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Importance of thyroid hormones in intrauterine programming

Saleh Zahediasl [1*]

[1] Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

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The editorial draws the attention again on the importance of thyroid hormones in development particularly during fetal life. This is important from basic as well as clinical points of view.

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Cross-sectional studies in humans and experimental data from animals have shown that a disturbed intrauterine environment can lead to morbidity in adult life. The phenomenon is known as Barker's theory, which was established almost 25 years ago (1-4). This concept has also been termed developmental programming (5), intrauterine programming (6), fetal programming (7), prenatal programming (8), and developmental origin of health and disease (DOHaD) (4) by different authors. Previous studies have revealed the effects of different types of alteration of the uterine environment on adulthood disease. Changes in intrauterine conditions can be due to malnutrition (9, 10), oxygen delivery capacity of the placenta (11), stress (12), and endocrine disorders (13). Among the endocrine disruptions during fetal life, thyroid abnormalities can cause a wide spectrum of morbidities during adult life. This is because thyroid hormones are crucial for development, differentiation, and metabolism (14).

The fetal thyroid gland matures by 11–12 weeks of fetal age and starts to secrete the hormones by 16 weeks (15). During this period, the demands of the developing fetus for thyroid hormones are met by the maternal thyroid (14). During fetal life, thyroid hormones can have significant impacts on different physiological characteristics of neonates as well as the offspring. The effect of fetal hypothyroidism on brain development is very well established (16), and it has been suggested that this can precipitate abnormalities in the cardiovascular development and function (17) and reproductive system (18) of the offspring. Evidently, the role of thyroid hormones on the development of muscle is also very important. In an animal model study in rats, it was shown that hypothyroidism during skeletal muscle development suppresses the transformation of myosin heavy chain isoforms (19). In another rat study, it was shown that propylthiouracil administered to mothers during pregnancy suppressed thyroid hormone levels in both the mother and the fetus. This led to a decreased response of the aorta rings (in vivo) of offspring to KCl and phenylephrine at the time of adulthood, and appears to be due to changes in smooth muscle structure in the intima (20). Furthermore, there are signs that the function of the endothelial cells might also be altered (data to be published). In a very recently published study, we showed that hypothyroidism induced during pregnancy affects both the mother and the fetus, leading

* *Corresponding author at:* Saleh Zahediasl, Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. Tel:+98-2122432500, Fax:+98-2122416264
E-mail: zahedi@endocrine.ac.ir

to abnormality of the glucose (in vitro) and reduced insulin secretion capacity of isolated islets (in vitro) in the male offspring (21).

It appears that fetal hypothyroidism can affect intrauterine programming more extensively than is believed. Further elucidation of this phenomenon will require extensive epidemiological and experimental studies.

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