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Association between Maternal HCV and Developing Thyroid Disorders: Achievements and Challenges

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BRIEF COMMUNICATION

Hepatitis C virus (HCV; a plus-stranded RNA virus) is recognized to the family Flaviviridae, infected > 200 million people worldwide (Waheed et al., 2009), and caused death in greater than 350,000 during 2012 (World Health Organization, 2012). 20% of acute viral hepatitis and 50% of chronic viral hepatitis (Alter et al., 1992; Kumar et al., 2005) can increase the risk of liver cirrhosis and hepatocellular carcinoma in about more than 170 million patients (World Health Organization, 1997; Kabbaj et al., 2006; Matsumori et al., 2010). The prevalence of HCV differs from area to area and there are 6 genotypes for HCV on the basis of nucleotides sequence divergence (Safi et al., 2010; Waheed, 2015). In pregnant women, the range of anti-hepatitis C virus (HCV) was from 0.7% to 4.4% (Hillemanns et al., 1998; Resti et al., 1998) and the rate of viremia was from 63% to 69% (Granovsky et al., 1998; Conte et al., 2000).

On the other hand, Many investigations reported that HCV infection was related to thyroid dysfunction (hypothyroidism and thyroid autoimmunity) (Antonelli et al., 2004; Muratori et al., 2005; Tran and Reeves, 2009; de Oliveira Andrade et al., 2011; Fallahi et al., 2014; Shukla et al., 2018). More importantly, other reports recorded that HCV infection can increase the prevalence of thyroid cancer (Antonelli et al., 2007; Giordano et al., 2007; Omland et al., 2010; Wang et al., 2017). These disturbances may be attributed to the following causes: **(1)** presence of thyroid autoantibodies and autoimmune thyroiditis due to HCV infection (Prummel and Laurberg, 2003; Antonelli et al., 2007); **(2)** HCV can infect thyroid cells (Bartolome et al., 2008); **(3)** HCV proteins can initiate apoptosis (Munshi et al., 2003; Balasubramanian et al., 2006); and **(4)** HCV can activate the pro-inflammatory cytokines (Balasubramanian et al., 2003; Akeno et al., 2008). Then, HCV can stimulate the disorders in the immune system and the development of thyroid cancer (Antonelli et al., 2007; Wang et al., 2017). On account of suitable gestational thyroid hormones (THs) signaling is necessary for the normal development (Ahmed, 2011, 2012a,b, 2013, 2014, 2015a-c, 2016a-d, 2017a-v, 2018a-w; Ahmed and Ahmed, 2012; Ahmed et al., 2013a,b, 2014, 2015a,b, 2018a,b; 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), any defects in the levels of 3,5,3'-triiodothyronine (T3) and thyroxine (T4) can cause pre-eclampsia, intrauterine/fetal growth restriction, abortion, preterm delivery, fetal distress, peripartum hemorrhage, and permanent neurodevelopmental dysfunctions (Cunningham et al., 2005; Kumar et al., 2009).

At the end of this commentary, it has been suggested that maternal HCV (chronic hepatitis C) may increase the risk of preterm delivery, teratogenic consequences, child death, and neonatal thyroid disorders (thyroiditis or cancer). The presence of positive thyroid antibodies and macrophages is the prognostic factors of the thyroid disorders. In addition, these disorders may cause several brain disabilities and inflammatory-immune diseases in fetuses, neonates, and childhood. In general, these disturbances may delay the development and growth depending on the severity of HCV and time of its infection. However, the disruption mechanisms of HCV during the different periods of development are still uncertain. Thus, following the state of the pregnancy and the levels of maternal T3, T4, thyroid-stimulating hormone (TSH), thyroid antibodies, and serum fibrosis markers in the

presence of HCV infection should be more significant to avoid or decrease the risk of teratogenic consequences and neonatal thyroid dysfunction. Hopefully, several pharmacogenomics methods will be used to recognize the activity of maternal thyroid gland during the gestation previous to the initiation of HCV treatments. Additional work is vital to determine the developmental (the metabolic pathways), molecular and biochemical disruption mechanisms of maternal HCV infection and its treatment during the fetal and neonatal development. Clinical examinations are still essential to understand the associations between the chronic HCV infection and the prevalence of maternofetal autoimmune thyroid disorders and thyroid cancer. As well, several studies are required to discover novel drugs for HCV treatment and new therapeutic approaches to improve the maternofetal and neonatal health consequences, and to decrease the morbidity and mortality in fetuses, neonates or child.

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