Maternal thyroid function and child IQ

We read with great interest the Article by Tim Korevaar and colleagues[1] showing that both high and low maternal free thyroxine in early pregnancy are associated with a significant decrease in child intelligence quotient (IQ). We previously reported that thyroid function in early pregnancy in Japanese women, who generally have sufficient iodine intake, had no relevance to parameters in neonates, scores of fetal maturation, or child development.[2]

Free thyroxine increase in early pregnancy is a physiologically adaptive change induced by circulating asialo-human chorionic gonadotropin[3] and is associated with severity of morning sickness.[4] Typical cases are characterised by gestational thyrotoxicosis and usually accompanied by hyperemesis gravidarum. Increased free thyroxine is often complicated by maternal malnutrition. Early fetal brain development might be affected by maternal nutrition and thus decreased IQ should also be assessed in relation to the possible presence of maternal nutritional disorders.

We declare no competing interests.

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2 Orito Y, Oku H, Kubota S, et al. Thyroid function in early pregnancy in Japanese healthy women: relation to urinary iodine excretion, emesis, and fetal and child development. *J Clin Endocrinol Metab* 2009; **94:** 1683–88.
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Authors' reply

We thank Nobuyuki Amino and Akane Ide for their comments about our recent Article.[1] The authors from the Kuma Hospital in Kobe, Japan, first reference their study of 544 pregnant women, in which they did not identify an association between early pregnancy maternal thyroid function and offspring neurocognition or thyroid function.[2] In two recent studies in much larger populations, we showed that maternal thyroid function is associated with offspring neurocognition (n=3839) and offspring thyroid function at birth and during childhood (n=4273).[1,3] Apart from differences in statistical power between our studies and the Japanese study, methodological differences could account for the different results, since we did regression analyses on the continuous exposures and outcomes, and took into account non-linearity.[1, 3] Amino and Ide suggest that hyperemesis gravidarum could potentially confound the association of high maternal free thyroxine with reduced offspring intelligence quotient (IQ),[1] for example via an increase of human chorionic gonadotropin (hCG) and stimulation of maternal free thyroxine on one hand, and via potential maternal malnutrition and effects on offspring IQ on the other. In our recent study we showed that after additional adjustments of the analysis for the association of high maternal free thyroxine (95th percentile) with child IQ for self-reported frequencies of vomiting, nausea, acid reflux or belching, and maternal hCG, the effect estimate for mean IQ of offspring from mothers with high free thyroxine was less than 0·1 point lower as compared with the original model (β change −3·5%). This finding shows that hyperemesis gravidarum is not a plausible confounder in the association of high maternal free thyroxine with offspring IQ. These results are in line with the conclusions of a recent systematic review, showing that there are slightly positive, rather than negative, effects of nausea and vomiting during pregnancy on pregnancy or child outcomes, including IQ.[4]

We declare no competing interests.

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Drug approvals in India

In their Comment, Atul Luthra and Anoop Misra[1] group together three distinct classes of drugs with different development and regulatory histories. We would like to respond with respect to the development of saroglitazar.

Saroglitazar is a rationally designed, novel drug developed with 12 years of intense scientific efforts and extensive preclinical[2] and clinical[3,4] investigations. Differentiating it from other peroxisome proliferator-activated receptor (PPAR) α and γ agonists, it has predominant PPARα and moderate PPARγ activity, which might result in advantages such as absence of markers of cardiac abnormalities, oedema, weight gain, and liver toxicity. Saroglitazar has been approved and marketed