International Journal of Endocrinology and Metabolism
Volume 21 · Issue 1 · e131081

OPEN PEER REVIEW

Physical Development at School Entry in Children with Congenital Hypothyroidism Diagnosed by the National Program of Newborn Screening in Iran

Shahin Yarahmadi, Bahram Nikkhoo, Hesam Parvizi, Rozhin Motaghi, Khaled Rahmani

SUBMITTED	REVISED	ACCEPTED	DOI
22 Aug 2022	20 Nov 2022	21 Nov 2022	10.5812/ijem-131081

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

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1 Original submission

1 comment · 12 Oct 2022

Associate Editor

MAJOR REVISION 12 Oct 2022

The authors have reported the physical development of children with congenital hypothyroidism (CH) at age 6 in the national newborn screening program in Iran. This manuscript has serious faults and limitations, which must be addressed before I can review it.

Major Comments:
1) The design of this study should be clarified. In what year did the deliveries occur, and in what year was the final study conducted? How many patients with CH were born in each province? Were all children with CH included, or had you selected only a few? Why? Is the number of children with CH in Mazandaran lower than in other provinces? What is the definition of transient CH, and how long were patients with CH treated with levothyroxine? What were the levels of fT4 and TSH during the 6 years of follow-up? How did you adjust for confounding variables? Please include the findings of the adjustments in the "Results" section.
2) There are discrepancies between the findings in the "Abstract" and those in the "text" and "tables". Differences in height (115.6±5.9 vs 116.7±6.1) or HC (50.8±1.7 vs 51.1±1.7) may not be significant, and even if significant, they may not have any clinical significance. What are the differences in anthropometric data at birth and at 6 years in each province, and are these changes (Δ) significantly different between children with CH and control children? Please repeat all statistical analyses.
3) The Discussion section cannot be evaluated because of the above comments. This part should also be rewritten, and more limitations should be added.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Professor Azizi,
Editor-in-chief at International Journal of Endocrinology and Metabolism,

Manuscript ID: 131081
Title: Physical development at school entry in children with congenital hypothyroidism diagnosed by the national program of newborn screening in Iran

First of all, we would like to thank you and the respected reviewers whose technical comments helped us to improve and revise our manuscript. We made the required changes in the manuscript and highlighted them in the text; additionally, in the table below we have listed the revisions and the responses to the comments.

	Comments	Response
Reviewer 1:	1-The anthropometric indices was different between CH and control; What was the reason for this difference? Please explain.	Thanks for your attention. In fact, t*he anthropometric indices were not significantly different between CH and control although we observe a minimally difference (not significant) difference*.
	2-The present research was retrospective, written informed consent was obtained from the children's parents before the data collection. How and why, from 480 parents? It is a bit exaggerated.	In fact, it took about two hours to collect the study data of each participant because in addition to measuring the anthropometric indicators, the IQ of the students was also measured using Wechsler *scale*, and the results of the comparison of their IQ have been published in a separate article. Accordingly, for each child, in addition to obtaining informed written consent, an incentive was also given to the children for participating in the study.
	3-Children should be matched as socio-economically. How, you didn't meet children, How did you trust?	As much as possible, the children of the two groups were tried to be similar in terms of socioeconomic status, and for this reason, the children of the control group were randomly selected from among the children born in the same

		area (neighborhood or village).
	4-You have written that preterm babies were excluded but table 1 shows included????	Many thanks for your comments. Preterm children were included in our study. We modified the exclusion criteria.
	5-Was the measuring tool the same in all provinces?	The measuring scale used in all provinces was same. OMRON scale (A confirmed tool by WHO) is our tool to obtain the values of weight and height
	6-The same results are presented in the form of a table and text .	Some of the results under the tables were modified to prevent the repetition of results.
	7-The subject of the discussion has not been well processed and should be written more and the reasons for the differences should be fully explained.	The discussion section was rewritten and some references were added.
	8-It would be better to make comparisons based on drug dosage, first TSH, time to start medication.	Since the starting dose are same (5-10microgram/kg) for all diagnosed cases based on surveillance system we could not analyze the data based on dose subgroup.
	9-Finally the manuscript must be rewritten; author should explain the reason for each result.	We modified the manuscript according to the comments.
Reviewer 2:	1) The design of this study should be clarified. What was the year of deliveries and year of final study? How many patients with CH were born in each province? And were all CH children included or you had selected a few? Why? Number of CH in Mazandaran is less than other Provinces? What is the definition of transient CH, and how long CH patients were treated with levothyroxine? What were the levels of fT4 and TSH during 6 years of follow up? How did you adjust for confounding variables? Please include finding of adjustments in the “Results” section.	Children selected for this study born in 2009 and we measured their anthropometrics indices at the time of entry school in 2015-2016. It was clarified and highlighted in the methods. CH children were selected based on PPS methods not based on the number of children born. (the reason for lower samples in Mazandaran). Transient CH denoted to the CH children who did not treatment after three years and permanent CH is denoted to the children that need treatment after three years and usually throughout life. Unfortunately, we did not access to values of TSH

		and T4 of two groups at school entry. the definition of transient and permanent CH was also added to the method section.
	2) There are discrepancies between finding in the “Abstract” with those of “text” and “tables”. Differences in height (115.6±5.9 vs 116.7±6.1) or HC (50.8±1.7 vs 51.1±1.7) may not be significant; and even significant may not have any clinical significance. What are the differences in anthropometric data at birth and 6 years in each province and are these changes (Δ) significant between CH and control children? Please repeat all statistical analysis.	Many thanks for your comments. We rechecked the result section of the abstract and the text and did not any discrepancies. It should be noted that we mentioned the CI of measures in the text but we did not it in the abstract in order to prevent the number of words in the abstract. All analyses were conducted again and no difference was observed between what mentioned in the manuscript and new analyses.
	3) Discussion section may not be evaluated because of above comments. This part should also be rewritten and more limitations should be added.	Some limitations such as lack of TSH and T4 values in the time of study was also added.

With Warmest Regards,
Corresponding Author

2 Revision 1

0 comments

No public comments in this round.

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

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With Warmest Regards,
Corresponding Author

3 Revision 2

0 comments

No public comments in this round.