

## Author's response to reviews

**Title:** Risk factors of thyroid abnormalities in bipolar patients receiving lithium: a case control study.

### Authors:

Seyed Ali Ahmadi-Abhari ([ahmadiab@sina.tums.ac.ir](mailto:ahmadiab@sina.tums.ac.ir))

Padideh Ghaeli ([mmppg@yahoo.com](mailto:mmppg@yahoo.com))

Dr Fanak Fahimi ([riazifahimi@yahoo.com](mailto:riazifahimi@yahoo.com))

Fatemeh Esfahanian ([f\\_esfahanian@yahoo.com](mailto:f_esfahanian@yahoo.com))

Hasan Farsam ([farsam@ams.ac.ir](mailto:farsam@ams.ac.ir))

Ahmad Reza Dehpour ([Dehpour@medscape.com](mailto:Dehpour@medscape.com))

Issa Jahanzad ([jahanzad@sina.tums.ac.ir](mailto:jahanzad@sina.tums.ac.ir))

Zinat Nadya Hatmi ([hatmizn@sina.tums.ac.ir](mailto:hatmizn@sina.tums.ac.ir))

Simin Dashti ([dashtikhalili@yahoo.com](mailto:dashtikhalili@yahoo.com))

**Version:** 4 **Date:** 28 Apr 2003

PDF covering letter

Dear editor,

I would like to thank for the very good comments on the manuscript entitled "Risk factors of thyroid abnormalities in bipolar patients receiving lithium: a case control study."

In response to your E-mail regarding "decision on my manuscript" please find the revised form as follows:

Referee 1:

Compulsory revisions:

1) Page 6, last two lines and page 7 first two lines: replaced by: With regard to thyroid function Rybakowski et al reported higher activity of lithium sodium counter-transport (LSC) in patients with higher TSH from a group of lithium-treated bipolar patients [17]. In the whole group and in female patients LSC was negatively correlated with LR [17]. Johnston et al found lower LRs in patients with side effects including hypothyroidism [14]. "

2) Valle et al (ref 29) was omitted. Page 7, lines 19 to 22 were replaced by: "Although Perrild et al reported no gender difference with regard to goiter and thyroid volume [28], several investigators showed higher incidences of lithium-induced thyroid abnormalities in women [26,27,28,29] which is in agreement with our findings. For instance, Johnston and Eagles reported a higher prevalence of clinical hypothyroidism in women [30]."

3) Conclusions rephrased as: " This study showed that LR could not be used as an indicator or a diagnostic tool for thyroid abnormalities. We suggest that monitoring thyroid size and function should take into account patient's gender, since being a female may be a risk factor to develop thyroid abnormalities. Further studies are needed to confirm our findings."

4) misprint: "anhedonya" (page 3, line 7) was corrected as "anhedonia";

On page 4, in the Patient selection section of Methods the first sentence changed as: "Patients with bipolar disorder, admitted at Roozbeh Mental Health Hospital, who did not receive any drug(s) affecting thyroid or TFT were enrolled in the study. "

The sentence "Patients with no significant difference in .... were selected." was replaced by (page 4, lines 11 to 13) " All the patients received equally similar doses of lithium. Additionally there was no significant difference in the number or the dose of other psychotropics (including benzodiazepines and haloperidol) among the patients."

"Pregnant women were excluded of the study" (page 4, line 14) was corrected as "Pregnant women were excluded from the study".

5) In the Sampling section (page 4, line 20), "12 ±1 hours after the last dose" rather than "at least 11 hours" was indicated.

Discretionary revisions:

1) Page 7, line 11:" Among potential sources of discrepancies regarding LR and side effects, possible ethnic differences may exist as reported by Strickland et al [24]." was added to the discussion section.

2) Page 7, last two lines and page 8 lines 1 to 8 were added at the end of the discussion section: "Bocchetta et al reported female gender and presence of thyroid autoimmunity as risk factors for developing lithium-induced thyroid abnormalities in a cohort study [31]. Environmental (iodine deficiency) or intrinsic (autoimmunity) risk factors may inhibit compensatory mechanisms in most patients and lead to thyroid dysfunction [31].

Probably, iodine deficiency does not play a significant role in thyroid abnormalities in Iran due to universal salt iodization since 1989 [32]. According to the report of Heydarian et al who conducted Tehran Thyroid Study, the frequencies of AbTPO+ and AbTG+ (antithyroid antibodies) were 15.9% in women versus 8.3% in men ( $p < 0.001$ ) and 21.5% in women versus 11% in men ( $p < 0.001$ ), respectively [33]. Therefore, the higher rate of

thyroid abnormalities in females observed in this study may be due to the autoimmunity effects.”

Editorial comments:

Confirmation of ethical approval was mentioned in the Methods section: Page 4, line 16.

The manuscript was edited to improve the English used. I hope it would obtain your satisfaction.

Although I tried my best to crop fig. 1 as closely as I could, white border still appears around it (this is because of the white background). Please let me know if there is any problem, so that I would correct.

I look forward to hearing from you soon.

Sincerely yours,

Fanak Fahimi, Pharm D, BCPS.

.