Reviewer’s report

Title: Biomonitoring of Bisphenol A Level in Maternal and Umbilical Cord Blood Relevant to Birth Outcomes and Adipokine Expression

Version: 2 Date: 2 June 2011

Reviewer: Lynn Goldman

Reviewer’s report:

Major Compulsory Revisions:

There are a number of areas where the manuscript continues to require more work. Line numbers refer to the revised “track changes” version of the manuscript.

1. Recruitment and sampling methods: This is clearer but is it true that 100% of subjects who were approached for the study consented to participate in the study? Is this true and if not what was the response rate?

2. Laboratory methods: The additional information is helpful in terms of reproducibility of the analyses. No information is given about recovery from blanks, an important issue in light of the situation with regards to background levels of BPA in laboratories generally.

3. Data analysis: The authors used LOD/2 to impute for non-detects. First they should report the percentage of samples that were reported as ND and second use of LOD/sqrt(2) is less biased for imputing ND when data are lognormally distributed.

4. Regression analysis: Lines 180-185 are not completely clear. The dependent variables are LBW, SGA, adiponectin and leptin. I appears that independent variables for LBW and SGA outcomes were selected based on two prior studies of leptin levels and neonatal growth, as well as empirically based on the data analysis. The last sentence in this section needs to be rewritten. The text implies that the authors found no significant differences in LBW or SGA vis a vis smoking or socioeconomic status; this would be rather unexpected. Looking at Table 2, I wonder if what was intended was to state that smoking and socioeconomic status were not associated with whether mothers were in “high” or “low” BPA groups and that is why these variables were not considered as potential confounders?

5. Results: In the authors’ response to the editors they draw a nice u-shaped dose response curve. However they do not address the points that I made about the extent to which their findings actually follow a u-shaped dose response. To be clear, here is an alternative interpretation, how the dose response curves would appear to me, based on the modeling by quartiles in Table 2:

a. Male Neonates

i. LBW: Q1: Control, Q2 significant increase in LBW, Q3 significant decrease in LBW, Q4: significant increase in LBW. Shape of curve: Z-shaped
ii. SGA: Q1: Control, Q2 significant decrease in SGA, Q3 significant decrease in SGA, Q 4: significant increase in SGA. Shape of curve: U-shaped but “adverse” effect only at highest exposure quartile.

iii. Adiponectin: Same as SGA.

iv. Leptin: Same as LBW only the decreased level at Q3 is not significant.

b. Female Neonates

i. LBW: No effect

ii. SGA: Q1: Control, Q2 significant increase in SGA, Q3 no effect, Q 4: significant increase in SGA. Shape of curve: Z-shaped and “adverse” effect occurs at 2nd and 4th exposure quartiles.

iii. Adiponectin: Q1: Control, Q2 significant decrease in adiponectin, Q3 non-significant decrease in adiponectin, Q4: significant decrease in adiponectin. Shape of curve: “threshold”

iv. Leptin: Q1: Control, Q2 significant decrease in leptin, Q3 significant decrease in leptin, Q 4: significant increase in leptin. Shape of curve: U-shaped but “adverse” effect only at highest exposure quartile.

Minor Essential Revisions:

1. There is still need for a thorough edit of the manuscript.

2. Background: Lines 89-91 contain more description about BPA levels in adipose tissue however the authors refer to levels found in adipose as “accumulation”. It would be more accurate to refer to these as follows: “BPA has been detected in adipose tissue.”

3. Results: As noted above some of the odds ratios in Figure 2 are “elevated”: and statistically significant and these (except one, the OR for leptin at Q2 for males) are labeled. Others are significantly lower than one but are not labeled: (e.g., male, LBW, Q3; male, SGA, Q2 and Q3; male, adiponectin, Q2 and Q3; female, adiponectin, Q2 and Q3; and female, leptin, Q2 and Q3). For consistency perhaps all significant findings (high and low) should be labeled.

4. Discussion: On line 375 and following that, please look more carefully at the paper that is cited that provides evidence that glucuronidated BPA has been “demonstrated’ to cross the placenta and be deconjugated in the fetus. This has been reported in only one study and needs to be cited more cautiously . Also in general be careful about appearing to infer causality on the basis of single studies (or your own study) including in lines: 75-80, 281-284, and 289-291.

Level of interest: An article of importance in its field

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

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.