Reviewer's report

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

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Reviewer: Connie Bish

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

Identification of risk factors associated with hypothyroidism and the influence of transient lifestyles during pregnancy to areas with varying levels of iodine is a novel yet important area of study. Military service is an example of a transient lifestyle, and the Department of Defense Birth and Health Registry is a unique dataset to study these associations.

Overall, this was a well written paper that was easy to read. The discussion points were well laid out and flowed in a logical order.

MINOR ESSENTIAL REVISIONS

BACKGROUND
1. There is no clear study objective stated in the background section. A brief statement should be the final sentence and is necessary for readers to understand where the study is headed.

METHODS
2. Reference 12 was cited as a source of information about the registry, but reference 12 is about “The Birth Defects Registry” and this paper refers to “The Birth and Infant Health Registry”. This is not clear without further details specific to the “Birth and Health Registry”. Please add brief clarifying information.

3. Since the number of military births identified by the regions included in the study only equals 96.8%, what was done with the other 3.2%? These are not mentioned in exclusion criteria. In table 1, the total of the sample by region does not equal 100%. Please account for how these observations were handled.

4. How was gestational age determined? Briefly mention whether clinical estimate or last menstrual period (LMP) or some other method was used.

RESULTS
5. The sentence “Hypothyroidism was increased in the setting of preterm birth …” implies directionality as written. Suggest rewording to a non directional associative sentence e.g., “Hypothyroidism was associated with preterm birth …” Further discussion reflected in comment #7 below.
DISCUSSION

6. The statement that most cases of hypothyroidism in this study are likely congenital is incongruent with the next paragraph’s discussion regarding transient hypothyroidism. Provide more definitional information. If the authors hypothesize transient congenital as the type most represented in their data, please describe how your data support that and what this means.

7. The paragraph that credits preterm birth as the “strongest risk factor” for hypothyroidism implies known directionality. While there is literature suggesting that preterm birth leads to incomplete thyroid gland development which can lead to transient hypothyroxemia, is it not also plausible that some unmeasured factors may lead to both congenital hypothyroidism (the type the study authors hypothesized was most prevalent in their data) and preterm birth? The data in this study do not clearly lend to conclusions of directionality – please discuss preterm and hypothyroidism as being associated only, or provide evidence based discussion of both directions.

8. In the next to the last sentence – “… exposure during the time of interest …” It would help the reader to have the actual time written rather than this general statement. What is the most important time for the iodine exposure? Is it the 1st, 2nd or 3rd trimester or the entire gestation period?

DISCRETIONARY REVISIONS

DISCUSSION

9. The discussion section that states this study found no association between race/ethnicity and hypothyroidism adequately referred to the limitation of the data regarding only having the military sponsor’s race/ethnicity. But since there were approximately 80,000 subjects who were in the military – presumably with known race/ethnicity – it would be interesting to present a subanalysis of these women testing for the race/ethnicity association. Was this considered/attempted?

CONCLUSIONS

10. Consider “prevention measures” or something similar rather than “interventions” in the second sentence.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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.