considering iron reserves at birth. However, in developing countries low birth weight (lbw) is most often the result of in utero malnutrition, and not the result of short gestational age. The prevalence of lbw in RR was 6.2%, and in IO it was 4.9%, so we considered that the influence these may have on the overall results did not grant a separate analyses, particularly as in this cross-sectional description of the overall micronutrient deficiencies found in this population we were not attempting to correlate any of them with specific risk factors. We also want to emphasize that our aim was to describe micronutrient deficiencies in the population younger than 2 years of age, so, although we present prevalences by age groups, we have eliminated the comparisons between them.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Discretionary Revisions (which the author can choose to ignore)
Do the authors have information about the usual length of breastfeeding in these populations?

At 4 months of age, 23.8% of children in RR and 46.2% in IO were reported to receive exclusive breast feeding. This prevalence was lowest in the Central Region (18.4% for RR and 32% for IO), and largest in the South (31.5% for RR and 48.4% for IO). We include this information on page 16 of the revised manuscript.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being Published

We have sent the article to a native English speaker, professional editor, before re-submission.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: 
I declare that I have no competing interests' below
### Table 3. Ferritin concentration and prevalence of iron deficiency, by region, age group and care regimen

<table>
<thead>
<tr>
<th>Region / Age groups</th>
<th>Regular Regimen (RR)</th>
<th>IMSS-Oportunidades (IO)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ferritin concentration µg/L</td>
<td>Prevalence of iron deficiency* %</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>95% CI</td>
</tr>
<tr>
<td>North</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>84</td>
<td>40776</td>
</tr>
<tr>
<td>6 to 11 months</td>
<td>268</td>
<td>138802</td>
</tr>
<tr>
<td>12 to 23 months</td>
<td>295</td>
<td>163476</td>
</tr>
<tr>
<td>Total North</td>
<td>647</td>
<td>343054</td>
</tr>
<tr>
<td>Center</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>147</td>
<td>55228</td>
</tr>
<tr>
<td>6 to 11 months</td>
<td>282</td>
<td>119726</td>
</tr>
<tr>
<td>12 to 23 months</td>
<td>348</td>
<td>177310</td>
</tr>
<tr>
<td>Total Center</td>
<td>777</td>
<td>352264</td>
</tr>
<tr>
<td>South</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>25</td>
<td>14352</td>
</tr>
<tr>
<td>6 to 11 months</td>
<td>239</td>
<td>79886</td>
</tr>
<tr>
<td>12 to 23 months</td>
<td>401</td>
<td>123384</td>
</tr>
<tr>
<td>Total South</td>
<td>665</td>
<td>217622</td>
</tr>
<tr>
<td>Mexico City and periurban area</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>64</td>
<td>30872</td>
</tr>
<tr>
<td>6 to 11 months</td>
<td>152</td>
<td>77977</td>
</tr>
<tr>
<td>12 to 23 months</td>
<td>195</td>
<td>88543</td>
</tr>
<tr>
<td>Total Mexico City and periurban area</td>
<td>411</td>
<td>197392</td>
</tr>
<tr>
<td>NATIONAL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Prevalence of iron deficiency calculated based on ferritin concentration.
<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number</th>
<th>Ferritin Level Median</th>
<th>Ferritin Level 95% CI</th>
<th>Ferritin Level Median</th>
<th>Ferritin Level 95% CI</th>
<th>Ferritin Level Median</th>
<th>Ferritin Level 95% CI</th>
<th>Ferritin Level Median</th>
<th>Ferritin Level 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 months</td>
<td>320</td>
<td>84.3</td>
<td>63.2, 105.5</td>
<td>9.0</td>
<td>5.6, 14.0</td>
<td>124</td>
<td>58.3</td>
<td>41.2, 75.4</td>
<td>25.2</td>
</tr>
<tr>
<td>6 to 11 months</td>
<td>941</td>
<td>28.6</td>
<td>23.9, 33.3</td>
<td>32.1</td>
<td>28.0, 36.5</td>
<td>374</td>
<td>53.4</td>
<td>21.7, 85.1</td>
<td>34.1</td>
</tr>
<tr>
<td>12 to 23 months</td>
<td>1239</td>
<td>17.8</td>
<td>15.1, 20.4</td>
<td>48.0</td>
<td>41.9, 54.2</td>
<td>861</td>
<td>34.0</td>
<td>17.9, 50.2</td>
<td>32.0</td>
</tr>
<tr>
<td>TOTAL NATIONAL</td>
<td>2500</td>
<td><strong>30.3</strong></td>
<td><strong>24.2, 36.4</strong></td>
<td><strong>37.0</strong></td>
<td><strong>33.6, 40.6</strong></td>
<td><strong>1359</strong></td>
<td><strong>41.1</strong></td>
<td><strong>20.0, 62.1</strong></td>
<td><strong>32.1</strong></td>
</tr>
</tbody>
</table>

* ferritin <12 µg/l

* Comparing between regions within each regimen, RR=0.004; IO=0.152.

* Comparing between regimens, national level, p=0.326.
Table 4. Iron nutritional status by hemoglobin and ferritin concentrations, by region, age group and care regimen

<table>
<thead>
<tr>
<th>Iron status</th>
<th>Total Regular Regimen n=2324 N=102247</th>
<th>North Region n=639 N=337,221</th>
<th>Center Region n=712 N=301,192</th>
<th>South Region n=574 N=193,493</th>
<th>Mexico City and periurban area n=399 N=190,340</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) IC 95%</td>
<td>n (%) IC 95%</td>
<td>n (%) IC 95%</td>
<td>n (%) IC 95%</td>
<td>n (%) IC 95%</td>
</tr>
<tr>
<td>Normal</td>
<td>1298 (57.0) 52.1, 61.7</td>
<td>375 (61.2) 50.3, 71.1</td>
<td>499 (67.7) 58.9, 75.4</td>
<td>207 (35.1) 32.4, 37.8</td>
<td>217 (54.7)</td>
</tr>
<tr>
<td>Iron deficiency without anemia</td>
<td>530 (22.0) 18.2, 26.3</td>
<td>168 (24.3) 17.8, 32.3</td>
<td>116 (17.0) 14.6, 19.8</td>
<td>169 (27.8) 16.0, 43.6</td>
<td>77 (19.7)</td>
</tr>
<tr>
<td>Anemia</td>
<td>496 (21.0) 17.1, 25.6</td>
<td>96 (14.5) 11.0, 18.8</td>
<td>97 (15.3) 10.1, 22.5</td>
<td>198 (37.2) 22.7, 54.5</td>
<td>105 (25.6)</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>248 (10.3) 8.6, 12.4</td>
<td>49 (7.1) 4.6, 10.9</td>
<td>59 (10.0) 7.0, 14.1</td>
<td>102 (17.8) 12.2, 25.4</td>
<td>38 (9.0)</td>
</tr>
<tr>
<td>Anemia due to other causes</td>
<td>248 (10.7) 8.0, 14.2</td>
<td>47 (7.3) 4.8, 11.1</td>
<td>38 (5.2) 2.5, 10.5</td>
<td>96 (19.4) 10.2, 33.7</td>
<td>67 (16.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Iron status</th>
<th>Total IMSS-Oportunidades n=1325 N=98150</th>
<th>North Region n=539 N=4195</th>
<th>Center Region n=479 N=10882</th>
<th>South Region n=307 N=83074</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) IC 95%</td>
<td>n (%) IC 95%</td>
<td>n (%) IC 95%</td>
<td>n (%) IC 95%</td>
</tr>
<tr>
<td>Normal</td>
<td>681 (60.73) 53.2, 70.2</td>
<td>294 (55.0) 46.8, 63.0</td>
<td>192 (42.9) 33.9, 52.4</td>
<td>195 (64.9) 54.6, 73.9</td>
</tr>
<tr>
<td>Iron deficiency without anemia</td>
<td>362 (20.5) 13.8, 29.2</td>
<td>132 (27.2) 21.0, 34.4</td>
<td>171 (39.0) 29.3, 49.6</td>
<td>59 (17.7) 10.9, 27.6</td>
</tr>
<tr>
<td>Anemia</td>
<td>282 (17.5) 13.2, 22.8</td>
<td>113 (17.8) 9.1, 31.9</td>
<td>116 (18.1) 8.0, 36.2</td>
<td>53 (17.4) 12.7, 23.4</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>137 (7.0) 4.7, 10.3</td>
<td>62 (10.5) 4.8, 21.4</td>
<td>57 (9.0) 4.2, 18.3</td>
<td>18 (6.6) 4.0, 10.5</td>
</tr>
<tr>
<td>Anemia due to other causes</td>
<td>145 (10.5) 7.4, 14.7</td>
<td>51 (7.3) 3.9, 13.2</td>
<td>59 (9.1) 3.6, 21.1</td>
<td>35 (10.8) 7.4, 15.7</td>
</tr>
</tbody>
</table>

N Population size (expanded sample)

*a Hemoglobin above the cut-off point for anemia and ferritin >= 10 µg/l
*b ferritin < 10 µg/l and Hb >= cut-off for anemia
*c Hb < cut-off for anemia
*d ferritin < 10 µg/l and Hb < cut-off for anemia
*e ferritin >= 10 µg/l and Hb < cut-off for anemia

Comparing nutritional iron status between regimens p=0.499
Comparing iron status between regions RR<0.001; IO=0.012
Reviewer's report-2
Title: Prevalence of anemia and deficiency of iron, folic acid, and zinc in children under 2 years of age and beneficiaries of the Mexican Social Security Institute.
Version: 1 Date: 12 July 2007
Reviewer: ann hill
Reviewer's report:
General
A nationwide health and nutrition survey of children under two years of age (n=35997) was conducted in Mexico between 1999 and 2001 and this article reports the iron, folate and zinc status of a sub-sample of children (n=4955) studied in 2000-01 who were beneficiaries of the Mexican Institute for Social Security. Benefits to families were delivered either through the ‘regular regimen’ (RR) for salaried non-government employees or though the ‘IMSS-Oportunidades’ (IO) for poor rural populations. The objective of the survey of the sub-sample was to determine the prevalences of anemia and iron, folate and zinc deficiencies at national and regional levels. Although socioeconomic, dietary, anthropometric, and health status data were collected, no attempt is made to relate these factors to regional differences in prevalence. This article is thus essentially a database with descriptive statistics.
Sampling method: The aim was to study a sample that was representative of the national population of beneficiaries.

The primary sampling appears to be sound, but the secondary sampling is beset with problems, only some of which the authors discuss. Of particular concern are the following:
a) the sub-sample was recruited from children attending clinic, rather than from the community

Attending to this concern, we have made specific clarifications to the sampling methodology in the Abstract, Introduction, Discussion and Conclusions sections of the revised manuscript. We have to keep in mind that the population that we wanted to represent in our sample was that which, being a subscriber of IMSS (either to RR or to IO), were users of the services. The reason behind this is that this is the population that may benefit from whatever policy implications or program implementation may derive from our study. In the case of IO, the lack of other medical services in localities covered by IO make it less likely that people living in those communities will use other services.

b) children with a history of illness in the previous two weeks were not included

The reviewer is right. The reason for doing so was due to the fact that children with recent or current acute infectious episodes will have their micronutrient status affected (particularly ferritin, Hb and Zn), thus giving a false estimate of the prevalence of deficiencies. Some studies have included the determination of acute phase infection reactants, like C Reactive Protein; we did not include this determination in our samples due to budgetary constraints. However, doing so would also have resulted in excluding children with present illness from the sample. We recognize this caveat in the Discussion.
c) the calculated sample size was not achieved, particularly in the South region (~50% achieved)

The reviewer is correct in pointing out this. The Southern part of the country is the less developed one, with the largest proportion of marginalized population, including that from indigenous origin. The under-representation that this region had in the total sample, for RR, was not statistically significant. However, for IO, the under-representation of this region may bear a weight. However, we also recognize that most of the social welfare programs, including food aid, are targeted to this area, and that may be the reason why the South region was not the worst off in terms of micronutrient deficiencies. We discuss these implications for the study in the Discussion section of the revised manuscript.

d) there was major under-representation of children aged 1-5 months and over-representation of children aged 6-11 months (e.g. 13% and 39% of the sub-sample were aged 1-5 and 6-11 months respectively compared with an expectation of ~21 and 25%)

The reviewer is correct in his appreciation. However, we have to point out that the study was not meant to have representativeness by age group (i.e., semester of life). Therefore, in the revised manuscript we have left out the statistical comparisons between age groups, keeping only those between regions and the country overall, as the sample was intended to represent these strata, and these may be the most meaningful in terms of policy decisions. We also want to point out that the group which was over-represented in the micronutrient sample was that between 12-23 months of age, as may be seen in the revised version of Table 1.

e) in the IO sample, there were many missing data for ferritin and zinc (~50% missing).

Actually, these were not missing data; due to budgetary constraints, we were not able to analyze all the samples, so we took a random sample of 50% for analysis, in all the regions except for the South, where we analyzed 100% of the samples because the sample size was only half of that estimated. We include this information in page 9 of the revised manuscript.

These limitations cast doubt as to the representativeness of the sub-sample and prevalences.

Taking into consideration the different points raised by this reviewer on this issue, on the revised manuscript we now present the analyses more in line with the study design, which intended to collect a sample representative of the regions and the nation as a whole. This does not solve the issue of the possible under-representation of the IO sample in the South region, which may introduce some bias. However, it should be noted that the
behavior of all other characteristics of this region, included anthropometric indicators, morbidity in the month previous to the interview, low birth weight, etc. (included in the larger study) was not different from the behavior that we observed for micronutrient status, in comparison with the rest of the country. These remarks are included on pages 15 and 16 of the Discussion section of the revised manuscript.

-------------------------------------------------------------------------------
Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
In the Discussion, the authors should add a), b) and e) above to their list of limitations and discuss the implications.

Points taken in the Discussion.

Details of the methods: These are mostly clear, apart from the following, which should be clarified:
a) prevalences calculated for the sub-sample were expanded to regional and national levels but it is not clear how this was done and no reference is given.

Expansion the larger population was done based on the number of primary sampling units for each stratum by region, divided by the number of primary sampling units that were randomly selected. This quotient was multiplied by the number of children assigned to each unit divided by the number of children who participated in the subsample for the micronutrient determinations. The analyses performed took into consideration the effect of the sampling design, running the “survey data analysis” routine in Stata. The corresponding references are included in the Analysis section.

In the Tables it is not stated what ‘N’ represents and the regional and age group N vary in each of the Tables, both in absolute terms and as proportions. Presumably N is linked with the expansion factor and perhaps with a weighting factor but until this is clarified the variability of N will remain puzzling.

N refers to the population size (expanded sample). “N” changes by age group and by region due to the fact that not all children had the same biochemical determinations. We have included comments to clarify these points on page 9 and in each of the corresponding tables.

b) recruitment needs to be clarified as in the Methods it is said to be from outpatient, vaccination and well-baby clinics but in the Discussion it is said to be from well-baby clinics

Patients were recruited from outpatient, vaccination and well-baby clinic services. We have specified this in the Discussion section of the revised manuscript.
c) the formula for adjusting Hb for altitude is unclear/incomplete

There was a typo on the formula, which has been corrected. The calculations were correct.

d) actions taken to ensure data quality should be added, particularly regarding blood sampling and blood analysis.

This has been clarified in the Methods section. Page 7.

Results: The following should also be reported:
a) number (%) of children excluded because of illness in the previous 2 weeks

This information is now included, in page 9 of the revised manuscript. Briefly, on the day that mothers were invited to participate with their children in the study, 15.7% of children in RR and 6.4% of children in IO had attended the clinic due to an illness episode. Additionally, in 20% of cases the mother reported some clinical sign of acute infectious disease (including acute diarrhea, cough, common cold or fever), so these children were not included in the sample.

b) number (%) of refusals, and whether they differed in their social background etc from those who participated

Unfortunately, we can not resolve this point; we do not have the required information on the children whose parents refused to participate. We present a comparison, in Table 1, between children who were included in the sample for micronutrient determinations and the sampled population, but we can only assume that those who refused to give a blood sample did not differed significantly from those who did.

c) the % of blood samples with missing data, and main reasons for loss

40% of children had one or another lab determination missing. The main reason was due to insufficient blood sample; only 3% of serum samples showed traces of lipids or hemolysis that precluded their analyses. Due to budgetary constraints, we were only able to analyze 50% of the samples collected in the North and Center region. The samples analyzed were selected at random. This is clarified on page 9 of the revised manuscript.

d) number (%) who had all four measurements (Hb, ferritin, folate and Zn).

As mentioned on page 9, 2,978 (60%) children had all four measurements taken.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
The following should be inserted/corrected:
• in the Abstract: ‘Methods’ should be positioned before ‘Results’
Correction made on the revised manuscript.

• throughout the manuscript, the comparison group should always be specified when making comparative statements (e.g. the sentence ‘Children with anaemia have higher percentages of folic acid deficiency.’ is incomplete as it does not indicate the comparative group
Correction made on the revised manuscript.

• throughout the manuscript, the term ‘fewer than’ should be used instead of ‘less than’ when referring to children or cases
Correction made on the revised manuscript.

• Background p2: ‘erythropoesis’ (not erithropoyesis)
Correction made on the revised manuscript.

• Background p2: ‘preterm’ (not premature)
Correction made on the revised manuscript.

• Methods p1: the sub-sample was taken from a larger sample of children aged 1-23 months, yet Hb cut-offs include children <2 weeks and children aged 2-3 weeks. If the sample starts at age 1 month, then these cut-offs should be removed from the text and Tables to avoid confusion.

We had included this information because, although not originally planned, we ended up having children under 1 month of age in the sample (n=50, 1.0% of the sample). Therefore, in the revised manuscript, we have substituted “1-6 months” for “<6 months”.

• Methods p2: ‘immunoradiometric assay’ (not essay)
Correction made on the revised manuscript.
• Results p2: ‘overall prevalence of iron deficiency’ (not global prevalence...)

Correction made on the revised manuscript.

• Results p4: the relevant region needs to be inserted in the sentence ‘prevalence of iron deficiency in was 23.4%’

We present the information on iron nutritional status by age groups, for RR and IO, in Figs. 1 and 2 (we considered it valuable to present information by age group, although we do not make the statistical comparisons by age groups, due to study design). Prevalence of iron deficiency for children 6-11 months old corresponded to 23.4%.

• Results p5 and p6: ‘significantly different when comparing RR with IO’ (not significant different..)

Correction made on the revised manuscript.

• Discussion p1: it is the age group 6-11 months that is notably over-represented (not those aged 12-23 months)

As shown on the revised Table 1, the over-represented group is the 12-23 month old

• Discussion p2: it is not possible to be confident that the sub-sample reflects the population that uses the IMSS health facilities, as children with recent illness were excluded and there is considerable under and over representation of certain age groups.

Please keep in mind that the sampling design was not meant to be representative of semesters of age, but rather of the under-2 year old population as a whole (we have addressed this issue in replying to a previous point). The largest proportion (80% of children in RR and over 90% in IO) of children in this age group were taken on the day of the interview to IMSS facilities seeking preventive services including vaccination and well-baby clinic. The possibility of bias due to the exclusion of children with recent or current illness from the micronutrient determination sample is included in the Results section (page 9) and discussed on page 15 of the revised manuscript.
<table>
<thead>
<tr>
<th>Age group</th>
<th>RR</th>
<th>IO</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 5</td>
<td>37.5</td>
<td>26.0</td>
</tr>
<tr>
<td>6 - 11</td>
<td>32.0</td>
<td>37.8</td>
</tr>
<tr>
<td>12 - 23</td>
<td>30.6</td>
<td>46.1</td>
</tr>
</tbody>
</table>

• Discussion p2: ‘sensitivity’ (not sensibility)

Correction made on the revised manuscript.

• Discussion p4: ‘children 6-11 months old..had a prevalence.. of 20.9%’ (not ‘children 2 years old.’)

Thank you for noticing this; we have made the corresponding correction (page 19, last paragraph).

• Discussion p4: it is not possible to claim that anaemia at 1-5 months reflects poor iron stores as well as poor complementary foods, as no data are presented to support this.

Correction made on the revised manuscript: Anemia at this early age has often been found to be related to a combination of the poor iron stores accumulated over the last trimester of pregnancy and to the poor quality of complementary foods, which may be either low in iron or in sources of highly bio-available iron.

• References: some errors exist e.g. spelling of names, and the references need careful checking.

Correction made on the revised manuscript.

When revising the manuscript, it would be helpful to insert page numbers.

Correction made on the revised manuscript.

--------------------------------------------------------------------------------------------------
Discretionary Revisions (which the author can choose to ignore)
Although identification of explanatory factors is not an aim of this article, it would be helpful to readers unfamiliar with Mexico to include a brief description of i) key contextual differences that exist among the North, Central and South regions, and ii) any differences in the service packages provided by RR and IO, including provision of haematinics.

The point has been taken in the Discussion section (page 15).

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being Published

We have sent the article to a native English speaker, professional editor, before re-submission.

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests.
Reviewer's report-3
Title: Prevalence of anemia and deficiency of iron, folic acid, and zinc in children under 2 years of age and beneficiaries of the Mexican Social Security Institute.
Version: 1 Date: 7 July 2007
Reviewer: Masahiro Hashizume

Reviewer's report:

General
This paper reported prevalence of anemia and of iron, folic acid, and zinc deficiencies in Mexican children under 2 years of age by region, age groups and care regimens. The topic of these micronutrient deficiencies is relevant and important. The data from a national level survey is a particular advantage of this study, given that that there are few large scale studies of these micronutrient deficiencies. I have some reservations about presentation of methods and results as described in specific comments.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Abstract: The order of subdivisions should be Background, Methods, Results and Conclusion.

Correction made on the revised manuscript.

2. Abstract, results: would clarify what you mean by “in direct relationship”.

Revised sentence: Iron stores were more depleted as age increased.

3. Abstract, results: not clear “Children with anemia have higher percentages of folic acid deficiency” than which population?

Revised sentence: Children with anemia have higher percentages of folic acid deficiency as compared with children with normal iron status.

4. Methods: The characteristics of out-patient clinic, vaccination clinic, and well-baby clinic are not clear. Although the characteristic of study subjects is described as “clinically healthy children” in abstract, I wonder if it is applicable to children who visited out-patient clinic.

On the day that mothers were invited to participate with their children in the study, 15.7% of children in RR and 6.4% of children in IO had attended the clinic due to an illness episode. Additionally, in 20% of cases the mother reported some clinical sign of acute infectious disease (including acute diarrhea, cough, common cold or fever), so these
children were not included in the sample. This information is now included, in page 9 of the revised manuscript.

5. Results: The authors may need to comment only on the important points in the text when results are presented in tables or figures. It is not necessary to repeat details in the text what is shown in the tables.

Point take in the revised manuscript.

6. Results: The authors performed numerous statistical tests to compare the prevalences between regions, age groups and care regimens, which is not appropriately defined in the objective of the study. Authors could consider omitting statistical tests which is not necessary according to the objective of the study.

The reviewer is right. In the revised manuscript, we have omitted comparisons by age groups, keeping only those warranted by the study design, i.e., between regions and between regimens.

7. Discussion: The authors mentioned the possible selection bias because of low response rate from the larger survey but not described the possible selection bias in relation that the subjects were chosen from children who visited health care facilities. It would be informative to know how much children who visited health care facilities were likely to be different from general population in the study area.

We are unable to provide this information, as the population that we wanted to represent in our sample was that which, being a suscriber of IMSS (either to RR or to IO), used the services. So, unfortunately, we do not have information about the general population. We have addressed this issue in the Introduction and Discussion sections of the revised manuscript.

8. Tables, overall: I feel difficult to follow what was compared by statistical tests, because numerous statistical tests were performed.

The information we present is rather ample and complex. Taking into consideration comments received during previous oral presentations of these data, we have tried to be as clear as possible in the footnotes to explain our statistical comparisons. Likewise, in the revised version of the paper we eliminated statistical comparisons between age groups, which should simplify the tables.
9. Tables 4 and 7 and Figures: The definition of iron deficiency is different from that in Table 3 and in the methods, which would confuse the reader. Could be changed to, for example, iron deficiency without anemia.

Following the reviewer’s suggestion, on tables 4 and 7 we changed “iron deficiency” for “iron deficiency without anemia”.

Minors Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

10. Tables, overall: not clear what “N” means. The tables should be self-explanatory.

N refers to the population size (expanded sample). We have included this definition in each of the corresponding tables.

11. Table 1: Media = Median?, IC 95% = 95% CI?

Correction made on the revised manuscript.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being Published

We have sent the article to a native English speaker, professional editor, before re-submission.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
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