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A Review on Post-Puberty Hypothyroidism: A Glance at Myxedema

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Abstract: Hypothyroidism, is a thyroid disorder accompanied by serum thyroid hormone reduction when thyroxin T4, the main thyroid hormone, reduced, it is followed by disruption of a negative-feed back auto regulatory mechanism on pituitary gland and subsequent thyroid stimulating hormone (TSH) which is released into the blood circulation to stimulate the thyroid gland to produce enough thyroid hormone to compensate for the body hormone requirements. Therefore, reduced serum thyroxin(T4) in principle, triidothyronine (T3) and elevated TSH are laboratory indices for the diagnosis of hypothyroidism. At early stage of hypothyroidism although laboratory measurements of thyroid function test are manifest the thyroid disorder but the patient clinical signs and symptoms may remain unnoticed. If the patient undiagnosed and untreated the condition of hypothyroidism worsen and the clinical manifestation begin to show itself and myxedema is a definition given to the whole picture of untreated hypothyroidism at very end stage the patients enter into myxedema comma with eventual death due to the sever symptoms of hypothyroidism. Among important causative factors leading to catastrophic events in myxedema is life threatening hypothermia, heart and cerebral dysfunctions.

Key words: Hypothyroidism, thyroid stimulating hormone, thyroxin, hypothermia, myxedema comma

HYPOTHYROIDISM

Hypothyroidism defined is a metabolic disorder in which the thyroid gland does not produce normal levels of thyroid hormones either thyroxin (T4) or triidothyronine (T3). The sever clinical manifestations accompanied with this type of thyroid malfunction in post-puberty is well known as myxedema. This latter abnormality was introduced in medicine in late ninteenth century. The myxedema which in practice is term for sever thyroid malfunction resulting with symptoms such as, skin, hair problems, speech difficulty slurry vision, gastrointestinal malfunction, intolerance to cold, imbalance of movement, reproductive and intellectual disabilities are all due to reduction of thyroid hormone synthesis which may have been followed by various reasons all with altering the concentration of either T4 and T3 to the level which the pathway of normal metabolism is negatively affected through this physiological changes due to thyroid malfunction (Hall and Scanlon, 1979; Ord, 1978; Evered *et al*., 1973; Watanakunakorn *et al*., 1965; Gull, 1874). Hypothyroidism is divided into 3 main sub-division as follow: (1) Primary hypothyroidism, in this type of thyroid malfunction the damages to the thyroid gland are responsible for the reduction of thyroid hormones of T4, T3 subsequently the production and release of Thyroid Stimulating Hormone (TSH), from pituitary is increased, this happen due to the absence of negative feed back control of TSH release by the T4 and T3 because when thyroid does not produce enough T4, T3 subsequently the negative feed back which is implied by T4 and T3 on the pituitary gland is not existed any more and therefore pituitary gland begin to synthesis and release TSH into the blood circulation. Thyroid is the only tissue which has receptor for the TSH therefore it binds to the receptor on the thyroid gland to stimulate the thyroid gland to produce enough T4 and T3 (Larsen, 1982; Wiersinga, 2004; Evered *et al*., 1973; Martino *et al*., 2000; Tunbridge *et al*., 1977a; Ford and Carter, 1990; Vanderpump *et al*., 1995; Bigos *et al*., 1978) TSH not only stimulate the synthesis of T4 and T3 but also it stimulate the thyroid tissue growth ending with thyroid enlargement of the thyroid which is called goiter. (2) The secondary form of hypothyroidism is a malfunction when the thyroid gland is not stimulated enough by TSH to produce adequate T4 and T3, this problem is due to pituitary disorder therefore pituitary is unable to synthesis and release enough TSH to stimulate T4 and T3 on the thyroid gland. (3) The tertiary hypothyroidism, in this type of hypothyroidism thyroid can not produce and release enough Thyrotrophic Releasing Hormone (TRH) the hormone which stimulate the pituitary gland to synthesis TSH, with subsequent production of T4 and T3 (Evered *et al*., 1973).

During the process of hypothyroidism depend to the nature and course of disease onset the severity of thyroid disorder varies according to the level of hormone reduction and the state of TSH (Larsen, 1982;

Samuels *et al*., 1990; Parle *et al*., 1991; Zulewski *et al*., 1997; Oliveira *et al*., 2001; Persani *et al*., 2000). The clinical manifestation differ from a mild, moderate to very advanced form of hypothyroidism. In mild to moderate the patients may even do not realize the disorder or hardly understand the symptoms but at the end stage the patients life is even at risk if the person involved remain untreated and enter the sever forms of hypothyroidism with all clinical presentation of myxedema.

Therefore, the best way to avoid, life threatening hypothyroidism, it is best to be diagnosed and treated properly to prevent the very serious form of disease. At very first stage of disease the diagnostic laboratory can give a very good assistance by determination of serum TSH, T4 and T3 concentrations. In condition where the thyroid hormones reduced with elevated TSH, hypothyroidism begin even if there are not any clinical manifestation and symptoms. As the process of disease onset continue the T4 and T3 reduced even further with elevation of TSH, also in some cases the T3 may remain at normal range. Therefore, the diagnosis of hypothyroidism start with measurement of TSH, T4 and T3, given the inverse relation between TSH and thyroid hormones due to the negative feed back exist between the T4, T3 and TSH, therefore when the level of T4 and T3 fall below the normal value, TSH begin to rise at that point the clinicians can adequately follow the pathway of disease onset by the laboratory report even if the patients do not manifest any proper clinical manifestation of the hypothyroidism to satisfy the clinical examinations (Samuels *et al*., 1990; Adriaanse *et al*., 1993).

The diagnostic laboratory is able to assist clinicians even before the mild hypothyroidism can practically happen and manifest its clinical symptoms and that assistance is as follow: there is another form of hypothyroidism and that is called sub-clinical hypothyroidism when from laboratory point of view the patient is in hypothyroid state because TSH is elevated but T4 and T3 are remain at normal range and this type of hypothyroidism where TSH is elevated but T4 and T3 are at normal range is defined as sub clinical hypothyroidism (Nilsson *et al*., 1976; Parle *et al*., 1992; Bonger *et al*., 1993). The clinician can not find any symptoms on clinical examination, but according to the laboratory thyroid function test thyroid disorder is existed already.

The above laboratory findings give an important information to prevent the onset of even mild form of hypothyroidism by applying proper treatment on condition of subclinical hypothyroidism and not to let the patients enter the proper hypothyroidism. Many direct symptoms and indirect disorder of hypothyroidism such as cardiovascular abnormality are due to lipid alteration. It have been demonstrated that hypothyroidism is associated with dyslipidemia. On condition of latter statement the hypothyroidism and this can be again another biochemical test to prevent the patients un-wantedly enter in the real state of hypothyroidism (Althaus *et al*., 1998; Caron *et al*., 1990; Brabant *et al*., 1994; Hak *et al*., 2000; Bakker *et al*., 2001; Hall and Scanlon, 1979).

It is also reported that women are more susceptible to hypothyroidism. Therefore in screening and management of hypothyroidism should have been taken under specific surveillance to help the women at risk (Geul *et al*., 1993).

Even as it was mentioned above the sub-clinical hypothyroidism a type of thyroid disorder which can be principally diagnosed with the laboratory findings and it is more common among women in the society. Biondi and Cooper (2008), Abrams and Grundy (1981), Kritchevsky (1960), Kurland *et al*. (1961), Staub *et al*. (1992), Gordin and Lamberg (1981) and Mansourian *et al*. (2008) worked on the topic and found the sub-clinical hypothyroidism is more common among women accompanied with dyslipidemia. Under any condition if any form of hypothyroidism is not treated properly it will enter the next stage with catastrophic syndrome and side-effects. It should have been mentioned that TSH and T4 are two main hormones regulating the thyroid function also T3 concentration fall at late stage of hypothyroidism. T3 in fact can be also produced in peripheral tissue by deiodinase enzyme which converting T4 in to T3 by deiodinating an iodine from T4 biochemical structure and for due to this conversion and keeping in mind the more intense biochemical activity of T3, it can keep the body requirement for thyroid hormone for while up to point where the T4 concentration fall below the point which can be able to permit this conversion adequately (Ishii *et al*., 1983; Laurberg, 1984; Lum *et al*., 1984).

Hypothyroidism and in particular the type which the thyroid gland itself is responsible for inadequate synthesis of T4 and T3 are common thyroid disorder particularly among women (Geul *et al*., 1993; Nystrom *et al*., 1981; Diekman *et al*., 1988; Mansourian *et al*., 2008). The iodine deficiency can be a cause for hypothyroidism. also the findings in this area are controversial (Mansourian *et al*., 2007). As it was already mentioned the onset of disease is more common among women than men and this findings universally accepted with age direct specific relation to the individuals (Dos Remedios *et al*., 1980; Sawin *et al*., 1985; Okamura *et al*., 1989; Sundbeck *et al*., 1991; Mansourian, 2010a-c).

As it was earlier mentioned hypothyroidism may happen due to disorder to the thyroid gland itself unable to produce (primary) or due to defect in the pituitary in lacking to produce TSH (secondary) and hypothalamus abnormality due to inability to produce TRH (terteriary). There are also rare cases which is not taken seriously into consideration when dealing with hypothyroidism management and that is the peripheral tissue resistance to the either of T4 or T3 receptor located either within the cell cytoplasm or nuclear. TSH is a pituitary hormone produced in response to the TRH a small peptide hormones synthesized in the hypothalamus, which enter the pituitary directly through a stem located between the hypothalamus and pituitary inside the brain (Larsen, 1982). When TSH is secreted from pituitary it enter the blood circulation, reaches the thyroid gland and binds to its receptor on the membrane of thyroid cells and stimulating the thyroid gland to produce T4 and T3. On condition of disorder on the axis of hypothalamus and pituitary or the disability of either of hypothalamus and pituitary to produce either of TSH or TRH, hypothyroidism of so-called secondary and tertiary occur, respectively (Arafah, 1986; Rose, 2001; Edwards and Clark, 1986). The main reasons for secondary hypothyroidism, can be either adenoma or pituitary operation due to benign or cancerous tumor and subsequent radiotherapy (Constine *et al*., 1993; Snyder *et al*., 1986). Also, other inflammation and any forms o autoimmunity to the pituitary may cause the pituitary tissue destruction accompanied by deficiency of pituitary hormones release, including TSH which may also be associated with secretion disorder of other hormone such as growth and hormone as well.

Also, the thyroid cell destruction due to any biological biochemical and drug induced are also are common cause of hypothyroidism best know as primary hypothyroidism (Lawrence *et al*., 1973). Hypothyroidism among other reasons also is gender and age dependent and the women more than men are susceptible individuals in this regard to afflict the hypothyroidism (Dos Remedios *et al*., 1980; Sawin *et al*., 1985; Okamura *et al*., 1989; Sundbeck *et al*., 1991). It is of a grate significant to determine the serum alteration of thyroid autoantibody level if a particular individual and specifically women subjects are undergoing some tests for hypothyroid assessment (Volpe, 1977; Geul *et al*., 1993). The other important issue which should have been look at it seriously is the iodine deficiency which is one of the causative factor developing into primary hypothyroidism. As it is well-recognized iodine is an element most needed by thyroid to synthesis tetraidothyronine (T4) and triidothyronine (T3). In fact the 4 and 3 in T4 and T3 are designated to show the number of iodine's present in the structure of these two thyroid hormones (Mansourian *et al*., 2007).

Among other reasons for primary hypothyroidism are either complete or partially thyroid surgery and thyroid relates surgery due to any lesion within the thyroid or its proximately (Braverman *et al*., 1969). Radio-therapy of thyroid by radioiodine also it is a significant non-surgical medical intervention in the primary hyperthyroidism due to cancerous, autoimmune disorder or any other problem but the patient may end up with undesired hypothyroidism which possibly can be reversed if not the patients have to be on thyroid hormone therapy for life otherwise (Braverman *et al*., 1969).

There are also various rare reasons for hypothyroidism which are not definitely front- runner in the induction of hypothyroidism such rare factors are infections, systemic sclerosis sarcoidosis which may causing primary hypothyroidism (Chau *et al*., 1970).

Among other rare but practical reasons for inducing primary hypothyroidism are genetic factors which may cause the genetic-related thyroid disorder and subsequent inability of thyroid to produce T4 and T3. If it is a congenital disorder and it may be due to trans-passing of blocking antibody to the thyroid stimulating hormone receptor from the placenta in fetus life.

Also as it is well-known that iodine deficiency eventually lead to hypothyroidism due to the requirement of T4 and T3 to iodine (Braverman, 1994; Markou *et al*., 2001; Mansourian *et al*., 2007), but there are some rare conditions in which the excess of iodine within the thyroid gland may cause the inhibition of T4 an T3. This pattern of events happen as follow: when T4 and T3 are produced within the thyroid gland from thyroglobulin molecules through the lysozomal reaction monoiodothyronine (MIT) and Diiodothyronins (DIT) are also released from thyroglobulin, these are the MIT and DIT,which are not coupled to become either T4 (DIT+DIT) or T3 (DIT+MIT) therefore subsequently the 2 iodines in DIT and 1 iodine in MIT are separated from DIT and MIT and released within the thyroid gland, the iodine's concentration within the thyroid gland is increased and this iodine elevation within the thyroid gland is a self -regulatory mechanism to either prevent or reduce the T4 and T3 synthesis. The logic behind this mechanism can be explained in this way: if thyroid should have continued to synthesis T4 and T3 therefore it should not release MIT and DIT and logically the thyroid at thyroglobuline level realize to convert MIT and DIT to T4 and T3. Therefore, if thyroid release DIT and MIT it means extra T4 and T3 are not needed according to the

physiological impulse and the body self regulatory system. There are rare cases in which when the level of T4 and T3 are reduced and at this time T4 and T3 should have been started to be synthesized, but this reverse mechanism does not happen, it means the T4 and T3 are not produced and thyroid finally enter into primary hypothyroidism state where the iodine excess within the thyroid and the routine dietary iodine and its absorption by the thyroid through the TSH mechanism which is an even extra factor in causing to elevate the iodine within the thyroid gland, finally ending up with hypothyroidism. The all event leaded to this type of hypothyroidism called iodine-induced hypothyroidism also well introduced as a Wolff-Chiakoff effect. This type of thyroid disorder physiologically can be either a reversible process or a one-way direction among some individuals leaving the affected person at hypothyroidism (Braverman *et al*., 1971; Gaitan *et al*., 1993; Wiersinga *et al*., 1986; Martino *et al*., 1984). The radioactive iodine and other radiation medical procedure applied in medicine which principally is used to treat some type of tumor either adenoma or carcinomas may at some point destroy those thyroid tissue are responsible for thyroid hormones and may leave behind the hyperthyroid or the patient with some tumor located within the thyroid gland at hypothyroid stage (Snyder *et al*., 1986; Rose, 2001; Braverman *et al*., 1969).

MYXEDOMA

Myxedoma is the ultimate clinical picture drawn by the eventual existence of hypothyroidism in adulthood. Myxedoma and its chinical manifestation are best known thyroid disorder in which the thyroid tissues are totally or partially are destroyed, due to infection, inflammation, autoimmune disease or even surgery to thyroid or neck (Bastenie *et al*., 1977; Ladenson *et al*., 1984; Yamamoto *et al*., 1999; Fliers and Wiersinga, 2003; Mansourian, 2010c). This disease afflict more female than male and the patient age onset of the disease mostly are at older probably more than 60 years of age, therefore as it was mentioned earlier the disease is age and gender dependant.

This metabolic disorder caused the reduced activity of the adult thyroid gland. The clinical manifestation accompanied by, dry skin swelling around the lips and nose puffy eyes and faces. It also associated with mental abnormalities and due to the direct effect of reduced thyroid hormone level the basal metabolic rate in affected person are dropped as well. In practice the myxedoma, which is a clinical manifestation of many type of hypothyroidism mainly associated with a particular type of coetaneous and dermal edema which is a direct consequence of elevated storages of connective tissue biochemical substances, such as glycosaminoglycans hyaluronic acid and also some varieties of mucopoly saccharides in subcutaneous tissues (Praving *et al*., 1979; Ord, 1978; Chau *et al*., 1970). In addition to the skin and subcutaneous disorder as it was earlier mentioned the affected individuals experiencing depression, mental disorder general weakness, fatigue bradycardia, intolerance to cold, constipation, muscle hypotonic, muscle cramps and joint pain weight gain and fluid retention (Praving *et al*., 1979). The latter symptoms can be summarized as early signs, subsequently at later stage difficulty in speech with hoarse type voice, face dry puffy skin in particular and amenoria among women can be the later signs and symptoms. Myxedema which practically is adults cretinism may also can be associated with other disorders which are common but can be found among myxedema patient the best well known are anemia which is a direct impairment of heamoglobin synthesis the desire for sleep, renal disorder with reduction in glomerular filteration rate, mood abnormality, psychosis, impairment of testosterone synthesis, gynecomastia are among the disorders which many be manifested in late myxedema. The one metabolic disorder, which commonly seen is the dyslipidemia and elevated serum cholesterol in particular, which if untreated eventually lead do cardiovascular disease of arthrosclerosis. Even the sub-clinical form of hypothyroidism accompanied with dyslipidemia especially among females subjects which it has been studied and reviewed word-wide (Mansourian *et al*., 2008; Biondi and Cooper, 2008; Nystrom *et al*., 1988; Dillann, 1983). At sub-clinical hypothyroidism, the signs and symptoms of thyroid disorder are not presented, but the individual on serum laboratory examination show elevated TSH with normal T4, T3, but the elevated serum lipid and in particular total cholesterol and LDL-Cholesterol are common findings particularly among females hypothyroid patients which have been studied and reviewed extensively. The other side-effects accompanied with elevated cholesterol and LDL-cholesterol is the elevation of free radical which is a factor for tissue injury and other complications of hypothyroidism (Marjani *et al*., 2008; Kurland *et al*., 1961; Mansourian *et al*., 2008; Mansourian, 2010a; Biondi and Cooper, 2008; Bough *et al*., 1978; Bell *et al*., 1985; Monzani *et al*., 1997; Nilsson *et al*., 1976; Dillann, 1983).

The other metabolic alterations which may happen are about protein and carbohydrate metabolism also the key role played by hypothyroidism on protein biosynthesis is not quiet well-understood and there are reports of reduction in both synthesis and catabolism of

proteins but the level of albumin which can be exchanged through the capillary wall are increased. It should be mentioned also the level of protein synthesis may be reduced but other such as glycosoaminoglycan and Thyroid Stimulating Hormone (TSH) which is a peptide hormone are increased (Lanberg and Grabeck, 1955; Lewallen *et al*., 1959; Smith *et al*., 1981, 1982). From protein point of view the subsequent of myxedema treatment is associated with trans-passing of extra-cellular fluid proteins (Lanberg and Grabeck, 1955; Crispell *et al*., 1965). In myxedema carbohydrate metabolism is also altered and intestinal absorption of glucose is reduced. In practice the patients experience some type of fasting hypoglycemia which may be due to reduction in gastrointestinal motility (Brauman and Corvilain, 1968; Shah *et al*., 1975; Shah and Cerchio, 1973; Hecht and Gershberg, 1968).

CLINICAL DIAGNOSIS OF MYXEDOMA

Hypothyroidism at very early stage is not a disease to show itself clinically; therefore, you may explain that this disease is a chronic and clinical symptom gradually develops. By the time the thyroid gland destroyed enough and thyroid producing cells hormones disrupts adequately up to point that which the hormones are not produced as required by the body regulatory system which the clinical signs begin to show themselves (Hayashi *et al*., 1985; Mintzer, 1992). Commonly the first sign can be intolerance to cold and this can be lasted for prolonged time prior to the catastrophic picture of hypothyroidism, sings and clinical manifestation which are knows as the myxedema begin to be demonstrated (Bastenie *et al*., 1971). The intolerance to cold can be followed by fatigue due to lack of energy, which can be the direct consequence of reducing appetite. The many other symptoms of hypothyroidism which was already mentioned followed as the disease course of events progress further are : puffy face, overweight, hair and skin abnormality, slurry speech, vision disorder, demand for an extra sleep, reproductive abnormality and many other symptoms are among the late stage of hypothyroidism which are the clear picture of myxedema and it is at very end stage of hypothyroidism the edema which it is well obvious at the patient face and appearance which begin to show the whole mark of myxedema with its catastrophic events if for any reason the disease left undiagnosed and untreated.

If the myxedema patients remain untreated the clinical manifestations and symptoms catastrophically altered further to the point which the patient eventually die due to infections and heart abnormality (Ord, 1978; Vanderpuma *et al*., 1996; Tunbridge *et al*., 1977b; Forfar *et al*., 1985).

LABORATORY DIAGNOSIS OF MYXEDOMA

The medical laboratory is the corner stone for the diagnosis of hypothyroidism at very early stage of disease onset also the laboratory assessment of thyroid hormone function test can be very helpful in the diagnosis of disease but the patient may not show any clinical sign related to the hypothyroid on clinical and physical examination by the physicians and endocrinologist, therefore it is the laboratory which play a key role in the diagnosis of hypothyroid patients by proper measurement of TSH, T4 and T3 at early stage. Also as hypothyroidism progress the clinical symptoms became more obvious and clinical examination provide enough information insight a metabolic disorder which if it remain untreated eventually enter into various syndrome with catastrophic scenario. Considering the cost- effectiveness of medical and laboratory treatment it seems, TSH is the best single test, to identify the hypothyroidism. In general the TSH measurement, may be is satisfactory enough, but it is most advisable to measure at least TSH and T4 simultaneously, also the assessment of T3 is advised as well to have a clear picture of disease progress from laboratory point of view with subsequent advice and recommendation to the clinicians and endocrinologists. In overt hypothyroidism, TSH and T4, T3, are increased and decreased, respectively (Spencer *et al*., 1990; Okamura *et al*., 1989). Further assessments of thyroid function test to manifest the presence of hypothyroidism is through careful determination of auto antibodies produced against thyroid gland various vital organelles, macromolecules and enzymes. It should be remembered, that some times,a simple factor such as the iodine deficiency which is a requirement of thyroid hormone biosynthesis can be the causative factor for hypothyroidism which can be assessed by the medical diagnostic laboratory to correct primary hypothyroidism at very first steps and prevent the patient from entering into a hypothyroidism which if unchecked and untreated eventually lead to myxedema.

The most obvious form of autoantibodies to thyroid gland is Hashimato which caused by autoantibody directed against thyroid peroxidase (Mansourian, 2010c). Under any condition, when hypothyroidism is proved to be happened regardless of its causative factor, to prevent the adverse side effect of this type of thyroid disorder it should be accompanied with hormone replacement therapy, most commonly by levothyroxine tablet with its sodium salts formulation which can easily be absorbed through intestine (Hays, 1988, 1991; Copper *et al*., 1984), also thyroxine itself also prescribed, but with reduced rate of absorption (Fish *et al*., 1987; Browning *et al*., 1988; Oliveria *et al*., 1997).

Those patients with mal- absorption and any disorder which can alter the drug metabolism should be taken under careful consideration and have to be consulted by the physicians and endocrinologist to adapt the proper dosage of drug and may alter other related factors, with should have been taken under serious consideration if the drug has to be consumed and effect properly, (Rosenbaum and Brazel, 1982; Cunningham and Barzel, 1984; Hays, 1988, 1991; Fish *et al*., 1987; Dong *et al*., 1997; Oliveria *et al*., 1997; Trip *et al*., 1991; Curran and DeGroot, 1991; Faber *et al*., 1985; Deluca *et al*., 1986; Isley, 1990; Contempre *et al*., 1991).

On condition of drug therapy the patients thyroid status should also have to be checked by laboratory measurement of thyroid function test, in addition to the physical and other Para- medical examinations. The laboratory assessment of TSH, T4 and T3 and comparison of thyroid hormone with proper laboratory results can help in deciding whether, the pattern of therapeutic treatment either is successful or the patient drug management should be modified by the related physicals and endocrinologist (Cunningham and Brazel, 1984; Rosenhaum and Brazel, 1982; Fish *et al*., 1987; Hays, 1988, 1991; Wennlund, 1986; Berens *et al*., 1970; Langer *et al*., 1998).

The procedure of continuous assessment of thyroid function is an important clue which should have been taken seriously, but certain individuals and conditions which can be considered as high risk situation such as pregnancy should have been under extra alarm and attention. The specific condition of pregnant women and the extra requirement for hormone replacement should have to be studied, if the adverse effects of hypothyroidism are to be avoided during the pregnancy period, which may have an adverse-effect to the growing fetus and pregnant women as well. The studies by the authors and many others confirm the seriousness of thyroid function proper assessment during pregnancy (Mansourian *et al*., 2010; Shahmohammadi *et al*., 2008).

As it was mentioned already dyslipidemia associated with the hypothyroidism and the related symptoms such as cardiovascular disorder can be also a side effect not only for the pregnant women but for any other individual as well (Mansourian, 2010a-c, Mansourian *et al*., 2010; Shahmohammadi *et al*., 2008; Mannisto *et al*., 2010).

Therefore, a need for continuous measurements of thyroid hormone while the related subjects and patients are on drug is a matter of importance if the therapeutic treatment is desired to be successful (Shimon *et al*., 2002; Arafah, 1994).

MYXEDOMA COMMA

Although, myxedema coma is a rare onset of disease but it is the most catastrophic clinical manifestation form of disease with high mortality rate, This latter state of myxedema occur if the hypothyroidism is progressed undiagnosed and untreated (Nicoloff and LoPresti, 1993; Jordan, 1995; Fliers and Wiersinga, 2003). Other organ abnormalities such as infection, cardiovascular and brain abnormalities are among all other problems which can interfere and facilitate the patient to be placed into a one direction pathway and eventual death (Bastenie *et al*., 1977; Bough *et al*., 1978; Ooi *et al*., 1980; Griffin, 1990; Muller *et al*., 2001; Obuobic *et al*., 2002; Fazio *et al*., 2004).

If hypothyroidism remain either unnoticed or un-managed for a considerable of time, the auto- regulatory mechanism collapse and affected individual cardiovascular, respiratory and central nervous system function all are disrupted. The clinical manifestations of afflicted patients and the subsequent symptom eventually enter the affected individual into the comatose myxdoma. The typical clinical manifestations including adverse modification of psychomotor ability, intolerance to cold and actual hypothermia to the level of life threatening state, finally other metabolic syndrome including heart and cerebral dysfunction are universally accepted conditions of sever hypothyroid patients, with possibility of entering into a myxedema comma with eventual death if the patient was left undiagnosed and untreated (Tsitouras, 1995; Mintzer, 1992; Nicoloff and LoPresti, 1993; Jordan 1995; Fliers and Wiersinga, 2003).

CONCLUSION

Hypothyroidism is the most probable thyroid disorder, affecting more women than men, which initially can be diagnosed by the laboratory when serum level of thyroxin (T4) and triiodothyronine the two thyroid hormones or mainly T4 is reduced, with subsequent elevation of Thyroid Stimulating Hormone (TSH) due to the absence of negative feed-back control of thyroid hormone on pituitary gland.

If hypothyroidism remain unchecked and unmanaged, on clinical examination the affected patients presenting themselves with clinical manifestations starting with hypothermia as initial sign followed by psychomotor, cardiovascular, gastrointestinal dysfunctions, skin, hair abnormalities and reproductive disorders among others.

If the overt hypothyroidism remain undiagnosed or not treated properly, the patients clinical manifestations worsen and eventually is presented with clinical signs and symptoms accompanied with particular coetaneous and dermal edema which is a direct consequence of elevated storage of connective tissue which is given the particular appearance of hypothyroid patient typically with skin swelling around lips and nose with ultimate puffy eye and faces, the whole clinical picture medically is known as myxedoma.

As the myxedema is worsen and the patient is not treated properly, there is possibility in which the affected individual enter into myxedema comma which is a disorder with high risk of mortality. The clinical manifestations of the patient is catastrophic due to collapse of auto-regulatory mechanism, which present itself by, bradycardia, hypotension, respiratory and central nervous system collapse, accompanied with lethal comma, well-known as myxedoma comma. It is a medical emergency with possibility of eventual death due to the clinical symptoms.

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