

# Maternal Thyroid Dysfunctions and Neonatal Bone Maldevelopment

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## LETTER TO EDITOR

Thyroid hormones (THs) play an essential role during the fetal and neonatal development (Gereben et al., 2008; Namba et al., 2008; El-bakry et al., 2010; Ahmed, 2011, 2012a,b, 2013, 2014, 2015a-c, 2016a-d, 2017a-v, 2018a-i; Ahmed et al., 2008, 2010, 2012, 2013a,b, 2014, 2015a,b, 2018; Ahmed and Ahmed, 2012; Ahmed and Incerpi, 2013; Van Herck et al., 2013; Ahmed and El-Gareib, 2014; Incerpi et al., 2014; Candelotti et al., 2015; De Vito et al., 2015; El-Ghareeb et al., 2016; Ahmed and El-Gareib, 2017), particularly the normal growth of bone cells (Kvistad et al., 2004). THs also induce the cellular proliferation of cartilage growth in the epiphyseal plate of long bones by stimulation the release of growth hormone (GH) (Kvistad et al., 2004; Sbaihi et al., 2007) and IGF (insulin-growth factor) (Awad, 2002; El-bakry et al., 2010). In addition, thyroid receptors (TRs;  $\alpha$  and  $\beta$ ) were found in chondrocytes, growth plate, and osteoblasts (Bradley et al., 1992; Ballock et al., 1999; Siddiqi et al., 2002; Bassett and Williams, 2003). It has also been revealed that 3,5,3'-triiodothyronine (T3) can activate the terminal differentiation of growth plate chondrocytes (Ballock et al., 2000), osteoclastic growth and the osteoblasts process (Allain et al., 1992; Britto et al., 1994).

On the other hand, bone shortening due to intrauterine growth retardation could be attributed to the endocrine disorders (Frost, 1987; Awad, 2002). My group reported that maternal hypothyroidism delayed the body growth and ossification in rat (El-bakry et al., 2010). In addition, hypothyroidism can reduce the bone turnover, osteoclast bone reabsorption, osteoblast formation, and remodeling process (Bassett et al., 2010; Cardoso et al., 2014). In general, administration of methimazole (MMI) (Albee et al., 1989), propylthiouracil (PTU) (Tamasy et al., 1986) or carbimazole (CMI) (El-bakry et al., 2010) to rats can cause growth retardation. Alternatively, the hyperthyroidism can accelerate the development of skeletal bones and premature closure of the epiphyseal growth plates (EGPs) (Kosińska et al., 2005), and subsequent diminish the longitudinal bone growth (Allain and McGregor, 1993; Harvey et al., 2002; O'Shea et al., 2003). Hyperthyroidism also results in increasing the osteoclastic response to TH (Jowsey and Gorrddan, 1971). Administration of thyroxine (T4) to pre- and post-menopausal women induces the osteogenic and osteoclastic processes (Kosińska et al., 2005), and osteoporotic fractures (Cardoso et al., 2014). In subclinical hyperthyroidism, bone fragility and bone recomposition was observed in the early adverse effect (Bassett and Williams, 2009; Gorka et al., 2013; Cardoso et al., 2014). During the early childhood, severe hyperthyroidism can induce the premature fusion of the sutures of the skull and craniosynostosis (Siddiqi et al., 1997). Low bone density values and high bone resorption rates were demonstrated at diagnosis of hyperthyroidism in children and adolescents (Mora et al., 1999). More importantly, the disturbances in the TR $\alpha$ 1 or TR $\beta$  can perturb and delay the development of epiphyseal growth plates and the ossification process (Gothe et al., 1999).

Thus, the maternal thyroid disorders may alter the general skeletal features during the prenatal and postnatal development. Additional examinations are desired to identify the gene expression and signaling of THs-bone axis during the development. Also, several experimental studies are required to test whether T3 can act directly or indirectly in osteoclasts.

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