International Journal of Research Studies in Medical and Health Sciences
Volume 2, Issue 11, 2017, PP 8-11
ISSN : 2456-6373

Commentary

Maternal Hypothyroidism and Lung Dysfunction

Ahmed R.G.

Division of Anatomy and Embryology, Zoology Department, Faculty of Science, Beni-Suef University, Beni-Suef, Egypt

***Corresponding Author:** Ahmed R.G., Division of Anatomy and Embryology, Zoology Department, Faculty of Science, Beni-Suef University, Beni-Suef, Egypt.*

Thyroid hormones (THs) are critical for the maintenance of the development (El-bakry et al., 2010; Ahmed, 2011, 2012a,b, 2013, 2014, 2015a-c, 2016a-d, 2017a-o; Ahmed et al., 2008, 2010, 2012, 2013a,b, 2014; 2015a,b; Ahmed and Ahmed, 2012; Ahmed and Incerpi, 2013;Van Hercket al., 2013; Ahmed andEl-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; Endendijk et al., 2017; Gigena et al., 2017), particularly the developing lung (Bernal and Pekonen, 1984; Ansari et al., 2000; Archavachotikul et al., 2002; Massaro and Massaro, 2002; van Tuyl et al., 2004). In the early embryonic period, THs control the growth, morphogenesis and functional maturation of lung by enhancing the differentiation of the mesenchymal and epithelial cell (Massaro et al., 1986; Holt et al., 1993; Göthe et al., 1999; Archavachotikul et al., 2002; van Tuyl et al., 2004). In the postnatal period, the elevation in the levels of THs concurs with the structural development of the lungs and acceleration of alveolar septation (Massaro and Massaro, 2002).

On the other hand, any deviation in the levels of maternal THs (maternal hypothyroidism) might cause the following: **(1)** pulmonary morbidity and overall mortality (Zwillich et al., 1975; Thvilumet al., 2013a,b; Dudhia and Dudhia BB 2014; Salomo et al., 2014; Sorensen et al., 2014);**(2)** retarded the developing fetal lung (Gonzales and Ballard, 1981; Bernal and Pekonen, 1984; van Tuyl et al., 2004); **(3)** diminished the diaphragmatic and abdominal muscle strength (Gorini et al., 1989; Siafakas et al., 1992; Duranti et al., 1993; Ansarin et al., 2011; Cakmak et al., 2011); **(4)** nocturnal breathing abnormalities (choking, restless sleep or sleep apnea) (Lin et al., 1992; Pelttari et al., 1994; Hira and Sibal, 1999; Jha et al., 2006); **(5)** decreased the breathing frequency in human and hamsters (Schlenker and Schultz, 2011 & 2012; Sykora et al., 2013); **(6)** reduced the levels of the dopamine receptor (D1 and D2) protein in the respiratory centers of the brain stem (paraventricular nucleus of the hypothalamus [PVN] and solitary nucleus), and the carotid glomus (Schlenker and Schultz, 2011 & 2012); and **(7)** decreased the energy transduction and glycolysis in the thoracic diaphragm due to reducethe activities of succinate dehydrogenase, hexokinase, 3-hyroxyl-CoA dehydrogenase, and phosphofructo kinase (Ianuzzo, 1984).More importantly, the harmful side effects of maternal hypothyroidism on the developing lung are nearly detectable during the postnatal period only, particular on thepulmonary gene expression (Haddow et al., 1999; Pop et al., 1999; Morreale de Escobar et al., 2000; van Tuyl et al., 2004).

On the basis of these data, it can be observed that thenormal availability of the maternal THs may vital for prenatal and postnatal development of lung. Also, the maternal hypothyroidism before the onset of fetal thyroid function may disrupt the morphological structure and function of the developing postnatal lung. Though, the mechanism of this disruption remains unknown. Further examinations are essential to clarify the effect of maternal hypothyroidism and L-thyroxine (L-T4) treatment on the fetal/neonatal respiratory system.

Conflict of Interest

The author declares that no competing financial interests exist.

References

[1] Ahmed, O.M., Abd El-Tawab, S.M., Ahmed, R.G., 2010. Effects of experimentally induced maternal hypothyroidism and hyperthyroidism on

the development of rat offspring: I- The development of the thyroid hormones-neurotransmitters and adenosinergic system interactions. Int. J. Dev. Neurosci. 28, 437-454.
[2] Ahmed, O.M., Ahmed, R.G., 2012. Hypothyroidism. In A New Look At Hypothyroidism. Dr. D. Springer (Ed.), ISBN:978-953-51-0020-1), In Tech Open Access Publisher, Chapter 1, pp. 1-20.
[3] Ahmed, O.M., Ahmed, R.G., El-Gareib, A.W., El-Bakry, A.M., Abd El-Tawaba, S.M., 2012. Effects of experimentally induced maternal hypothyroidism and hyperthyroidism on the development of rat offspring: II-The developmental pattern of neurons in relation to oxidative stress and antioxidant defense system. Int. J. Dev. Neurosci. 30, 517–537.
[4] Ahmed, O.M., El-Gareib, A.W., El-bakry, A.M., Abd El-Tawab, S.M., Ahmed, R.G., 2008. Thyroid hormones states and brain development interactions. Int. J. Dev. Neurosci. 26(2), 147-209. Review.
[5] Ahmed, R.G., 2011. Perinatal 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin exposure alters developmental neuroendocrine system. Food Chem. Toxicology, 49, 1276–1284.
[6] Ahmed, R.G., 2012a. Maternal-newborn thyroid dysfunction.In the Developmental Neuro endocrinology, pp. 1-369. Ed R.G. Ahmed. Germany: LAP LAMBERT Academic Publishing GmbH & Co KG.
[7] Ahmed, R.G., 2012b. Maternal-fetal thyroid interactions, Thyroid Hormone, Dr. N.K. Agrawal (Ed.), ISBN: 978-953-51-0678-4, In Tech Open Access Publisher, Chapter 5, pp. 125-156.
[8] Ahmed, R.G., 2013. Early weaning PCB 95 exposure alters the neonatal endocrine system: thyroid adipokine dysfunction. J. Endocrinol. 219 (3), 205-215.
[9] Ahmed, R.G., 2014. Editorial: Do PCBs modify the thyroid-adipokine axis during development? Annals Thyroid Res. 1(1), 11-12.
[10] Ahmed, R.G., 2015a. Chapter 1: Hypothyroidism and brain development. In advances in hypothyroidism treatment.Avid Science Borsigstr.9, 10115 Berlin, Berlin, Germany. Avid Science Publications level 6, Melange Towers, Wing a, Hitec City, Hyderabad, Telangana, India. pp. 1-40.
[11] Ahmed, R.G., 2015b. Hypothyroidism and brain developmental players.Thyroid Research J. 8(2), 1-12.
[12] Ahmed, R.G., 2015c. Editorials and Commentary: Maternofetal thyroid action and brain development. J. of Advances in Biology; 7(1), 1207-1213.
[13] Ahmed, R.G., 2015d.Developmental adipokines and maternal obesity interactions. J. of Advances in Biology; 7(1), 1189-1206.
[14] Ahmed, R.G., 2016a. Maternal bisphenol A alters fetal endocrine system: Thyroid adipokine dysfunction. Food Chem. Toxicology, 95, 168-174.
[15] Ahmed, R.G., 2016b. Gestational dexamethasone alters fetal neuroendocrine axis. Toxicology Letters, 258, 46–54.
[16] Ahmed, R.G., 2016c. Maternal iodine deficiency and brain disorders.Endocrinol.Metab.Syndr.5, 223.http://dx.doi.org/10.4172/2161-1017.1000223.
[17] Ahmed, R.G., 2016d. Neonatal polychlorinated biphenyls-induced endocrine dysfunction. Ann. Thyroid. Res. 2 (1), 34-35.
[18] Ahmed, R.G., 2017a. Developmental thyroid diseases and GABAergic dysfunction. EC Neurology 8.1, 02-04.
[19] Ahmed, R.G., 2017b. Hyperthyroidism and developmental dysfunction.Arch Med. 9, 4.
[20] Ahmed, R.G., 2017c. Anti-thyroid drugs may be at higher risk for perinatal thyroid disease. EC Pharmacology and Toxicology 4.4, 140-142.
[21] Ahmed, R.G.,2017d. Perinatal hypothyroidism and cytoskeleton dysfunction. Endocrinol Metab Syndr 6, 271.doi:10.4172/2161-1017.1000271
[22] Ahmed, R.G., 2017e. Developmental thyroid diseases and monoaminergic dysfunction. Advances in Applied Science Research 8(3), 01-10.
[23] Ahmed, R.G., 2017 f. Hypothyroidism and brain development. J. Anim Res Nutr.2 (2), 13.
[24] Ahmed, R.G., 2017g. Antiepileptic drugs and developmental neuroendocrine dysfunction: Every why has A Wherefore.Arch Med 9(6), 2.
[25] Ahmed, R.G., 2017h. Gestational prooxidant-antioxidant imbalance may be at higher risk for postpartum thyroid disease. Endocrinol Metab Syndr 6, 279. doi:10.4172/2161-1017.1000279.
[26] Ahmed, R.G., 2017i. Synergistic actions of thyroid- adipokines axis during development. Endocrinol Metab Syndr 6, 280.doi:10.4172/ 2161-1017.1000280.
[27] Ahmed, R.G., 2017j. Thyroid-insulin dysfunction during development. International Journal of Research Studies in Zoology 3(4), 73-75. DOI: http://dx.doi.org/10.20431/2454-941X.0304010.
[28] Ahmed, R.G., 2017k. Developmental thyroid diseases and cholinergic imbalance. International Journal of Research Studies in Zoology 3(4), 70-72. DOI: http://dx.doi.org/10.20431/2454-941X.0304009.
[29] Ahmed, R.G., 2017l. Thyroid diseases and developmental adenosinergic imbalance.Int J ClinEndocrinol 1(2), 053-055.
[30] Ahmed, R.G., 2017m. Maternal anticancer drugs and fetal neuroendocrine dysfunction in experimental animals. EndocrinolMetabSyndr 6, 281.doi:10.4172/2161-1017.1000281.
[31] Ahmed, R.G., 2017n. Letter: Gestational dexamethasone may be at higher risk for thyroid disease developing peripartum. Open Journal Of Biomedical & Life Sciences (Ojbili) 3(2), 01-06.

[32] Ahmed, R.G., 2017o. Deiodinases and developmental hypothyroidism. EC Nutrition 11.5, 183-185.
[33] Ahmed, R.G., Abdel-Latif, M., Ahmed F., 2015b.Protective effects of GM-CSF in experimental neonatal hypothyroidism. International Immuno pharmacology 29, 538–543.
[34] Ahmed, R.G., Abdel-Latif, M., Mahdi, E., El-Nesr, K., 2015a. Immune stimulation improves endocrine and neural fetal outcomes in a model of maternofetal thyrotoxicosis. Int. Immunopharmacol. 29, 714-721.
[35] Ahmed, R.G., Davis, P.J., Davis, F.B., De Vito, P., Farias, R.N., Luly, P., Pedersen, J.Z., Incerpi, S., 2013b. Nongenomic actions of thyroid hormones: from basic research to clinical applications. An update. Immunology, Endocrine & Metabolic Agents in Medicinal Chemistry, 13(1), 46-59.
[36] Ahmed, R.G., El-Gareib, A.W. 2014.Lactating PTU exposure: I- Alters thyroid-neural axis in neonatal cerebellum. Eur. J. of Biol. and Medical Sci. Res. 2(1), 1-16.
[37] Ahmed, R.G., El-Gareib, A.W., 2017.Maternal carbamazepine alters fetal neuroendocrine-cytokines axis. Toxicology 382, 59–66.
[38] Ahmed, R.G., El-Gareib, A.W., Incerpi, S., 2014. Lactating PTU exposure: II- Alters thyroid-axis and prooxidant-antioxidant balance in neonatal cerebellum. Int. Res. J. of Natural Sciences 2(1), 1-20.
[39] Ahmed, R.G., Incerpi, S., 2013. Gestational doxorubicin alters fetal thyroid–brain axis. Int. J. Devl. Neuroscience 31, 96–104.
[40] Ahmed, R.G., Incerpi, S., Ahmed, F., Gaber, A., 2013a. The developmental and physiological interactions between free radicals and antioxidant: Effect of environmental pollutants. J. of Natural Sci. Res. 3(13), 74-110.
[41] Ansari, M.A., de Mello, D.E., Devaskar, U.P. 2000.Effect of prenatal glucocorticoid on fetal lung ultrastructural maturation in hyt/hyt mice with primary hypothyroidism.Biol. Neonate 77, 29– 36.
[42] Ansarin, K., Niroomand, B., Najafipour, F., Aghamohammadzadeh, N., Niafar, M., Sharifi, A., Shoja, M.M., 2011. End-tidal CO (2) levels lower in subclinical and overt hypothyroidism than healthy controls; no relationship to thyroid function tests. Int J Gen Med 4, 29-33.
[43] Archavachotikul, K., Ciccone, T.J., Chinoy, M.R., et al., 2002. Thyroid hormone affects embryonic mouse lung branching morphogenesis and cellular differentiation. Am. J. Physiol. Lung Cell. Mol. Physiol. 282, L359– L369.
[44] Bernal, J., Pekonen, F. 1984. Ontogenesis of the nuclear 3,5,3'-triiodothyronine receptor in the human fetal brain. Endocrinology 114, 677– 679.
[45] Cakmak, G., Saler, T., Saglam, Z.A., Yenigun, M., Ataoglu, E., Demir, T., Temiz, L.U., 2011. Pulmonary functions in patients with subclinical hypothyroidism. J Pak Med Assoc 61, 951-953.
[46] Candelotti, E., De Vito, P., Ahmed, R.G., Luly, P., Davis, P.J., Pedersen, J.Z., Lin, H-Y., Incerpi, I., 2015. Thyroid hormones crosstalk with growth factors: Old facts and new hypotheses. Immun., Endoc. & Metab. Agents in Med. Chem., 15, 71-85.
[47] De Vito, P., Candelotti, E., Ahmed, R.G., Luly, P., Davis, P.J., Incerpi, S., Pedersen, J.Z., 2015.Role of thyroid hormones in insulin resistance and diabetes. Immun., Endoc.&Metab. Agents in Med. Chem., 15, 86-93.
[48] Dudhia, S.B., Dudhia, B.B., 2014. Undetected hypothyroidism: A rare dental diagnosis. J Oral MaxillofacPathol 18, 315-319.
[49] Duranti, R., Gheri, R.G., Gorini, M., Gigliotti, F., Spinelli, A., Fanelli, A., Scano, G., 1993.Control of breathing in patients with severe hypothyroidism.Am J Med 95, 29-37.
[50] El-bakry, A.M., El-Ghareeb, A.W.,Ahmed, R.G., 2010.Comparative study of the effects of experimentally-induced hypothyroidism and hyperthyroidism in some brain regions in albino rats.Int. J. Dev. Neurosci. 28, 371-389.
[51] El-Ghareeb, A.A., El-Bakry, A.M., Ahmed, R.G., Gaber, A., 2016.Effects of zinc supplementation in neonatal hypothyroidism and cerebellar distortion induced by maternal carbimazole. Asian Journal of Applied Sciences 4(04), 1030-1040.
[52] Endendijk, J.J., Wijnen, H.A.A., Pop, V.J.M., van Baar, A.L., 2017. Maternal thyroid hormone trajectories during pregnancy and child behavioral problems. Hormones & Behav. 94, 84–92.
[53] Gigena, N., Alamino, V.A., Montesinos, M.M., Nazar, M., Louzada, R.A., Wajner, S.M., Maia, A.L., Masini- Repiso, A.M., Carvalho, D.P., Cremaschi G.A., Pellizas, C.G., 2017.Dissecting thyroid hormone transport and metabolism in dendritic cells. J. Endocrinology 232, 337–350.
[54] Gonzales, L.W., Ballard, P.L. 1981. Identification and characterization of nuclear 3,5,3'-triiodothyronine- binding sites in fetal human lung. J. Clin. Endocrinol.Metab.53, 21– 28.
[55] Gorini, M., Spinelli, A., Cangioli, C., Gigliotti, F., Duranti, R., Arcangeli, P., Scano, G., 1989. Control of breathing in patients with short-term primary hypothyroidism. Lung 167, 43-53.
[56] Göthe, S., Wang, Z., Ng, L., et al., 1999. Mice devoid of all known thyroid hormone receptors are viable but exhibit disorders of the pituitary thyroid axis, growth, and bone maturation. Genes Dev. 13, 1329– 1341.
[57] Haddow, J.E., Palomaki, G.E., Allan, W.C., et al., 1999.Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child.N. Engl. J. Med. 341, 549– 555.
[58] Hira, H.S., Sibal, L., 1999. Sleep apnea syndrome among patients with hypothyroidism. J Assoc Physicians India 47, 615-618.

[59] Holt, J., Canavan, J.P., Goldspink, D.F. 1993. The influence of thyroid hormones on the growth of the lungs in perinatal rats. Int. J. Dev. Biol. 37, 467–472.

[60] Ianuzzo, C.D., Chen, V., O'Brien, P., Keens, T.G., 1984. Effect of experimental dysthyroidism on the enzymatic character of the diaphragm. J ApplPhysiolRespir Environ ExercPhysiol 56, 117-121.

[61] Incerpi, S., Hsieh, M-T., Lin, H-Y., Cheng, G-Y., De Vito, P., Fiore, A.M., Ahmed, R.G., Salvia, R., Candelotti, E., Leone, S., Luly, P., Pedersen, J.Z., Davis, F.B., Davis, P.J., 2014. Thyroid hormone inhibition in L6 myoblasts of IGF-I-mediated glucose uptake and proliferation: new roles for integrin αvβ3. Am. J. Physiol. Cell Physiol. 307, C150–C161.

[62] Jha, A., Sharma, S.K., Tandon, N., Lakshmy, R., Kadhiravan, T., Handa, K.K., Gupta, R., Pandey, R.M., Chaturvedi, P.K., 2006. Thyroxine replacement therapy reverses sleep-disordered breathing in patients with primary hypothyroidism. Sleep Med 7, 55-61.

[63] Lin, C.C., Tsan, K.W., Chen, P.J., 1992. The relationship between sleep apnea syndrome and hypothyroidism. Chest 102, 1663-1667.

[64] Massaro, D., Massaro, G.D. 2002. Invited Review: pulmonary alveoli: formation, the ‘‘call for oxygen,’’ and other regulators. Am. J. Physiol Lung Cell.Mol. Physiol. 282, L345–L358.

[65] Massaro, D., Teich, N., Massaro, G.D. 1986. Postnatal development of pulmonary alveoli: modulation in rats by thyroid hormones. Am. J. Physiol. 250, R51–R55.

[66] Morreale de Escobar, G., Obregon, M.J., Escobar del Rey, F. 2000. Is neuropsychological development related to maternal hypothyroidism or to maternal hypothyroxinemia? J. Clin. Endocrinol. Metab. 85, 3975–3987.

[67] Pelttari, L., Rauhala, E., Polo, O., Hyyppa, M.T., Kronholm, E., Viikari, J., Kantola, I., 1994. Upper airway obstruction in hypothyroidism. J Intern Med 236, 177-181.

[68] Pop, V.J., Kuijpens, J.L., van Baar, A.L., et al., 1999. Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. Clin.Endocrinol.50, 149– 155.

[69] Salomo, L.H., Laursen, A.H., Reiter, N., Feldt-Rasmussen, U., 2014.Myxoedema coma: an almost forgotten, yet still existing cause of multiorgan failure. BMJ Case Rep.

[70] Schlenker, E.H., Schultz, H.D., 2011. Hypothyroidism attenuates SCH 23390-mediated depression of breathing and decreases D1 receptor expression in carotid bodies, PVN and striatum of hamsters. Brain Res 1401,40-51.

[71] Schlenker, E.H., Schultz, H.D., 2012. Hypothyroidism stimulates D2 receptor-mediated breathing in response to acute hypoxia and alters D2 receptors levels in carotid bodies and brain. RespirPhysiolNeurobiol 180,69-78.

[72] Siafakas, N.M., Salesiotou, V., Filaditaki, V., Tzanakis, N., Thalassinos, N., Bouros, D., 1992.Respiratory muscle strength in hypothyroidism. Chest 102, 189-194.

[73] Sorensen, J.R., Hegedus, L., Kruse-Andersen, S., Godballe, C., Bonnema, S.J., 2014. The impact of goitre and its treatment on the trachea, airflow, oesophagus and swallowing function. A systematic review. Best Pract Res ClinEndocrinolMetab 28, 481-494.

[74] Sykora, C., Amor, M., Schlenker, E., 2013. Age and hypothyroidism affect dopamine modulation of breathing and D(2) receptor levels. Respir Physiol Neurobiol 185, 257-264.

[75] Thvilum, M., Brandt, F., Almind, D., Christensen, K., Brix, T.H., Hegedus, L., 2013b.Type and extent of somatic morbidity before and after the diagnosis of hypothyroidism.a nationwide register study. PLoS One 8, e75789.

[76] Thvilum, M., Brandt, F., Almind, D., Christensen, K., Hegedus, L., Brix, T.H., 2013a. Excess mortality in patients diagnosed with hypothyroidism: a nationwide cohort study of singletons and twins. J Clin Endocrinol Metab 98, 1069-1075.

[77] Van Herck, S.L.J., Geysens, S., Bald, E., Chwatko, G., Delezie, E., Dianati, E., Ahmed, R.G., Darras, V.M., 2013.Maternal transfer of methimazole and effects on thyroid hormone availability in embryonic tissues. Endocrinol. 218, 105-115.

[78] vanTuy, M., Blommaart, P.E., de Boer, P.A.J., Wert, S.E., Ruijter, J.M., Islam, S., Schnitzer, J., Ellison, A.R., Tibboel, D., Moorman, A.F.M., Lamers, W.H., 2004. Prenatal exposure to thyroid hormone is necessary for normal postnatal development of murine heart and lungs. Developmental Biology 272, 104–117.

[79] Zwillich, C.W., Pierson, D.J., Hofeldt, F.D., Lufkin, E.G., Weil, J.V., 1975. Ventilatory control in myxedema and hypothyroidism. N Engl J Med 292, 662-665.

Citation: *Ahmed R.G. Maternal Hypothyroidism and Lung Dysfunction. International Journal of Research Studies in Medical and Health Sciences. 2017;2(11):8-11.*