The impact of thyroid autoimmunity on IVF/ICSI outcome: re-evaluation of the findings

Sir,

It is with great interest that we read the work by Busnelli et al. published in the June issue of Human Reproduction Update (Busnelli et al., 2016). The authors designed and conducted a systematic review and meta-analysis on the outcome of IVF/ICSI cycles in relation to the presence or absence of thyroid autoimmunity (TAI). This is an interesting clinical question, though attempts to address it in the past did not show consistent results (Toulis et al., 2010; He et al., 2016).

The present meta-analysis presents some points that have to be further clarified. First, the primary outcome of the meta-analysis was live birth rate (LBR) per woman, defined as the number of deliveries that resulted in at least one live birth. However, the definition of LBR is not fully clarified, as it is unclear if the denominator is biochemical pregnancy or clinical pregnancy (the latter needing further definition). Similarly, secondary outcomes are not clearly defined (fertilization rate, implantation rate). Second, careful observation of Fig. 2 reveals a discrepancy in the data extraction phase. Specifically, the LBR in women with TAI in a study from our own group (Mintziori et al., 2014) is expressed in live births per woman that underwent IVF, whereas the LBR of women without TAI is expressed in live births per woman that has achieved clinical pregnancy after IVF. This, unavoidably, leads to a miscalculated odds ratio.

In an effort to provide a better insight, we recalculated the primary outcome, after correcting the data that were entered from our study. It should be noted that after this new analysis, the heterogeneity has significantly reduced ($I^2 = 41\%$ from $66\%$, $P = 0.1$). The reduction in LBR in women with positive TAI compared with women with negative TAI remains significant, though marginally (OR 0.73; 95% CI 0.54–0.99, $P = 0.04$). Of note, Mintziori et al. (2014) was not included in the secondary outcomes, though reporting in detail oocytes derived and biochemical pregnancies.

In conclusion, the meta-analysis by Busnelli et al. (2016) is a nice effort to systematically review the evidence on the association of the presence of TAI and IVF/ICSI outcome. Even after our re-analysis, there is a significant reduction in LBR in women with TAI, and we do agree with the authors that these finding should be discussed with all women with TAI undergoing ovarian stimulation for IVF/ICSI, though further evidence is needed before any call of action for these women.

Conflict of Interest

None declared.

References


Reply: The impact of thyroid autoimmunity on IVF/ICSI outcome: re-evaluation of the findings

Sir,

We would like to thank Mintziori et al. for their interesting comments and to apologize for our inaccuracies. In our meta-analysis (Busnelli et al., 2016a), the live birth rate (LBR) per woman was defined as the number of deliveries that resulted in at least one live birth divided by the number of clinical pregnancies. These data, as reported in the ‘data extraction and analysis section’, should be considered as pregnancies diagnosed by ultrasonographic intrauterine visualization of one or more gestational sacs. As correctly stated by Mintziori et al. (2016), we wrongly extracted data from the study of their group (Mintziori et al., 2014) and, as a consequence, we erroneously calculated the LBR in women with thyroid autoimmunity (TAI). We would like to thank Mintziori et al. for recalculating the primary outcome, after correcting the data that were entered from their study. The recalculated LBR (OR 0.73; 95% CI [0.54–0.99], $P = 0.04$) should now be considered as correct. The Journal has published a Corrigendum correcting all mistakes (Busnelli et al., 2016b).

As for secondary outcomes, clear definitions are not systematically reported in the selected studies. In general, for the implantation rate (IR), we used the definition reported by Lukaszk et al. (2015); i.e. the number of sacs with fetal heart beat divided by the total number of embryos transferred. Fertilization rate was defined as the number of oocytes with two pronuclei (2PN) per oocyte injected (for ICSI) or inseminated (for conventional

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IVF). This information could unfortunately not be retrieved from most of the selected studies, including the contribution from Mintziori et al. (2014).

Finally, it is worth noting that the above-reported adjustments have not resulted in any change in the overall findings or the conclusions of our review.

Conflict of interest
None declared.

References


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