

Maternal Iodine Deficiency and Late Outcomes in Child's Development

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Iodine is a fundamental component of thyroxine (T4) and tri-iodothyronine (T3), thyroid hormones which are essential for the natural growth and development of the child. Pregnant women are required to generate higher amounts of thyroid hormones in order to meet both their own and their children's needs, therefore iodine intake should be enhanced by over 50% during this period. The normal neurodevelopment of the fetus is made possible through sufficient amounts of T3 available in the fetal brain, which are derived from the mother's own free T4. Low levels of maternal free T4 that can be witnessed in iodine deficiency contribute to the poor neurodevelopment of the fetus. The most severe outcome of maternal iodine deficiency is, without doubt, cretinism. This review is therefore meant to highlight the necessity for more rigorous investigations into the extent and importance of maternal iodine deficiency in the child's development.

Keywords: iodine deficiency, thyroxine (T4), tri-iodothyronine (T3), cretinism

Iodine is an essential constituent of the thyroid hormones, thyroxine (T4) and tri-iodothyronine (T3), which are crucial molecules for the baby's physiological development of the brain [1]. Maternal iodine deficiency results in serious consequences in the fetus, which range from goitre to hypothyroidism, retarded growth and general developmental delay [2]. Moreover, infant mortality is highly increased as a result of iodine deficiency, which makes up the main preventable origin of mental retardation in children [3]. It has been shown since long that iodine prophylaxis limits the development of goitre in children [4], while the introduction of iodised salt has unmistakably decreased overall infant mortality rates as well as the proportion of cretinism cases [5]. However, despite remarkable improvement over the last couple of decades, iodine deficiency remains one of the most frequent micronutrient deficiencies worldwide [1].

The Role of Iodine in the Human Body

It is well known that iodine deficiency is the primarily preventable cause of mental retardation in newborns [6]. Iodine can be present in water (especially seawater) and in food in variable quantities, depending on the type of soil in which fruits and vegetables grew, whether fertilizers have been used and on the irrigation [7]. The highest content of iodine can be found in seaweed and in fish, followed by dairy products and white bread [2].

After ingestion it is absorbed from the stomach and duodenum and together with the iodide that remained after deionization of the thyroid hormones, forms the extrathyroidal pool of inorganic iodide [8]. Iodine is mostly used by the thyroid to synthesize hormones by binding it to the tyrosine residues of the molecules of thyroglobulin, forming monoiodotyrosine (MIT) and diiodotyrosine (DIT) that later combine to create triiodothyronine (T3) and thyroxine (T4) [9].

Although iodine is found primarily in the thyroid gland, it can be also observed in various tissues, such as the salivary glands, mammary glands and the gastric mucosa. In the mammary glands, apart from its role during breast feeding, iodine has antioxidant properties, protecting the breast against free oxygen radicals [10]. About 90% of the excess iodine is eliminated by the kidneys and the rest is excreted in the sweat and feces [7].

The Impact of Iodine Deficiency on the Pregnancy and the Newborn

During gestation, the iodine demand is higher due to certain changes that occur in the maternal organism, such as the increase of estrogen levels that lead to higher thyroxine-binding globulin (TBG) serum concentrations that furthermore cause an accelerated production of thyroid hormones. It has also been observed an increase in the excretion of iodine due to glomerular hyperfiltration and higher levels of human chorionic gonadotropin (hCG) that have a direct stimulatory effect on the thyroid [8]. These changes, associated with an inadequate supply of iodine during pregnancy can lead to miscarriage or still birth of the fetus, and an increased perinatal and infant mortality [9].

It has been proven that the iodine deficiency that occurs during gestation can cause endemic cretinism, neonatal goiter and congenital disorders [7]. There have been defined two types of endemic cretinism, a neurological one and a myxedematous form. The neurological form is believed to be caused by early gestational iodine deficiency and it is defined by severe cognitive impairment, deafness, pyramidal tract syndrome with paresis and muscle spasticity essentially in the lower limbs [7]. The myxedematous form is associated with mild mental

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retardation, severe growth retardation and hypothyroidism [7].

Maternal Iodine Deficiency and Late Outcomes in Child's Development

It is a well-known fact that iodine deficiency during the first trimester of pregnancy can have a big impact on the baby's neurological and behavioral development, if the mother does not receive adequate supplementation. During this period, the presence of the fetus stimulates the mother's thyroid to produce an excess of hormones, especially T₄, at the same time keeping the TSH levels in the normal range [6]. This effect occurs due to high levels of serum hCG and other related molecules, which replace the mother's TSH, to the point of suppression and even thyroid hormone resistance [11, 12]. The increase of maternal fT₄ during the first trimester of pregnancy appears in order to provide the fetus with the means to produce its own T₃, which is essential for the development of their brain and neural network [13, 14].

Prior studies have shown that children born from mothers who didn't receive the appropriate amounts of iodine during pregnancy, are very likely to develop a wide spectrum of conditions, such as deafness, congenital abnormalities, cretinism, behavioral and neurological delay, mental retardation, as well as attention deficit and hyperactivity disorder [6, 15]. Also, the idea that these children are at risk of developing autism spectrum disorders is supported by several recent papers stating that pollutants and other substances that have the potential to inhibit the mother's thyroid function during pregnancy, could lead to such conditions in their offspring [16, 17].

The first symptoms of neurobehavioral delay that can be observed in these children have been studied at the age of 18 months [18], using the Brunet-Lezine scale, which is comprised of 4 parts, testing the motor coordination – both fine and gross, language skills and socialization. Results indicate that children born from mothers who have received iodine supplementation during the first trimester are more likely to have a normal development, in comparison to those born from mothers that started receiving the treatment in the second or third trimester, or even at the end of pregnancy [18].

Later on during a child's development, the effects of iodine deficiency can be observed by measuring the IQ or school performances. At this stage, the deficit can come either from the gestation period, or from the insufficient iodine intake by the child, especially in areas where there is a documented natural iodine deficiency [9, 19, 20]. Prior analyses have shown that the IQ of children with iodine deficiency tend to have their mean IQ 13.5 points lower than the average IQ of those who have a sufficient iodine intake [15]. At the same time, in terms of performances in school, all the studies indicate reductions in reading abilities, grammar, spelling and literacy [20], as well as overall learning abilities and motivation [21]. Furthermore, scientists have tried to figure out whether iodine supplementation in school-aged children could have a beneficial effect over these drawbacks. Unfortunately, results are inconclusive, some indicating an improvement in short-term memory [22], others in overall cognitive performances [23], and others showed no improvement at all [24].

The beneficial effects of iodine supplementation in salt

Around the world there are numerous countries that have a well-documented iodine deficiency. In 2013, the WHO

was reporting that 36.4% of all children that go to school present an inadequate iodine intake. Overall, the prevalence of this deficit is highest in Europe (59.9%) [25], Romania being amongst the countries that encounter such a problem [26].

The effects of iodine deficiency occur early during pregnancy and are possibly the most severe at this stage, therefore all mothers should receive adequate iodine supplementation, which, according to the World Health Organization, is estimated at 250 µg/day during pregnancy and lactation. Besides the effects discussed earlier in this paper, severe lack of iodine during pregnancy can also lead to spontaneous abortions and stillbirths [27]. In the case of children, the amount of iodine necessary is 90 µg/day for infants 0-5 years old, 120 µg/day for young school children 6-12 years old and 150 µg/day for those over 12 years old [28].

Initiatives have been taken in order to reduce the unfortunate outcomes of iodine deficiency, such as salt iodization. The overall results show that this has been a very effective strategy, being able to provide the necessary iodine requirements, even for pregnant women in spite of their higher necessities [26, 29]. According to their salt iodization strategy, countries have been divided into 3 categories: those who have a well-implemented iodization strategy (over 90% coverage), those who have areas that are not covered by the strategy and the ones that either didn't start the program or have massive gaps in their coverage. The last two categories should still recommend iodine supplementation to their population, especially for pregnant women and infants [30].

Conclusions

Iodine is one of the most important micronutrients in our organism. Its role is essential for performing the thyroid functions in adults and also for the neurological and behavioral development during pregnancy and early childhood. Iodine deficiency, especially during the first trimester of pregnancy can have disastrous outcomes and can lead to irreversible conditions, but the WHO initiatives taken in order to prevent such outcomes have proven efficient. Whether there is a chance to reverse some of the effects of this deficit is still to be studied by more in depth analyses, but prevention is definitely easier and more reliable.

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