Author's response to reviews

Title: Hypothyroidism Among Military Infants Born in Countries of Varied Iodine Nutrition Status

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Author's response to reviews: see over
Dr. Alam:

I am writing in response to the peer review of our article “Hypothyroidism Among Military Infants Born in Countries of Varied Iodine Nutrition Status”. We greatly appreciate the time commitment and helpful feedback provided by both referees. Please find below, the point-by-point response to the concerns raised by each referee.

Referee 1 Concerns:

1. A closing sentence has been added to the background section, stating the study objective.

2. The DoD Birth and Infant Health Registry previously was titled the DoD Birth Defects Registry. A sentence in the background section has been modified to explain this fact.

3. The third sentence in the study population section was modified to better clarify that geographic location was an inclusion/exclusion criteria for this study. The n for each geographic region equals the total N for the study population. The percentages total 100.1% after rounding.

4. Estimated gestational age was based on ICD-9-CM codes in the 765 series. A sentence has been modified in the hypothyroid risk factors section to explain how estimated gestational age was defined and classified.

5. Modifications have been made to the manuscript to define the relationship between preterm birth and hypothyroidism as a non-direction association.

6. Unfortunately the study database does not allow determination of the outcome for each subject to define which are transiently vs. permanently hypothyroid. A sentence has been added to the discussion providing information regarding the timing of ICD-9-CM entries, supporting the assumption that the majority represent cases of congenital, rather than acquired, hypothyroidism, regardless of the ICD-9-CM code for hypothyroidism entered by the provider.

7. Please see explanation in #5 above.

8. This sentence has been altered to clarify the fact that birth location likely represents the location of iodine exposure that impacts thyroid function at the time of birth.

9. Our primary limitation regarding the association with parental race/ethnicity was only having race/ethnicity data for one parent, the active-duty sponsor. The parental race/ethnicity information was available for 96.7% of the infants, but always limited to that of only one parent.
If the mother was active-duty military or civilian, we still only had race/ethnicity data attached to the infant based on that of the active-duty sponsor. In addition, even in the setting of military maternal status, the military sponsor may be the mother or the father depending on the military status of the father and the parents’ decision as to whom to link the child’s medical benefits.

10. The term intervention was left in the manuscript as it was the authors’ desire to address, in addition to prevention measures, diagnostic screening and disease treatment.

Referee 2 Concerns:

1. The word change from differences to deficiencies was made.

2. The word change from sponsor to parent was made in the abstract. The definition of military sponsor was kept in the Methods section and the term sponsor used later in the manuscript, as it provides added information, specifically in cases in which both parents are military.

3. The referee raises a very interesting potential explanation for the finding in this study. We have added a sentence in the discussion to clarify that we are only able to examine the association between hypothyroidism and geographic location and not able to assess iodine intake or certain factors that may have impacted iodine intake. Specifically, we are not able to examine the potential impact of iodine-containing prenatal vitamin use. We have the ability to link prenatal vitamin prescriptions to the infant’s mother. However, the Department of Defense does not have a single supplier of prenatal vitamins and many different suppliers were used during the period of this study. Some of the suppliers had iodine in their prenatal vitamins and others did not. Interestingly, it appears that the minority of prenatal vitamins would have contained iodine. However, we are not able to determine the specific supplier for each prenatal vitamin prescription to determine which mothers had prenatal vitamins that contained iodine and which mothers did not.

4. Once again we agree with the premise of the referee’s suggestion, but do not feel that our data would allow the recommended analysis. Although separate ICD-9-CM codes exist defining congenital and acquired hypothyroidism, we do not have confidence that the codes were used appropriately and accurately by providers. We believe that the overwhelming majority of the hypothyroidism cases in this study are congenital cases, despite the frequent use of the ICD-9-CM code244 for acquired hypothyroidism by providers. We have added further explanation in the second paragraph of the Discussion section to clarify our concern.

5. We greatly appreciate the suggested article and have reviewed it and included reference where appropriate.

Once again we are very thankful for the input provided by each referee and would be happy to respond to any remaining concerns that they may have.
Sincerely,

Marcus M. Cranston, MD, MPH