ARC Journal of Pharmaceutical Sciences (AJPS)
Volume 4, Issue 1, 2018, PP 20-24
ISSN No.: 2455-1538
DOI: http://dx.doi.org/10.20431/2455-1538.0401005
www.arcjournals.org

Maternal Hypothyroidism and Fetal Hepatic Diseases: Ongoing Debates and Key Issues

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.*

COMMUNICATION

The normal activities of maternal thyroid hormones (THs) are needed for the fetal/ neonatal development (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& 2018a,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; Gigena et al., 2017), particularly the hepatic function, lipid homeostasis, the basal metabolic rate of hepatocyte, and the bilirubin metabolism (Huang and Liaw, 1995; Malik and Hodgson, 2002; Tindall et al., 2007; Paquette et al., 2011; Yao et al., 2014).In addition, the liver has a significant action in THs metabolism by deiodinases (D1, D2 and D3) (Malik and Hodgson, 2002; Tindall et al., 2007; Paquette et al., 2011; Ahmed, 2012b; Bano et al., 2016). The alterations in hepatic lipid homeostasis due to the abnormality in thyroid states might cause a non-alcoholic fatty liver disease (NAFLD; a very common liver disorder) (Liu et al., 2007; Burra, 2013). These changes were a dose-dependent manner (Chung et al., 2012). Though, the direct relationship between the pathogenesis of NAFLD and thyroid disorders is still unknown. On the other hand, thyroid disorders may disturb the liver function (Malik and Hodgson, 2002), glycogen accumulation and hepatic fatty acid composition (Yao et al., 2014), and elevate the alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase (Huang and Liaw, 1995).

The association between the hypothyroidism and cholestatic jaundice and gallstones can be attributed to the following (Van Steenbergen et al., 1989; Huang and Liaw, 1995; Gaitan and Cooper, 1997; Inkinen et al., 2000; Malik and Hodgson, 2002): (1)diminished the bilirubin UDP-glucuronyltransferase; (2) decreased bilirubin and bile excretion; (3) increased the membrane cholesterol-phospholipid ratio; (4) decreased the membrane fluidity; (5) altered the membrane transporters and the activity of Na^+, K^+-ATPase; and (6)hypotonia and hypercholesterolaemia of the gall bladder. These abnormalities can be reversible with a short-term replacement with thyroxin (T4) (Huang and Liaw, 1995; Gaitan and Cooper, 1997; Malik and Hodgson, 2002). Alternatively, the elevations in the levels of T4 and thyroxine-binding globulin (TBG), reductions in the activity of D1 [decrease the conversion of T4 to 3,5,3′-triiodo-L-thyronine (T3)] were associated with the liver diseases such as Hepatitis C virus infection (HCV) (Huang and Liaw, 1995) or acute hepatitis of mild or moderate severity (Hegedus, 1986; Kano et al., 1987; Malik and Hodgson, 2002). On the other hand, therapy by anti thyroid drugs might cause hepatitis, transient subclinical hepatotoxicity or cholestasis, while therapy with interferon (IFN) in liver diseases might cause thyroid dysfunctions (Benelhadj et al., 1997; Deutsch et al., 1997).

On the basis of these data, it can be concluded that there is a significant relationship between the maternofetal thyroid gland and the liver in normal or abnormal states. It is recommended to detect the levels of T4 and thyroid-stimulating hormone (TSH) with liver disorders, to include or exclude the thyroid disorders with unexplained liver abnormalities. Further studies are essential to elucidate the prospective relations with human health.

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 neuro-endocrine 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. Endocrinal. 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 Meta bSyndr 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. EndocrinolMetabSyndr 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., 2017p.Maternofetal thyroid hormones and risk of diabetes. Int. J. of Res. Studies in Medical and Health Sciences 2(10), 18-21.

[34] Ahmed, R.G., 2017r.Association between hypothyroidism and renal dysfunctions. International Journal of Research Studies in Medical and Health Sciences 2(11), 1-4.

[35] Ahmed, R.G., 2017s.Maternal hypothyroidism and lung dysfunction. International Journal of Research Studies in Medical and Health Sciences 2(11), 8-11.

[36] Ahmed, R.G., 2017t.Endocrine disruptors; possible mechanisms for inducing developmental disorders. International journal of basic science in medicine (IJBSM) 2(4), 157-160.

[37] Ahmed, R.G., 2017u.Maternal thyroid hormones trajectories and neonatal behavioral disorders. ARC Journal of Diabetes and Endocrinology 3(2), 18-21.

[38] Ahmed, R.G., 2017v.Maternal thyroid dysfunction and neonatal cardiac disorders. Insights Biol Med. 1, 092-096.

[39] Ahmed, R.G., 2018a. Maternal hypothyroidism and neonatal testicular dysfunction. International Journal of Research Studies in Medical and Health Sciences 3(1), 8-12.

[40] Ahmed, R.G., 2018b. Maternal hypothyroidism and neonatal depression: Current perspective. International Journal of Research Studies in Zoology 4(1), 6-10. DOI: http://dx.doi.org/10.20431/2454-941X.0401002.

[41] Ahmed, R.G., 2018c. Non-genomic actions of thyroid hormones during development. App Clin Pharmacol Toxicol: ACPT-108. DOI: 10.29011/ACPT-109. 100008.

[42] Ahmed, R.G., 2018d. Maternal thyroid function and placental hemodynamic. ARC Journal of Animal and Veterinary Sciences 4(1), 9-13. DOI: http://dx.doi.org/10.20431/2455-2518.0401002.

[43] Ahmed, R.G., 2018e.Interactions between thyroid and growth factors during development. ARC Journal of Diabetes and Endocrinology 4(1), 1-4. DOI: http://dx.doi.org/10.20431/2455-5983.0401001.

[44] Ahmed, R.G., 2018f. Maternal thyroid hormones and neonatal appetite. ARC Journal of Nutrition and Growth 4(1), 18-22. DOI: http://dx.doi.org/10.20431/2455-2550.0401005.

[45] Ahmed, R.G., 2018g. Genomic actions of thyroid hormones during development. ARC Journal of Diabetes and Endocrinology 4(1), 5-8. DOI: http://dx.doi.org/10.20431/2455-5983.0401002.

[46] Ahmed, R.G., 2018h. Dysfunction of maternal thyroid hormones and psychiatric symptoms. American Research Journal of Endocrinology. 2(1), 1-6.

[47] Ahmed, R.G., 2018i. Is there a connection between maternal hypothyroidism and developing autism spectrum disorders? ARC Journal of Neuroscience 3(1), 5-8. DOI: http://dx.doi.org/10.20431/2456-057X.0301002.

[48] Ahmed, R.G., Abdel-Latif, M., Ahmed F., 2015b.Protective effects of GM-CSF in experimental neonatal hypothyroidism. International Immunopharmacology 29, 538–543.

[49] 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.

[50] 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.

[51] 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.

[52] Ahmed, R.G., El-Gareib, A.W., Shaker, H.M., 2018a.Gestational 3, 3′, 4, 4′, 5-pentachlorobiphenyl (PCB 126) exposure disrupts fetoplacental unit: Fetal thyroid-cytokines dysfunction. Life Sciences 192, 213–220.

[53] Ahmed, R.G., El-Gareib, A.W., 2017.Maternal carbamazepine alters fetal neuroendocrine-cytokines axis. Toxicology 382, 59–66.

[54] Ahmed, R.G., El-Gareib, A.W., Incerpi, S., 2014. Lactating PTU exposure: II- Alter's thyroid-axis and prooxidant-antioxidant balance in neonatal cerebellum. Int. Res. J. of Natural Sciences 2(1), 1-20.

[55] Ahmed, R.G., Incerpi, S., 2013. Gestational doxorubicin alters fetal thyroid–brain axis. Int. J. Devl. Neuroscience 31, 96–104.

[56] 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.

[57] Ahmed, R.G., Walaa G.H., Asmaa F.S., 2018b.Suppressive effects of neonatal bisphenol A on the neuroendocrine system. Toxicology and Industrial Health Journal (in press).

[58] Bano, A., Chaker, L., Plompen, E.P., Hofman, A., Dehghan, A., Franco, O.H., Janssen, H.L., Darwish Murad, S., Peeters, R.P., 2016. Thyroid Function and the Risk of Nonalcoholic Fatty Liver Disease: The Rotterdam Study. J ClinEndocrinolMetab.101 (8), 3204-3211.

[59] Benelhadj, S., Marcellin, P., Castelnau, C., Colas-Linhart, N., Benhamou, J.P., Erlinger, S., Bok, B., 1997.Incidence of dysthyroidism during interferon therapy in chronic hepatitis C. Horm Res. 48, 209–14.

[60] Burra, P, 2013. Liver abnormalities and endocrine diseases. Best Pract Res ClinGastroenterol. 27, 553–563.

[61] 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.

[62] Chung, G.E., Kim, D., Kim, W., Yim, J.Y., Park, M.J., Kim, Y.J., Yoon, J.H., Lee, H.S., 2012.Non-alcoholic fatty liver disease across the spectrum of hypothyroidism.J Hepatol. 57, 150–156.

[63] 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.

[64] Deutsch, M., Dourakis, S., Manesis, E.K., Gioustozi, A., Hess, G., Horsch, A., Hadziyannis, S., 1997. Thyroid abnormalities in chronic viral hepatitis and their relationship to interferon alfa therapy. Hepatology 26, 206–10.

[65] 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.

[66] 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.

[67] Gaitan, E., Cooper, D.S., 1997. Primary hypothyroidism. CurrTherEndocrinolMetab 6, 94-98.

[68] 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.

[69] Hegedus, L., 1986. Thyroid gland volume and thyroid function during and after acute hepatitis infection. Metabolism 35, 495-498.

[70] Huang, M.J., Liaw, Y.F., 1995.Clinical associations between thyroid and liver diseases.J Gastroenterol Hepatol. 10(3), 344-350.

[71] 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.

[72] Inkinen, J., Sand, J., Nordback, I., 2000. Association between common bile duct stones and treated hypothyroidism. Hepatogastroenterology 47, 919-921.

[73] Kano, T., Kojima, T., Takahashi, T., Muto, Y., 1987. Serum thyroid hormone levels in patients with fulminant hepatitis: usefulness of rT3 and the rT3/T3 ratio as prognostic indices. GastroenterolJpn 22, 344-353.

[74] Liu, Y.Y., Heymann, R.S., Moatamed, F., Schultz, J.J., Sobel, D., Brent, G.A., 2007. A mutant thyroid hormone receptor alpha antagonizes peroxisome proliferator-activated receptor alpha signaling in vivo and impairs fatty acid oxidation. Endocrinology 148, 1206–1217.

[75] Malik, R., Hodgson, H., 2002. The relationship between the thyroid gland and the liver. Q J Med 95, 559–569.

[76] Paquette, M.A., Dong, H., Gagné, R., Williams, A., Malowany, M., Wade, M.G., Yauk, C.L., 2011. Thyroid hormone-regulated gene expression in juvenile mouse liver: identification of thyroid response elements using microarray profiling and in silico analyses. BMC Genomics 2011, 12, 634.

[77] Tindall, A.J., Morris, I.D., Pownall, M.E., Isaacs, H.V., 2007. Expression of enzymes involved in thyroid hormone metabolism during the early development of Xenopustropicalis. Biol Cell. 99(3), 151-163.

[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] Van Steenbergen, W., Fevery, J., De Vos, R., Leyten, R., Heirwegh, K.P., De Groote, J., 1989.Thyroid hormones and the hepatic handling of bilirubin. I. Effects of hypothyroidism and hyperthyroidism on the hepatic transport of bilirubin mono- and diconjugates in the Wistar rat. Hepatology 9, 314-321.

[80] Yao, X., Hou, S., Zhang, D., Xia, H., Wang, Y-C., Jiang, J., Yin, H., Ying, H., 2014.Regulation of fatty acid composition and lipid storage by thyroid hormone in mouse liver. Cell & Bioscience 4, 38.

Citation: *Ahmed R.G. "Maternal Hypothyroidism and Fetal Hepatic Diseases", ARC Journal of Pharmaceutical Sciences (AJPS), vol. 4, no. 1, p. 20-24, 2018. http://dx.doi.org/10.20431/2455-1538.0401005*