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Short Communication

Maternal Hypothyroidism and Multiple Sclerosis: Disruption the Developing Neuroendocrine System

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Maternal thyroid hormones (THs; 3,5,3'-triiodothyronine (T3) and thyroxin (T4)) have dynamic trophic actions during the perinatal development [1-76], in particular the developing brain and myelination process [5,66,77-81]. It is widely known that the appropriate myelinated growth, at postnatal day 25 in the rat, is responsible for protection and insulation of axons and is vital for the function of Central Nervous System (CNS), in particular the learning and memory function [82-84]. Alternatively, there is a link between the hypothyroidism and the vulnerability of the CNS to inflammatory diseases by the thymus or spleen (cells of the immune system). In maternal hypothyroidism, the dysfunction in the thymic selection increases the accumulation of autoimmune T cells and the risk of autoimmune-inflammatory disorders in the offspring [85], such as multiple sclerosis [86]. Multiple sclerosis is a long-lasting, neuroinflammatory demyelinating dysfunction of the CNS that mostly disturbs young adults [87,88]. The etiology of multiple sclerosis might be due to a disturbance in the genetic process, immunological (autoimmune disorders), infectious, or environmental factors [89]. Symptoms of multiple sclerosis during pregnancy are urinary insistence, fatigue, lower extremities paresthesias and gait difficulties [90,91].

On the other hand, deficiency in the levels of maternal THs during the gestation can decrease the growth and differentiation of myelinated axons [86,92], and cause permanent defects in the developing CNS including a mental retardation and cognitive disturbances [5,84,93,94]. In mild-moderate iodine insufficiency, maternal and neonatal hypothyroxinemia, a low circulating free T4 with no change in free T3 or thyroid stimulating hormone (TSH), can disrupt the levels of nuclear Myelin Binding Protein (MBP) and increase the apoptosis causing a reduction in the cellular survival [95]. More importantly, Wei et al. [94] reported that hypothyroxinemia due to the maternal mild iodine decreases the expression of myelin-related proteins and delays the growth of neonatal myelination. Notably, a reduction in the levels of gestational THs can increase the severity of multiple sclerosis [86,96].

From the preceding results, the present overview presumed that any disorders in the activity of maternal thyroid gland during the gestation may increase the demyelination (hypomyelination) and decrease the thickness of the myelin sheath. These disruptions may increase the vulnerability of the CNS to multiple sclerosis and several inflammatory-immune impairments.

As well, the gestational hypothyroidism associated with the multiple sclerosis may cause the following:

(1) Perturb the neural organization and synaptogenesis,

(2) Delay the development and progress of the fetal and neonatal neuroendocrine system (thyroid-brain axis),

(3) increase the teratogenic consequences;

(4) increase the risk of developing brain disorders (mental retardation or cognitive disorders); and

(5) Delay the fetal and neonatal development generally.

Thus, both diseases may be a major avoidable health problem worldwide. These conditions may be depending on the severity, distribution and time of both diseases. Though, their molecular mechanisms are obscure. To date, it is not obvious whether the described effects of both diseases on the fetal or neonatal neuroendocrine system in experimental animal models might be fitted to human health. These observations strongly recommend assessing maternal THs and treating hypothyroidism before or during the gestation to avoid the vulnerability to any inflammatory diseases, in particular, multiple sclerosis in the fetal or neonatal CNS. Further experiments are influential to examine the impact of maternal hypothyroidism and multiple sclerosis on the fetal and neonatal neuroendocrine system (thyroid-brain axis). Moreover, the molecular and immunological variation due to both diseases during the gestation and lactation periods should be addressed. This could assist to understand the pathogenesis of both diseases and planning new therapeutic approaches.

References

1. El-bakry AM, El-Ghareeb AW, Ahmed RG. Comparative study of the effects of experimentally-induced hypothyroidism and hyperthyroidism in some brain regions in albino rats. Int. J. Dev. Neurosci. 2010; 28: 371-389.
2. Ahmed OM, Abd El-Tawab SM, Ahmed RG. 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. 2010; 28: 437-454.
3. Ahmed OM, Ahmed RG, Springer D. Hypothyroidism. In A New Look At Hypothyroidism. In Tech Open Access Publisher. 2012; 1-20.
4. Ahmed OM, Ahmed RG, El-Gareib AW, El-Bakry AM, Abd El-Tawab SM. 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. 2012; 30: 517-537.
5. Ahmed OM, El-Gareib AW, El-bakry AM, Abd El-Tawab SM, Ahmed RG. Thyroid hormones states and brain development interactions. Int. J. Dev. Neurosci. 2008; 26: 147-209.

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6. Ahmed RG. Perinatal 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin exposure alters developmental neuroendocrine system. Food Chem. Toxicology. 2011; 49: 1276-1284.

7. Ahmed RG. Maternal-newborn thyroid dysfunction. In the Developmental Neuroendocrinology. Ed RG Ahmed. Germany: LAP LAMBERT Academic Publishing GmbH & Co KG. 2012; 1-369.

8. Ahmed RG, Agrawal NK. Maternal-fetal thyroid interactions, Thyroid Hormone. In Tech Open Access Publisher. 2012; 125-156.

9. Ahmed RG. Early weaning PCB 95 exposure alters the neonatal endocrine system: thyroid adipokine dysfunction. J. Endocrinol. 2013; 219: 205-215.

10. Ahmed RG. Editorial: Do PCBs modify the thyroid-adipokine axis during development? Annals Thyroid Res. 2014; 1: 11-12.

11. Ahmed RG. Chapter 1: Hypothyroidism and brain development. In advances in hypothyroidism treatment. Avid Science Borsigstr.9, 10115 Berlin, Germany. Avid Science Publications level 6, Melange Towers, Wing a, Hitec City, Hyderabad, Telangana, India. 2015; 1-40.

12. Ahmed RG. Hypothyroidism and brain developmental players. Thyroid Research J. 2015; 8: 1-12.

13. Ahmed RG. Editorials and Commentary: Maternofetal thyroid action and brain development. J. of Advances in Biology. 2015; 7: 1207-1213.

14. Ahmed RG. Gestational dexamethasone alters fetal neuroendocrine axis. Toxicology Letters. 2016; 258: 46-54.

15. Ahmed RG. Neonatal polychlorinated biphenyls-induced endocrine dysfunction. Ann. Thyroid. Res. 2016; 2: 34-35.

16. Ahmed RG. Maternal iodine deficiency and brain disorders. Endocrinol. Metab. Syndr. 2016; 5: 223.

17. Ahmed RG. Maternal bisphenol A alters fetal endocrine system: Thyroid adipokine dysfunction. Food Chem. Toxicology. 2016; 95: 168-174.

18. Ahmed RG. Developmental thyroid diseases and GABAergic dysfunction. EC Neurology. 2017; 8.1: 02-04.

19. Ahmed RG. Hyperthyroidism and developmental dysfunction. Arch Med. 2017; 9: 4.

20. Ahmed RG. Anti-thyroid drugs may be at higher risk for perinatal thyroid disease. EC Pharmacology and Toxicology. 2017; 4.4: 140-142.

21. Ahmed RG. Perinatal hypothyroidism and cytoskeleton dysfunction. Endocrinol Metab Syndr. 2017; 6: 271.

22. Ahmed RG. Developmental thyroid diseases and monoaminergic dysfunction. Advances in Applied Science Research. 2017; 8: 01-10.

23. Ahmed RG. Hypothyroidism and brain development. J. Anim Res Nutr. 2017; 2: 13.

24. Ahmed RG. Antiepileptic drugs and developmental neuroendocrine dysfunction: Every why has A Wherefore? Arch Med. 2017; 9: 2.

25. Ahmed RG. Gestational prooxidant-antioxidant imbalance may be at higher risk for postpartum thyroid disease. Endocrinol Metab Syndr. 2017; 6: 279.

26. Ahmed RG. Synergistic actions of thyroid-adipokines axis during development. Endocrinol Metab Syndr. 2017; 6: 280.

27. Ahmed RG. Thyroid-insulin dysfunction during development. International Journal of Research Studies in Zoology. 2017; 3: 73-75.

28. Ahmed RG. Developmental thyroid diseases and cholinergic imbalance. International Journal of Research Studies in Zoology. 2017; 3: 70-72.

29. Ahmed RG. Thyroid diseases and developmental adenosinergic imbalance. Int J Clin Endocrinol. 2017; 1: 053-055.

30. Ahmed RG. Maternal anticancer drugs and fetal neuroendocrine dysfunction in experimental animals. Endocrinol Metab Syndr. 2017; 6: 281.

31. Ahmed RG. Letter: Gestational dexamethasone may be at higher risk for thyroid disease developing peripartum. Open Journal of Biomedical & Life Sciences (Ojbili). 2017; 3: 01-06.

32. Ahmed RG. Deiodinases and developmental hypothyroidism. EC Nutrition. 2017; 11.5: 183-185.

33. Ahmed RG. Maternofetal thyroid hormones and risk of diabetes. Int. J. of Res. Studies in Medical and Health Sciences. 2017; 2: 18-21.

34. Ahmed RG. Association between hypothyroidism and renal dysfunctions. International Journal of Research Studies in Medical and Health Sciences. 2017; 2: 1-4.

35. Ahmed RG. Maternal hypothyroidism and lung dysfunction. International Journal of Research Studies in Medical and Health Sciences. 2017; 2: 8-11.

36. Ahmed RG. Endocrine disruptors; possible mechanisms for inducing developmental disorders. International Journal of Basic Science in Medicine (IJBSM). 2017; 2: 157-160.

37. Ahmed RG. Maternal thyroid hormones trajectories and neonatal behavioral disorders. ARC Journal of Diabetes and Endocrinology. 2017; 3: 18-21.

38. Ahmed RG. Maternal thyroid dysfunction and neonatal cardiac disorders. Insights Biol Med. 2017; 1: 092-096.

39. Ahmed RG. Maternal hypothyroidism and neonatal testicular dysfunction. International Journal of Research Studies in Medical and Health Sciences. 2018; 3: 8-12.

40. Ahmed RG. Maternal hypothyroidism and neonatal depression: Current perspective. International Journal of Research Studies in Zoology. 2018; 4: 6-10.

41. Ahmed RG. Non-genomic actions of thyroid hormones during development. App Clin Pharmacol Toxicol: ACPT-108. 2018.

42. Ahmed RG. Maternal thyroid function and placental hemodynamic. ARC Journal of Animal and Veterinary Sciences. 2018; 4: 9-13.

43. Ahmed RG. Interactions between thyroid and growth factors during development. ARC Journal of Diabetes and Endocrinology. 2018; 4: 1-4.

44. Ahmed RG. Maternal thyroid hormones and neonatal appetite. ARC Journal of Nutrition and Growth. 2018; 4: 18-22.

45. Ahmed RG. Genomic actions of thyroid hormones during development. ARC Journal of Diabetes and Endocrinology. 2018; 4: 5-8.

46. Ahmed RG. Dysfunction of maternal thyroid hormones and psychiatric symptoms. American Research Journal of Endocrinology. 2018; 2: 1-6.

47. Ahmed RG. Is there a connection between maternal hypothyroidism and developing autism spectrum disorders? ARC Journal of Neuroscience. 2018; 3: 5-8.

48. Ahmed RG. Maternal thyroid dysfunctions and neonatal bone mal development. American Research Journal of Endocrinology (in press). 2018.

49. Ahmed RG. Maternal thyroid disorders and risk of neonatal seizure: Current perspective. ARC Journal of Neuroscience. 2018; 3: 21-25.

50. Ahmed RG. Gestational dioxin acts as developing neuroendocrine-disruptor. EC Pharmacology and Toxicology. 2018; 6.3: 96-100.

51. Ahmed RG. Maternal thyroid dysfunction and risk of neonatal stroke. ARC Journal of Animal and Veterinary Sciences. 2018; 4: 22-26.

52. Ahmed RG. Maternal thyroid disorders and developing skin dysfunctions. ARC Journal of Dermatology. 2018; 3: 13-17.

53. Ahmed RG. Maternal hypothyroidism-milk ejections: What is the link? ARC Journal of Nutrition and Growth. 2018; 4: 29-33.

54. Ahmed RG. Does maternal antepartum hypothyroidism cause fetal and neonatal hyponatremia? ARC Journal of Diabetes and Endocrinology. 2018; 4: 7-11.

55. Ahmed RG. Maternal hypothyroidism and rheumatoid arthritis. International Journal of Research Studies in Medical and Health Sciences. 2018; 3: 1-5.

56. Ahmed RG. Developmental thyroid and skeletal muscle dysfunction. ARC Journal of Diabetes and Endocrinology. 2018; 4.

57. Ahmed RG. Hyperthyroidism and renal disorders. ARC Journal of Animal and

Veterinary Sciences. 2018; 4: 1-5.

58. Ahmed RG. Maternal hypothyroidism and developing hyperhomocysteinemia. ARC Journal of Nutrition and Growth. 2018; 4: 5-9.

59. Ahmed RG. Maternal hyperthyroidism and neonatal testicular dysfunction. ARC Journal of Urology. 2018; 3: 6-10.

60. Ahmed RG. Maternal hypothyroidism-developing dyslipidemia: What is the connection? ARC Journal of Pharmaceutical Sciences (AJPS). 2018: 4; 1-6.

61. Ahmed RG. Maternal iodine deficiency and pregnancy complications: Still a health issue for the pregnant and fetuses. ARC Journal of Pharmaceutical Sciences (AJPS). 2018: 4; 7-11.

62. Ahmed RG, Abdel-Latif M, Ahmed F. Protective effects of GM-CSF in experimental neonatal hypothyroidism. International Immunopharmacology. 2015; 29: 538-543.

63. Ahmed RG, Abdel-Latif M, Mahdi E, El-Nesr K. Immune stimulation improves endocrine and neural fetal outcomes in a model of maternofetal thyrotoxicosis. Int. Immunopharmacol. 2015; 29: 714-721.

64. Ahmed RG, Davis PJ, Davis FB, De Vito P, Farias RN, Luly P, Pedersen JZ, Incerpi S, et al. Nongenomic actions of thyroid hormones: from basic research to clinical applications. An update. Immunology, Endocrine & Metabolic Agents in Medicinal Chemistry. 2013; 13: 46-59.

65. Ahmed RG, El-Gareib, AW. Lactating PTU exposure: I- Alters thyroid-neural axis in neonatal cerebellum. Eur. J. of Biol. and Medical Sci. Res. 2014; 2: 1-16.

66. Ahmed RG, El-Gareib AW. Maternal carbamazepine alters fetal neuroendocrine-cytokines axis. Toxicology. 2017; 382: 59-66.

67. Ahmed RG, El-Gareib AW, Incerpi S. Lactating PTU exposure: II- Alters thyroid-axis and prooxidant-antioxidant balance in neonatal cerebellum. Int. Res. J. of Natural Sciences. 2014; 2: 1-20.

68. Ahmed RG. El-Gareib, AW, Shaker HM. Gestational 3,3′,4,4′,5-pentachlorobiphenyl (PCB 126) exposure disrupts fetoplacental unit: Fetal thyroid-cytokines dysfunction. Life Sciences. 2018; 192: 213-220.

69. Ahmed RG, Incerpi S. Gestational doxorubicin alters fetal thyroid–brain axis. Int. J. Devl. Neuroscience. 2013; 31: 96-104.

70. Ahmed RG, Incerpi S, Ahmed F, Gaber A. The developmental and physiological interactions between free radicals and antioxidant: Effect of environmental pollutants. J. of Natural Sci. Res. 2013; 3: 74-110.

71. Ahmed RG, Walaa GH, Asmaa FS. Suppressive effects of neonatal bisphenol A on the neuroendocrine system. Toxicology and Industrial Health Journal (in press). 2018.

72. Van Herck SLJ, Geysens, S, Bald E, Chwatko G, Delezie E, Dianati E, et al. Maternal transfer of methimazole and effects on thyroid hormone availability in embryonic tissues. Endocrinol. 2013; 218: 105-115.

73. Incerpi S, Hsieh MT, Lin HY, Cheng GY, De Vito P, Fiore AM, et al. Thyroid hormone inhibition in L6 myoblasts of IGF-I-mediated glucose uptake and proliferation: new roles for integrin αvβ3. Am. J. Physiol. Cell Physiol. 2014; 307: 150-161.

74. Candelotti E, De Vito P, Ahmed RG, Luly P, Davis PJ, Pedersen JZ, et al. Thyroid hormones crosstalk with growth factors: Old facts and new hypotheses. Immun, Endoc & Metab. Agents in Med. Chem. 2015; 15: 71-85.

75. De Vito P, Candelotti E, Ahmed RG, Luly P, Davis PJ, Incerpi S, et al. Role of thyroid hormones in insulin resistance and diabetes. Immun, Endoc & Metab. Agents in Med. Chem. 2015; 15: 86-93.

76. El-Ghareeb AA, El-Bakry AM, Ahmed RG, Gaber A. Effects of zinc supplementation in neonatal hypothyroidism and cerebellar distortion induced by maternal carbimazole. Asian Journal of Applied Sciences. 2016; 4: 1030-1040.

77. Zoeller RT, Dowling ALS, Herzig CTA, Iannacone EA, Gauger KJ, Bansal R. Thyroid hormone, brain development, and the environment. Environ. Health Perspect. 2002; 110: 355-361.

78. Zoeller RT. Editorial: Local control of the timing of thyroid hormone action in the developing human brain. J. Clin. Endocrinol. Metab. 2004; 89: 3114-3116.

79. Gilbert ME, Sui Li. Dose-dependent reductions in spatial learning and synaptic function in the dentate gyrus of adult rats following developmental thyroid hormone insufficiency. Brain Res. Arch. 2006; 1069: 10-22.

80. Hogan NS, Crump KL, Duarte P, Lean DRS, Trudeau VL. Hormone cross-regulation in the tadpole brain: developmental expression profiles and effect of T3 exposure on thyroid hormone- and estrogen responsive genes in Rana pipiens. Gen. Comp. Endocrinol. 2007; 154: 5-15.

81. Andersen SL, Laurberg P, Wu CS, Olsen J. Maternal thyroid dysfunction and risk of seizure in the child: A Danish nationwide cohort study. Journal of Pregnancy. 2013; 2013: 1-10.

82. Meier S, Bräuer AU, Heimrich B, Nitsch R, Savaskan NE. Myelination in the hippocampus during development and following lesion. Cell Mol Life Sci. 2004; 61: 1082-1094.

83. Huang Z, Liu J, Cheung PY, Chen C. Long-term cognitive impairment and myelination deficiency in a rat model of perinatal hypoxic-ischemic brain injury. Brain Res. 2009; 1301: 100-109.

84. Jarjour AA, Zhang H, Bauer N, Ffrench-Constant C, Williams A. *In vitro* modeling of central nervous system myelination and remediation. Glia. 2012; 60: 1-12.

85. Zhou D, Hemmer B. Specificity and degeneracy: T cell recognition in CNS autoimmunity. MolImmunol. 2004; 40: 1057-1061.

86. Albornoz EA, Carreño LJ, Cortes CM, Gonzalez PA, Cisternas PA, Cautivo KM, et al. Gestational hypothyroidism increases the severity of experimental autoimmune encephalomyelitis in adult offspring. Thyroid. 2013; 23: 1627-1636.

87. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. N Engl J Med. 2000; 343: 938-952.

88. Tsui A, Lee MA. Multiple sclerosis and pregnancy. CurrOpinObstet Gynecol. 2011; 23: 435-439.

89. Compston A, Coles A. Multiple sclerosis. Lancet. 2008; 372: 1502-1517.

90. Voskuhl R, Giesser BS. Gender and reproductive issues in multiple sclerosis. In: Primer on Multiple Sclerosis. Giesser BS (Ed). Oxford University Press, NY, USA. 2011; 221-240.

91. Alwan S, Sadovnick AD. Multiple sclerosis and pregnancy: maternal considerations. Women's Health. 2012; 8: 399-414.

92. Schoonover CM, Seibel MM, Jolson DM, Stack MJ, Rahman RJ, Jones SA, et al. Thyroid hormone regulates oligodendrocyte accumulation in developing rat brain white matter tracts. Endocrinology. 2004; 145: 5013-5020.

93. Henrichs J, Bongers-Schokking JJ, Schenk JJ, Ghassabian A, Schmidt HG, Visser TJ, et al. Maternal thyroid function during early pregnancy and cognitive functioning in early childhood: The generation R study. J ClinEndocrinolMetab. 2010; 95: 4227-4234.

94. Wei W, Wang Y, Dong J, Wang Y, Min H, Song B, et al. Hypothyroxinemia induced by maternal mild iodine deficiency impairs hippocampal myelinated growth in lactational rats. Environ Toxicol. 2015; 30: 1264-1274.

95. Babu S, Sinha RA, Mohan V, Rao G, Pal A, Pathak A, et al. Effect of hypothyroxinemia on thyroid hormone responsiveness and action during rat postnatal neocortical development. Exp Neurol. 2011; 228: 91-98.

96. Marrie RA. Environmental risk factors in multiple sclerosis aetiology. Lancet Neurol. 2004; 3: 709-718.