International Journal of Research Studies in Medical and Health Sciences
Volume 3, Issue 1, 2018, PP 8-12
ISSN : 2456-6373

Letter to Editor

Maternal Hypothyroidism and Neonatal Testicular 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) including thyroxine (T4) and 3,5,3'-triiodothyronine (T3) are dynamic for the vertebrate 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 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; Endendijk et al., 2017; Gigena et al., 2017), particularly the developing Leydig, germ (steroidogenesis) and Sertoli cells, blood-testis barrier, gap junction and testicular function (van Haaster et al., 1993; Cooke et al., 1994; De Franca et al., 1995; Gao et al., 2014; Rijntjes et al., 2017). In addition, the testicular cells can express the thyroid transporters, thyroid hormone receptors (TRs; α1, α2, α3, and β1, β2, β3) and deiodinases (Ds; D1, D2 and D3), and can keep the steady levels of THs in the seminiferous epithelium for the spermatogenesis (Buzzard et al., 2000; Jannini et al., 2000; O'Shea and Williams, 2002; Mendis-Handagama and Siril Ariyaratne, 2005; Hernandez et al., 2006; Schneider et al., 2006; Meeker et al., 2007; Wajner et al., 2007; Weng et al., 2007; Krassas et al., 2008 & 2010; Wagner et al., 2009; Pelletier, 2011; Zamoner et al., 2011; Tarulli et al., 2012; Gao et al., 2009 & 2014; Mayerl et al., 2014). More importantly, the coordination between THs, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) might regulate the testicular development (Leydig and Sertoli cell) and function (Gao et al., 2014; Picut et al., 2015; Rijntjes et al., 2017).

On the other hand, hypothyroidism can disrupt the testicular development and function as the following (Cooke and Meisami, 1991; Cooke et al., 1991; van Haaster et al.,1992; De Franca et al., 1995; Mendis-Handagama et al., 1998; Chaio et al., 2000; Cristovao et al., 2002; Dermott, 2004; Mendis-Handagama et al., 2007; Shibutani et al., 2009; Auharek and De Franca, 2010; Gao et al., 2014; Rijntjes et al., 2017):

- Stimulate the proliferation of Sertoli cell;
- Delay the differentiation of Sertoli cell;
- Inhibit the blood–testis barrier;
- Increase the neonatal testis weight;
- Hypertrophy of fetal Leydig cells;
- Arrest the formation of neonatal Leydig cell progenitor;
- Inhibit the development of germ cells;
- Reduce the level of plasma testosterone (Jahan et al., 2012);
- Decrease the activity of 17β-hydroxy steroid dehydrogenase (17β-HSD) and post c-AMP pathways;
- Delay the puberty and fertility;
- Delay the spermatogenesis; and
- Increase the apoptotsis of spermatocytes.

On the basis of these investigations, it can be inferred that the steady activities of the maternal THs may noteworthy for the developing testis. Also, the maternal hypothyroidism may disturb the testicular development and function during the postnatal period. Hypothyroidism may act a negative role on the neonatal thyroid-reproductive axis. However, the mechanism of this disorder needs more examinations. Further examinations are crucial to clarify the variations in developing blood-testis barrier, dynamics of gap junctions and Sertoli-germ cell axis due to the effect of goitrogen-induced hypothyroidism model.

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 Neuroendocrinology, 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., 2017f. 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 Clin Endocrinol 1(2), 053-055.

[30] Ahmed, R.G., 2017m. Maternal anticancer drugs and fetal neuroendocrine dysfunction in experimental animals. Endocrinol Metab Syndr 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 Immunopharmacology 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] Auharek S.A., De Franca, L.R., 2010. Postnatal testis development, Sertoli cell proliferation and number of different spermatogonial types in C57BL/6J mice made transiently hypo- and hyperthyroidic during the neonatal period. J. Anat. 216, 577–588.

[42] Buzzard, J.J., Morrison, J.R., O'Bryan, M.K., Song, Q., Wreford, N.G., 2000. Developmental expression of thyroid hormone receptors in the rat testis. Biol Reprod 62, 664-669.

[43] 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.

[44] Chiao, C.Y., Chao, L.H., Huang, W.S., Wang, S.P., 2000. Direct effects of propylthiouracil on testosterone production in monkeys. Chin. J. Physiol. 43, 55-59.

[45] Cooke, P.S., Hess, R.A., Porcelli, J., Meisami, E., 1991. Increased sperm production in adult rats after transient neonatal hypothyroidism. Endocrinology 129, 244248.

[46] Cooke, P.S., Meisami,E., 1991. Early hypothyroidism in rats causes increased adult testis and reproductive organ size but does not change testosterone levels. Endocrinol 129, 237-243.

[47] Cooke, P.S., Zhao, Y.D., Bunick, D., 1994. Triiodothyronine inhibits proliferation and stimulates differentiation of cultured neonatal Sertoli cells: possible mechanism for increased adult testis weight and sperm production induced by neonatal goitrogen treatment. Biol Reprod 51, 1000-1005.

[48] Cristovao, F.C., Bisi, H., Mendonca, B.B., Bianco, A.C., and Bloise, W., 2002. Severe and mild neonatal hypothyroidism mediate opposite effects on Leydig cells of rats. Thyroid 12, 13–18.

[49] De Franca, L.R., Hess, R.A., Cooke, P.S., Russell, L.D., 1995. Neonatal hypothyroidism causes delayed Sertoli cell maturation in rats treated with propylthiouracil:evi- dence that the Sertoli cell controls testis growth. Anat Rec 242, 57–69.

[50] 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.

[51] Dermott, J.M., Ha, J.H., Lee, C.H., Dhanasekaran, N., 2004. Differential regulation of Jun N-terminal kinase and p38MAP kinase by Ga12. Oncogene. 23, 226-232.

[52] 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.

[53] 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.

[54] 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.

[55] Galton, V.A., Schneider, M.J., Clark, A.S., StGermain, D.L., 2009. Life without thyroxine to 3,5,3'-triiodothyronine conversion: studies in mice devoid of the 5'-deiodinases. Endocrinology 150, 2957-2963.

[56] Gao, Y., Lee, W.M., Cheng, C.Y., 2014. Thyroid hormone function in the rat testis. Front.Endocrinol. 5:188. doi: 10.3389/fendo.2014.00188.

[57] 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.

[58] Hernandez, A., Martinez, M.E., Fiering, S., Galton, V.A., StGermain, D., 2006. Type 3 deiodinase is critical for the maturation and function of the thyroidaxis. J Clin Invest 16, 476–484.

[59] 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.

[60] Jahan, S., Ahmed, S., Emanuel, E., Fatima, I., Ahmed, H., 2012. Effect of an anti-thyroid drug, 2,8-Dimercapto-6-hydroxy purine on reproduction in male rats. Pak. J. Pharm. Sci.25(2), 401-406.

[61] Jannini, E.A., Crescenzi, A.,Rucci, N., Screponi, E., Carosa, E., deMatteis, A., et al., 2000. Ontogenetic pattern of thyroid hormone receptor expression in the human testis. J Clin Endocrinol Metab 85, 3453-3457.

[62] Krassas, G.E., Papadopoulou, F., Tziomalos, K., Zeginiadou, T., Pontikides, N., 2008. Hypothyroidism has an adverse effect on human spermatogenesis: a prospective, controlled study. Thyroid 18, 1255-1259.

[63] Krassas, G.E., Poppe, K., Glinoer, D., 2010. Thyroid function and human reproductive health. Endocr Rev 31, 702-755.

[64] Mayerl, S., Muller, J., Bauer, R., Richert, S., Kassmann, C.M., Darras, V.M., et al., 2014.Trans- porters MCT8 and OATP1C1 maintain murine brain thyroid hormone homeostasis. J Clin Invest 124, 1987-1999.

[65] Meeker, J.D., Godfrey-Bailey, L., Hauser, R., 2007. Relationships between serum hormone levels and semen quality among menfroman in fertility clinic. J Androl 28, 397-406.

[66] Mendis-Handagama, S.M., Ariyaratne, H.B., Teunissen van Manen, K.R., Haupt, R.L., 1998. Differentiation of adult Leydig cells in the neonatal rat testis is arrested by hypothyroidism. Biol. Reprod. 59, 351–357.

[67] Mendis-Handagama, S.M., Ariyaratne, H.B.S., Mrkonjich, L., Ivell, R., 2007. Expression of insulin-like peptide 3 in the postnatal rat Leydig cell lineage: timing and effects of triiodothyronine-treatment. Reproduction 133, 479–485.

[68] Mendis-Handagama, S.M., Siril Ariyaratne, H.B., 2005. Leydig cells, thyroid hormones and steroidogenesis. Indian J Exp Biol 43, 939–62.

[69] O'Shea, P.J., Williams, G.R., 2002. Insight into the physiological actions of thyroid hor- mone receptors from genetically modified mice. J Endocrinol 175, 553-570.

[70] Pelletier, R.M., 2011. The blood-testis barrier: the junctional permeability, the proteins and the lipids. Prog Histochem Cytochem 46, 49–127.

[71] Picut, C.A., Remick, A.K., De Rijk, E.P., Simons, M.L., Stump, D.G., and Parker, G.A., 2015. Postnatal development of the testis in the rat: morphologic study and correlation of morphology to neuroendocrine parameters. Toxicol. Pathol. 43, 326–342.

[72] Rijntjes, E., Gomes, M.L.M., Zupanič, N., Swarts, H.J.M., Keijer, J., Teerds, K.J., 2017. Transient hypothyroidism: Dual effect on adult-type Leydig cell and Sertoli cell development. Front. Physiol. 8:323. doi: 10.3389/fphys.2017.00323

[73] Schneider, M.J., Fiering, S.N., Thai, B., Wu, S.Y., StGermain, E., Parlow, A.F., et al., 2006. Tar- geted disruption of the type 1 selenodeiodinasegene(Dio1) results in marked changes in thyroid hormone economy in mice. Endocrinol 147, 580-589.

[74] Shibutani, M., Woo, H.G., Fujimoto, H., Suegusa, Y., Takahashi, M., Inoue, K., Hirose, M., Nishikawa, A., 2009. Assessment of developmental effects of hypothyroidism in rats from in utero and lactation exposure to anti-thyroid agents. Reprod. Toxicol. 28, 297-307.

[75] Tarulli, G.A., Stanton, P.G., Meachem, S.J., 2012. Is the adult Sertoli cell terminally differentiated? Biol Reprod 87, 1–11.

[76] van Haaster, L.H., De Jong, F.H., Docter, R., De Rooij, D.G., 1992. The effect of hypothyroidism on Sertoli cell proliferation and differentiation and hormone levels during testicular development in the rat. Endocrinology 131, 1574–1576.doi: 10.1210/ endo.131.3.1505485

[77] van Haaster, L.H., de Jong, F.H., Docter, R., de Rooij, D.G., 1993. High neonatal triiodothyronine levels reduce the period of Sertoli cell proliferation and accelerate tubular lumen formation in the rat testis, and increase serum inhibin levels. Endocrinol 133, 755-760.

[78] 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.

[79] Wagner, M.S., Wajner, S.M., Maia, A.L., 2009. Is there a role for thyroid hormone on spermatogenesis? Microsc ResTech 72, 796–808.

[80] Wajner, S.M., dosSantos Wagner, M., Melo, R.C., Parreira, G.G., Chiarini-Garcia, H., Bianco, A.C., et al., 2007. Type 2 iodothyronine deiodinase is highly expressed in germ cells of adult rat testis. J Endocrinol 194, 47–54.

[81] Weng, Q., Saita, E., Watanabe, G., Takahashi, S., Sedqyar, M., Suzuki, A.K., et al., 2007. Effect of methimazole-induced hypothyroidism on adrenal and gonadal functions in male Japanes equail (Coturnix japonica). J Reprod Dev 53, 1335-1341.

[82] Zamoner, A., Pessoa-Pureur, R., Silva, F.R., 2011. Membrane-initiated actions of thyroid hormones on the male reproductive system. Life Sci 89, 507-514.

Citation: *Ahmed R.G. Maternal Hypothyroidism and Neonatal Testicular Dysfunction. International Journal of Research Studies in Medical and Health Sciences. 2018;3(1):8-12.*