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OPEN PEER REVIEW

Medication Adherence of Children with Congenital Hypothyroidism in Iran: A National Cross-Sectional Study

Shahin Yarahmadi, Bahram Nikkhoo, Shiva Bararpour, Parisa Marabi, Khaled Rahmani

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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.

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1 Original submission

1 comment · 13 Jul 2024

Ladan Mehran Reviewer

MINOR REVISION 13 Jul 2024

In the current study, the authors investigated adherence to treatment among patients with congenital hypothyroidism born between 2019 and 2023 in Iran using national registry data and showed that medication compliance in about two-thirds of hypothyroid children diagnosed by national newborn screening is good. The following points should be addressed.

- In the introduction, the authors should mention the prevalence of CH in Iran to present its importance and the economic and social burdens of the disease on families and populations.
- The following changes in the order of paragraphs in the introduction would improve the manuscript.
- Line 52: "Prescribing thyroid hormone" should be replaced with Levothyroxine, not thyroid hormones; the drugs are synthetic, not hormones.
- Line 61: "At the global level, the studies conducted are minimal". Please give references for these studies.
- In the results section, all units should be mentioned in the figures and tables; e.g., in Figure 1, the unit of the vertical axis (%) should be indicated, and in Table 2, n (%) for each variable should be presented.
- In Table 3, in the multivariate analysis of the association between the studied variables and medical adherence, the authors selected Ardebil as the reference. Why?

Also, the authors should complete all the legends of tables and figures; e.g., in Table 3, the dichotomous levels of medical adherence should be defined. Each table and figure should be self-explanatory.

- Discussion: In the first paragraph of the Discussion, the authors should present their main findings (adherence and important factors), and then, in the second paragraph, they can continue with the importance of medical care and adherence in CH and compare their results with the previous literature. Therefore, change the first paragraph accordingly.
- The results of the univariate analysis showed that the educational level of the mother was a major factor in increasing adherence to treatment among hypothyroid children. However, in the multivariate analysis, maternal education was not a significant factor, although it yielded an odds ratio greater than 2.5 for good medical adherence, with wide confidence intervals. Please check for missing data for this variable, as a high rate of missing data might yield non-significant results, and discuss this in the discussion section. In lines 161-162, the authors said, "As shown in Table 3, CH type and place of residence were two significant factors associated with adherence when modeling the data". However, I think maternal education is very important (the high odds ratio and wide CIs show the effect and the low power of the statistical analysis due to sample size or missing data).

Grammatical mistakes

There are many grammatical mistakes throughout the manuscript, e.g.:

- Line 156: "Guillan and Hamadan with 156 90% and Yazd with 27.27 had higher and lower adherence among studied province"; the correct form is "Guillan and Hamadan with 90% and Yazd with 27.27 had highest and lowest adherence among the studied province".

- Lines: 81, 82 "and place of residence were collected using a checklist tailored to the variables 82 and objectives studied." Do the authors mean the study's objectives?

- The conclusion should be changed, as about two-thirds is correct instead of more than two-thirds in Lines 213: "The results of this study showed that medication adherence is good in more than two-thirds of hypothyroid children diagnosed through national newborn screening."

- In the conclusion, the authors should emphasize that about 30% of patients do not have suitable adherence to therapy; therefore, it is recommended to implement intervention plans, including educational programs,

together with active follow-up of patients to increase compliance.

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

Manuscript ID: 150329
Title: Medication Adherence of Children with Congenital Hypothyroidism in Iran: a national cross-sectional study

First, 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 point by point.

Reviewer	Comments	Response
Reviewer #1	¬ *In the introduction, the authors should mention the prevalence of CH in Iran to present its importance and the economic and social burdens of the disease on the families and populations.*	CH is one of the most important health problems in Iran. The average incidence of this disease in the country is 2.6 per 1000 live births. These sentences were added to the introduction.
	¬ *The following changes in the order of paragraphs in the introduction would improve the manuscript.* ¬ *Line 52 : "Prescribing thyroid hormone" should be replaced with Levothyroxine not thyroid hormones, the drugs are synthetic not hormones* ¬ *Line 61: "At the global level, the studies conducted are minimal". Please give any reference /references for these studies*	Line 52: the thyroid hormone was replaced by Levothyroxine. Line 61: In the literature review, we fund only one study that we cited it.
	¬ *In the results section, all units should be mentioned in the figures and tables e.g. Figure 1 unit of the vertical axis (%) should be indicated and Table 2 n(%) for each variable should be presented* ¬ *In Table 3 , multivariate analysis for the association between studied variables and medical adherence, the authors selected Ardebil as the reference??? Why?...* *Also the authors should complete all the legends of tables and figures e.g. Table 3 dichotomous level of medical adherence should be defined. Each table and figure should be self-explanatory.*	The unit in figure 1 (compliance) is percent that we added it to the title of figure. In table 2, n(%) of each group is mentioned in first row. Ardebil is selected because it has lower code in our dataset, and there is no any further reason. Dichotomous variable for treatment compliance is adherence below 6 and >=6 that we mentioned it in the text and in the table 2.
	¬ *Discussion; In the first paragraph of the*	-The discussion section was

	Discussion, the authors should present their main findings of the study (adherence and important factors) and then in the second paragraph, they can continue with the importance of medical care and adherence in CH and compare their results with the previous literature and. Therefore, change the first paragraph regarding this point. *¬ The results of the univariate analysis showed that the educational level of the mother was a major factor in increasing adherence to the treatment of hypothyroid children. However, in multivariate analysis, mother education was not a significant factor while induced more than a 2.5 odds ratio for good medical adherence, with wide confidence intervals. Please check for the missing in this variable as a high rate of missing data might yield non-significant results and discuss this in the discussion section.* *In lines 161-162 the authors said "As shown in Table 3, CH type and place of residence were two significant factors associated with adherence when modeling the data" However, I think mother's education is very important (high odds ratio and wide CIs show the effect and low power of statistical analysis due to sample size or missing data)*	revised as your comments. -We have no any missing data in our analysis. We rechecked the dataset. You can see the table 1 for this fact. -You are right. Mother education is a main influencing factor and higher sample size could lead to significant P value. Mother education is an important factor and we discussed it in different sections of results, discussion and conclusion.
	Grammatical mistakes *There are many grammatical mistakes all over the manuscript e.g.* *¬ Line 156: "Guillan and Hamadan with 156 90% and Yazd with 27.27 had higher and lower adherence among studied province", the correct form is "Guillan and Hamadan with 90% and Yazd with 27.27 had highest and lowest adherence among the studied province"* *¬ Lines: 81, 82 "and place of residence were collected using a checklist tailored to the variables 82 and objectives studied." Do the authors mean the study's objectives??*	These mistakes were corrected. We mean study's objectives. The sentence was revised. (many thanks for your attention).
	¬ The conclusion should be changed as about two-thirds is correct instead of more than two-thirds in Lines 213: "The results of this study showed that medication adherence is good in more than two-thirds of hypothyroid children diagnosed through national newborn screening."	It was revised and highlighted as the comment.
	¬ In the conclusion the authors should emphasize on the point that about 30 % of patients have not suitable adherence to therapy, therefore, it is recommended to implement intervention plans, including educational programs, together with active follow-up of patients to increase compliance	**It was revised and these sentences are replaced:** Since nearly 30% of patients still do not adhere adequately to their therapy, and considering that in most cases

		the treatment period is long, it is recommended to implement intervention plans, including educational programs, together with active follow-up of patients to increase compliance.

With Warmest Regards,
Dr Khaled Rahmani,
Corresponding Author

2 Revision 1

1 comment · 21 Jul 2024

Ladan Mehran Reviewer

ACCEPT 21 Jul 2024

The authors addressed the suggested comments; however, the manuscript needs English language editing.