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A Review on the Metabolic Disorders of Iodine Deficiency

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Abstract: Iodine is in the crucial parts of two hormones of T4 and T3 produced by the thyroid glands which are essential for all the aspects of human metabolisms. It is demonstrated that iodine deficiency can be considered as sole cause of many thyroid abnormalities including mental disorders. Iodine deficiency of sufficient degree to cause hypothyroidism during fetus life and early infancy will be accompanied with brain abnormality possibly to the stage of mental retardation. The iodine deficiency among subjects in their early stage of childhood is not as severe as those in their fetus or infancy. In adult subjects the sever iodine deficiency can be also associated with mental disorders due to the direct side effects of hypothyroidism occurred by lack of iodine. The clinical manifestation of iodine deficiency show itself with psychological disorders in adult subjects. The status of iodine within blood can be evaluated through measurement of urinary iodine level and the low urinary concentration is an indicative of hypothyroidism. Mental retardation and brain damage due to iodine deficiency can be prevented if iodine supplementation prescribed duly on time.

Key words: Hypothyroidism, infant, adult, mental retardation, brain damage

INTRODUCTION

Thyroid gland produces two important hormones tetra idothyronin or thyroxine (T4) and triidothyronine (T3). These two hormones are essential for human physiological process and metabolisms (Reinehr, 2010; Reinehr *et al*., 2008; Mansourian *et al*., 2008; Mansourian, 2010b-e).

Thyroid hormone deficiency accompanied with serious adverse effects and it will have an catastrophic consequences particularly among infants and young children. In some circumstances, the physical and mental status of infant both are affected. The biosynthesis of thyroid hormones exclusively depends on the presence of iodine which is entirely thyroid based element and the thyroid is the sole site of iodine absorption and storage (Mansourian, 2011a; Mansourian *et al*., 2007; Mansourian, 2010e).

The oxidized iodine within thyroid is transferred on the tyrosyle residues of thyroglobulin and converted into tyrosyle iodinated substances monoido and diido tyrosyle (MIT, DIT) on thyroglobuline. The coupling process followed between MIT and DIT, DIT and DIT produce T3 and T4, respectively still on the thyroglobuline molecules. It is therefore, interestingly obvious that 4 and 3 in T4 and T3 are designated for the number of iodine atoms present in the biochemical structure of thyroid hormones and this is why the iodine reside in crucial center of thyroid hormones and in fact T4, T3 without iodine atom are only amino acids derivatives. Thyroglobuline is hydrolyzed subsequently by the lysozome enzymes within the extra follicular space of thyroid and eventually T4 and T3 are secreted into blood circulation (Mansourian, 2011a).

Iodine therefore, reside in the central core of manufacturing T4 and T3 in thyroid and iodine deficiency in human eventually lead to serious metabolic disorders. Iodine deficiency caused tremendous headaches for health care providers world wide which can be occurred from early stage of fetus life (Zimmermann and Andersson, 2011; Delange, 2002; Laurberg *et al*., 2006; Kapil, 2010; Andersson *et al*., 2010; Rajatanavin, 2007; Kurtoglu *et al*., 2004; Jaruratanasirikul *et al*., 2006; Kung, 2007; Luton *et al*., 2011; Delange *et al*., 2002; Vern *et al*., 2003). Iodine deficiency eventually lead to hypothyroidism, only in rare cases it can cause hyperthyroidism but it is not absolutely common (Pearce *et al*., 2004; Haldimann *et al*., 2005; El-Ghawi and Al-Sadeq, 2006; Thomson *et al*., 2008; Chavasit *et al*., 2002; Mansourian, 2010b, c, e).

The level of thyroid hormones dictate the amount of iodine for the production of T4, T3. The iodine level also depends on the age, physiological status of each individual (Glinoer, 2007, 2003, 1999, 2001; Luton *et al*., 2011; Delange, 1994; Laurberg *et al*., 2000, 2001, 2007; Zarei *et al*., 2009).

It seems that pregnancy, fetus life, infancy and childhood, are the periods with highest requirement of

iodine, respectively due to higher level of thyroid hormones which are duly required (Sidibeel, 2007; Glinoer, 2007, 1999; Delange, 1998). Various studies indicated the vital and crucial requirement of iodine intake for the proper amount of thyroid hormone to prevent particularly the brain damage during fetus and infancy. It is therefore, absolutely necessary to have enough iodine supplementation during pregnancy and in early stage of infancy and childhood to prevent the occurrence of mentally retarded newborns (Delange, 1998; Glinoer, 2007, 2003, 1999; Eftekhari *et al*., 2007).

The role of iodine in fetus life and early infancy: Iodine is absorbed into thyroid gland through an active transport mediated by Na/K pump which itself regulated and stimulated by Thyroid Stimulating Hormone (TSH) a pituitary hormone. The situation of iodine deficiency seems to be even worse during pregnancy, due to mental and physical growth adverse effects. It is widely advised that pregnant women dietary regiment should be supplemented with enough iodine to prevent possible hypothyroidism which can happen due the iodine shortage (Berbel *et al*., 2007; Zimmermann, 2007a; Maberly, 1994). It should be mentioned that in addition to iodine deficiency, any other metabolic disorders which occur genetically on the biochemical structure of thyroid hormone translocator protein and receptor which are present on the cell surface and nucleus of T4 and T3 target tissues also can have a similar adverse effects, because in either cases thyroid hormones messages are not relayed into the tissues (Glinoer, 1999, 2001, 2007). In addition to mental and physical disturbances iodine deficiency of large extend to cause hypothyroidism will interfere with the physiological status of pregnancy accompanied with catastrophic event in some cases and fetus death eventually (Berbel *et al*., 2007; Zimmermann, 2007a; Maberly, 1994). It should be also mentioned that the stage at which iodine deficiency occur can play an important role in the presentation of signs and symptoms of iodine deficiency during pregnancy. The first and the early stage of second trimester of pregnancy and early infancy is an utmost importance in regard to iodine deficiency and much damage to the fetus occur during this phase of pregnancy due to onset of maternal hypothyroidism in first and early second trimester of pregnancy (DeLong *et al*., 1985; Vulsma *et al*., 1989; Christensen and Davis, 2004). Under any condition iodine deficiency accelerate the rate of hypothyroidism in maternal life up to 10-12 times, therefore, to prevent the side effects of fetus damage due to maternal iodine deficiency maternal hypothyroidism should be checked out regularly to prevent any possible mental and physical retardation of fetus, although the newborns should be assessed for their blood thyroid hormone shortly after delivery to prevent similar consequences (Delange, 1997; Glinoer, 1997).

The role of iodine deficiency in brain tissues: In case of iodine deficiency the anatomy of brain tissues are not properly formed, the cell production and differentiation altered due to iodine deficiency. Iodine deficiency enough to cause hypothyroidism during fetus life and early infancy eventually cause mental disturbance with possible mental retardation (Eayrs and Taylor, 1951; Madeira *et al*., 1988a, b). Thyroid hormone also play an important roles in nervous system metabolic pathway, therefore it seems the lack of iodine if converted to hypothyroidism can eventually leave the newborn with mental abnormality (Ambrogini *et al*., 2005; Desouza *et al*., 2005; Lemkine *et al*., 2005; Montero-Pedrazuela *et al*., 2006; Emder and Jack, 2011; Jaruratanasirikul *et al*., 2006; Rajatanavin, 2007).

The metabolic pathway of thyroid hormones within the brain follow almost the same pathways to other tissues and it is the free thyroid hormones within blood circulation which play an important role in regulating metabolic pathways. It means T4 and T3 following biosynthesis within thyroid gland secreted into blood circulation, transported by transporting protein which are synthesized in the liver, reach the target tissues and bind to the receptors following passage through cell membrane by thyroid hormone translocator protein. Like other peripheral tissues in brain, T4 can also be converted into T3 which is a more potent hormone with different speed to accommodate itself with brain actual requirement (Escobar-Morreale *et al*., 1995, 1999; Mansourian, 2011a, b; Mansourian 2010a, c).

T4 and T3 play an utmost important role in growing fetus physiological life and particularly in the brain formation during the first trimester of pregnancy which fetus completely depends to the maternal thyroid hormone also the requirement is decreased as fetus grow further but it is a slow process which need extra attention to have normal mental and physical status (Kurtoglu *et al*., 2004; De Escobar *et al*., 1987, 1990, 1985, 2004; Obregon *et al*., 1984; Porterfield and Hendrich, 1992; Woods *et al*., 1984; Contempre *et al*., 1993; Bernal and Pekonen, 1984; Vulsma *et al*., 1989).

Malnutrition may lead to iodine deficiency hypothyroidism: One of main problem of thyroid disorder end-up with hypothyroidism is iodine deficiency due to the nutritional status and the deficiency of iodine in the dietary regiment. A high portion of thyroid deficiency

leading to the clinical manifestation of cretinism among newborn and children are due to maternal dietary iodine deficiency during pregnancy and early phase of infancy which is also caused by the fact that in many region of the world the nutrient used as daily dietary consumption are iodine deficient as well and the iodine supplementation in such region is a urgent matter to be considered (Zimmermann and Andersson, 2011; Delange, 2002; Zhong *et al*., 1983; Hetzel and Hay, 1979; McMichael *et al*., 1980). Experimentally hypothyroidism are produced during pregnancy by omitting the iodine from daily dietary. These studies demonstrated the whole clinical manifestation of thyroid hormone deficiency on the growing fetus following iodine deletion from nutritional regiment. The other studies indicated that the scenario was reversed, by iodine supplementation (Kapil, 2010; Laurberg *et al*., 2006, 2001; Potter *et al*., 1981).

Although the fetus physical and mental growth in early phase of pregnancy entirely depends to the maternal circulation of thyroid hormones but experimental evidence, proved that in latter stage of pregnancy also the growing fetus itself is able to produce thyroid hormones but the hormones should be supplemented also by maternal circulation to have a fetus with normal mental and physical growth (McMichael *et al*., 1980; Hetzel *et al*., 1988; Delange, 1998; Glinoer, 1999; Mansourian, 2010e, d; Shahmohammdi *et al*., 2008; Mansourian *et al*., 2010a, b; Mansourian *et al*., 2007, Marjani *et al*., 2008; Mansourian and Ahmadi, 2010).

It should be kept in mind that although thyroid hormone or iodine supplementation may eventually improve physical growth but the fetus and newborn mental disorder, caused by T4 and T3 deficiency, might be an irreversible pathway (Auso *et al*., 2004; Koibuchi and Chin, 2000; Chan and Kilby, 2000; Delange, 2000, 2001).

The iodine deficiency associated with various abnormalities ranging from pregnancy disorder affecting the fetus with various anomalies and in some cases, accompanied with fatal outcome (Glinoer, 2007; Sidibeel, 2007; Delange, 1994, 1998; Andersson *et al*., 2010; Zimmermann, 2007a, 2009; Mansourian, 2010e). Even following giving birth to the child by iodine deficient mother the newborn can be accompanied with possible risk of mental retardation. The iodine deficiency during adulthood up to the elderly is accompanied with goiter and associated consequences of hypothyroidism. Accordingly iodine related malnutrition, malabsorbtion and related nutritional status in any stage of life can be accompanied with hypothyroidism adverse effects (Auso *et al*., 2004; Koibuchi and Chin, 2000; Chan and Kilby, 2000; Delange, 2000, 2001).

The mechanism behind brain damage during fetus and early life due to iodine deficiency relay on the fact that, lack of iodine eventually accompanied with hypothyroidism which will be resulted in the reduction of T4 and T3 serum concentration, followed by adverse alteration of gene expression particularly within the brain and nerves tissues, of fetus and neonate (Auso *et al*., 2004; Koibuchi and Chin, 2000; Chan and Kilby, 2000; Delange, 2000, 2001).

The reversibility of brain damage is not certain, by thyroid hormone, it is this dilemma which manifest the importance of iodine supplementation during pregnancy and early stage of infancy which is absolutely crucial particularly for the mental function (Auso *et al*., 2004; Koibuchi and Chin, 2000; Chan and Kilby, 2000; Delange, 2000, 2001).

As it was mentioned above the different stage of pregnancy is of utmost importance for the fetus mental growth (Dobbing and Sands, 1973). Following termination of pregnancy and in early phase of infancy, the brain still is not developed properly and during both stages of fetus life and early infancy the presence of thyroid hormones, crucially are required and lack of iodine prevent or at least slow the process of brain formation into proper shape. It is vital to remember that the brain development in the early stage of fetal life entirely relay on the maternal circulation of enough thyroid hormone but as fetus grows further it is less dependent on the maternal thyroid hormones circulation (Dobbing and Sands, 1973). Under any circumstance, the lack of iodine which lead to the thyroid hormone deficiency may eventually ended with mentally retard infant (Dobbing and Sands, 1973). It should be mentioned that in some cases iodine excess is accompanied with adverse effects and following iodine overload the signs and symptoms of hypothyroidism and hyperthyroidism are both can be exhibited and this is why iodine intake should be only on physician and nutritionists recommendation (Carceller *et al*., 2011; Kurtoglu *et al*., 2009; Khashu *et al*., 2005; Ergur *et al*., 2011; Teng *et al*., 2011).

The significant role which played by the fetal and maternal T4 and T3, prove that the clinical care should be taken during pregnancy on the amount of iodine supplementation to prevent any thyroid abnormalities. Also fetus can produce thyroid hormone to substitute the maternal thyroid hormones but one should remember, that the circulating maternal thyroid hormones always support the fetus thyroid hormones requirements particularly during first half of pregnancy and it seems maternal thyroid hormone partly required up to the very last days of pregnancy (Zimmermann, 2007b; Zimmermann, 2009;

Bernal and Pekonen, 1984; Kooistra *et al*., 2006; Vulsma *et al*., 1989). The gene expression which occurred through the combination of T4 and T3 to their nuclear receptor is considered as a cornerstone to our understanding in how thyroid hormone facilities their effects in producing various proteins required for brain development. Although thyroid hormones are binding to their receptor, within nuclear region of brain cell but the free hormone reaches the receptor through a passage, assisted by a translocation protein present on the brain cell membrane (Delange *et al*., 1989).

Various degrees of iodine deficiency and Brain development during pregnancy: Iodine deficiency can be subdivided into sever, mild and moderate, if sever iodine deficiency was demonstrate itself it can be accompanied by serious physical and mental disturbance during fetus life. There are controversial arguments on condition of mild and moderate iodine deficiency but pregnant women possible hypothyroidism due to iodine deficiency may eventually cause the fetus physical and mental disturbances but this area of studies is not absolutely clear and it is matter for further investigations (Kooistra *et al*., 2006; Vulsma *et al*., 1989; Delange *et al*., 1989).

Under any condition iodine deficiency during fetal life may lead to fatal outcome and studies showed the iodine supplementation reduce the severity of scenario and such circumstance are reversed on iodine prescription. Various studies from different part of the world indicated that the fatal outcome of iodine deficiency in infancy also reduced following iodine supplementation (Pharoah and Connolly, 1987; Cobra *et al*., 1997; Thilly *et al*., 1980, 1986; Delong *et al*., 1997; Dobbing, 1974).

The iodine supplementation in such circumstance, enable the thyroid to produce enough T4 and T3 for the proper functioning and stimulation of healthy brain development. The throughout studies confirmed that iodine deficiency is not only belong to the poor and developing countries, but the iodine deficiency and possible brain damage can be observed even in well developed countries but it should be emphasized that the most adverse effects of iodine deficiency are seen among infant and it is why higher iodine requirement is necessary for younger population due to their higher metabolic rate and growth developments (Zimmermann and Andersson, 2011; Delange, 2002, 1990; Dobbing, 1974).

Iodine deficiency among children: The iodine deficiency among subjects in their early stage of childhood, is not sever as those in their fetus or neonatal life. It has been shown that cognition of children are not adversely affected but it has to be mentioned that the iodine supplementation enhance the intelligence ability of children (Aghini-Lombardi *et al*., 1995; Santiago-Fernandez *et al*., 2004). Other studies indicated the clinical manifestation have been improved to some acceptable range after iodine supplementation among children with iodine deficiency (Zimmermann *et al*., 2006). The intelligence capacity of those children, that their fetus life were associated with sever iodine deficient mother was lower, compared to those children that their fetus life was accompanied with moderate maternal iodine deficiency (Fierro-Benitez *et al*., 1974; Kochupillai *et al*., 1986; Huda *et al*., 1999). Under any circumstances, some reports indicated the iodine deficiency of even moderate to sever cases can be accompanied by reducing the intellectual capacity among children to some extend (Bleichrodt and Born, 1994; Qian *et al*., 2005). In addition to the earlier reported studies, other investigation indicated that mild to moderate iodine deficiency cause the reducing psychomotor and mental development, neuromuscular disorders, reducing learning capability, slowing psychomotor development and many similar results which mostly related with the level iodine deficiency compared with the control subjects. It has also been demonstrated that iodine supplementation in some instance enhance the rate of intelligence and psychomotor ability (Bleichrodt *et al*., 1989; Vermiglio *et al*., 1990; Fenzi *et al*., 1990; Tiwari *et al*., 1996; Shresta, 1994; Van den Briel *et al*., 2000; Aghini-Lombardi *et al*., 1995).

In spit of all documented reports on the positive role played by iodine supplementation, on the cognitive and psychomotor abilities but this area of research are controversially discussed (Zimmermann *et al*., 2007; Zimmermann, 2009; Mansourian, 2010e; Mansourian *et al*., 2010b; Mansourian and Ahmadi, 2010).

Iodine deficiency among adults population: In has been reported that iodine deficiency of enough degree to be considered as a sever, can profoundly associated with mental disorder due to the direct side effects of thyroid hypo function and subsequent overt hypothyroidism with possible, cerebral abnormalities in adult population. The iodine deficiency, eventually, show itself with psychological disorder, to such extend that daily life and routine procedure of adults subjects can be effected negatively (Hollowell and Hannon, 1997; Mansourian *et al*., 2007; Mansourian, 2010c; Mansourian, 2011a). Although iodine deficiency do not demonstrate a fatal outcome among adults but the adult iodine deficiency is associated with problems, that can adversely interfere with routine procedure of daily life

and normal metabolism (Aghini-Lombardi *et al*., 1999; Vanderpump *et al*., 1995; Laurberg *et al*., 1998; Szabolcs *et al*., 1997; Garcia-Mayor *et al*., 1999; Mansourian *et al*., 2008; China, Marjani *et al*., 2008; Mansourian, 2010b).

In rare cases iodine supplementation trigger hyperthyroidism: Surprisingly, iodine supplementation programs in some cases, stimulate the thyroid gland towards hyperthyroidism. The concept behind this observation, derived from this fact that the iodine deficiency itself contribute the thyroid cells proliferation, thyrocyte and Thyroid Stimulating Hormone (TSH) receptor mutation. TSH is a pituitary hormone which stimulate thyroid gland to produce T4 and T3 after binding to the TSH Receptor (TSHR) on the thyroid gland. The thyroid gland begin to produce T4 and T3 following TSH binds to TSHR (Ergur *et al*., 2011; Carceller *et al*., 2011; Kurtoglu *et al*., 2009; Delange *et al*., 1999; Baltisberger *et al*., 1995; Mansourian, 2011a).

It seems, that in some from of moderate to sever iodine deficiency iodine supplementation possibly stimulated the iodine-induced hyperthyroidism but this is a pathway which can be reversed eventually (Dremier *et al*., 1996).

The other possibilities of excessive iodine supplementation, is the adverse effect of such supplementation, on inducing the immune system to be become activated against thyrocyte in genetically susceptible indivisual. In some other studies, the iodine supplementation stimulate the auto -immunity against the thyroid and possible production of auto antibodies against thyroid gland (Jonckheer *et al*., 1992; Delange and Lecomte, 2000; McConahey *et al*., 1962; Mansourian, 2010a).

The iodine supplementation of excessive amount even in healthy subjects, can stimulate the healthy thyroid into a condition in which the immune system activate against the peroxidase enzyme responsible for iodine peroxidation prior to T4 and T3 production within the thyroid gland. This observation which is adversely affect the thyroid, is reversed into normal condition eventually. The findings of this area of research are not and globally homogenously are agreed (Kahaly *et al*., 1998; Hollowell *et al*., 2002; Braverman, 1994; Pearce *et al*., 2002; Yang *et al*., 2007; Teng *et al*., 2006; Mansourian, 2010e).

There are also some reports indicating that if excessive amount of iodine taken for a long period of times the iodine overload hypothyroidism, can be a eventual outcome, of such undesired dietary regiments. It is also reported that iodine excess to the level which stimulate the thyroid into goiter condition is done either by iodine stimulation of auto immunity against thyroid gland or the excess iodine and the eventual absorption by the thyroid, lead to the temporary inhibition of T4 and T3 synthesis through the Wolff- Chikoff effect, in those individual which are prone to such adverse effect. (Roti *et al*., 1981; Suzuki *et al*., 1965; Tonglet *et al*., 1992; Knudsen *et al*., 2000a).

As whole the adverse effects of iodine excess on the thyroid gland are of both hypo and hyperthyroid disorder as explained above. It seems that the iodine deficiency and iodine overload both can interfere with proper mechanism of thyroid gland and in susceptible subjects either of iodine deficiency and excess can possibly accompanied with side effects of thyroid disorders (McGuire and Galloway, 1994).

How circulating blood T4 and T3 do their physiological function in the targets tissues: Most of T4 and T3 are transported through blood circulation by proteins which are synthesized within the liver (Mansourian, 2011b) and the free hormone which are the true active hormones pass through target tissues via a translocator protein complex resided on the membrane of target tissues. In addition to what it was mentioned the T4 and T3 nuclear receptor is shown to play a crucially important passage in this mechanism for the function of thyroid hormone in the brain in fetus and early infancy (Laterra and Goldstein, 2000; Dumitrescu *et al*., 2004; Friesema *et al*., 2004, 2005; Perez-Castillo *et al*., 1985; Schwartz and Oppenheimer, 1978; Strait *et al*., 1990).

Any physiological modification to this system can also cause some abnormalities to the tissues involved and if the brain and nervous system associated with this above mentioned disorder the fetus and infant manifest a sever clinical symptoms resulting from hypothyroidism due to iodine deficiency.

The thyroid hormones do their physiological function by regulation which take place through genetical manipulation to give the satisfactory speed to the various biochemical reactions of the brain and other tissues, through related enzymes of a specified reaction at specific genes. It should be mentioned that in general the exact scenario in how T4 and T3 behave to exercise their influence on gene manipulation particularly during fetus life is a subject for further investigation in this area of medical science and major portion of our knowledge in this region is through experimental research on animal models (Schwartz *et al*., 1997; Krebs *et al*., 1996; Sampson *et al*., 2000; Dowling *et al*., 2001; Sinha *et al*., 2008; Farsetti *et al*., 1992; Zou *et al*., 1994). The present experimental data on how T4 and T3 influence gene

manipulation indicate that during infancy the brain tissues are more prone towards thyroid hormones and it seems that the brain development in this stage of life do happen through the gene expression regulated by thyroid hormones. The thyroid hormone clearly play an important role in regulation of adults psychological status up to the late stage of life and it is demonstrated that hormone therapy to treat hypothyroidism reveres the patient condition to the large extend (Diez *et al*., 2008; Bauer *et al*., 2002; Simon *et al*., 2002; Baumgartner *et al*., 1994; Bauer *et al*., 2005).

Serum iodine evaluation can be assessed through urinary iodine measurement: Iodine within blood circulation can be assessed through, measurement of urinary iodine-concentration, the low level of urinary concentration is a indicative of hypothyroidism (Mansourian *et al*., 2007; Mansourian, 2010e; Shahmohammdi *et al*., 2008).

The simple goiter is a clinical manifestation explaining the possibility of reduced amount of intake iodine (Mansourian, 2010b, c). The TSH and Thyroglubulin (Tg), are also two indicators which can demonstrate the physiological status of thyroid gland with potential indication of iodine status.

TSH, measurement and its negative correlation with thyroid hormones of T4 and T3 clearly can give a clue to the thyroid function tests. In iodine deficiency the Tg which is an thyroid follicular space protein is released within blood circulation and its measurement can be an indicative iodine status of human body. The combination of TSH and Tg measurement are useful indicative for the assessment of iodine concentration (Spencer and Wang, 1995; Knudsen *et al*., 2001; Mansourian, 2011a).

The estimation of thyroid hormone of T4 and T3 can not give a prices clue to the iodine level and should not be used precisely to assess the iodine status. TSH serum level physiologically is controlled by the amount of T4 and T3 but on the other hand the level of T4 and T3 may in some way reflect the amount of iodine and alternatively the TSH measurement can in some cases also be an indicative of iodine level. It should be mentioned that TSH can not be thoroughly trusted at different age groups to estimate serum iodine level but its concentration most probably can be used as serum iodine status. Due to the utmost importance of thyroid hormones and iodine assessment in early infancy TSH assessment as single test seems to be a valuable probe into in how newborn thyroid function at crucial days of life. It is therefore, suggested that serum T4 and T3 level in infants can ultimately be examined by TSH measurements at a time when the newborns require the optimal thyroid hormones level to prevent brain damage (Andersen *et al*., 2008; Knudsen *et al*., 2000b; Jaruratanasirikul *et al*., 2009; Jaruratanasirikul *et al*., 2006).

CONCLUSION

- Thyroid gland produce two important hormones, of tetra idothyronin or thyroxine (T4) and triidothyronine (T3). These hormones are essential for all the aspect of human physiological process and metabolisms
- Iodine deficiency to the degree leading to hypothyroidism during fetus life and early infancy causing the brain malfunction to the stage which brain tissues are not properly formed with possible mental retardation outcome
- The iodine deficiency among subjects in their early stage of childhood is not as severe as those in their fetus or neonatal life. It has been shown that cognition of children are not adversely affected but it has to be mentioned that the iodine supplementation enhance the intelligence ability of children
- It has been reported that iodine deficiency of enough degree to be considered as a sever, can profoundly associated with mental disorder in adult population due to the direct side effects of overt hypothyroidism with possible, cerebral abnormalities. The clinical manifestation of iodine deficiency eventually show itself with psychological disorders, to the such extend that the daily life and routine procedure of adults subjects can be effected seriously
- The status of iodine within blood can be evaluated through measurement of urinary iodine level and the low urinary concentration is a indicative of hypothyroidism. Some of the side effects of thyroid malfunction in such conditions can be corrected particularly among adults subjects by iodine supplementation if it is done on time.

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