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Obesity in Hypothyroidism and Their Management

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KEYWORDS
Hypothyroidism, Obesity, BMI, Management.

ABSTRACT:

Purpose :- Hypothyroidism is a common endocrinal disorder , mostly occurs in women & elderly person and it has traditionally been most commonly related with obesity. Hypothyroidism is a disease of thyroid gland . if any person have hypothyroidism that means the thyroid gland is under active. The term hypothyroidism is made from the word "hypo" – means "under" or " below the normal" & "Thyroidism" – mean "thyroid function". There are very few studies have assessed these associations. The main aim of this study is to evaluate the relation between thyroid dysfunction and body mass index (BMI) at pre-test and post test (after normalization of the hormone levels).

Patients and methods:- This is a observational study of hypothyroid patients that were referred for evaluation of thyroid dysfunction to the school of health sciences C.S.J.M. University Kanpur , India was conducted. We collected data of BMI and thyroid hormone levels before treatment and after normalization of thyroid function within a follow-up period of 6 months.

Results: :- A total of 312 patients were referred to the School of health science (C.S.J.M. University , Kanpur: India) for the thyroid dysfunction measurement during the study. From this,220 patients were excluded from this study for further analysis due to some exclusion criteria. (Eg.:- due to pregnancy, weight loss , recent surgery, (96 patients had already initiated treatment for thyroid dysfunction, 38 were experiencing transient thyroid dysfunction , 47 excluded due to the hypertension, 39 were rejected due to lost to follow – up). 41 patients were excluded from this study due to hyperthyroidism. And then finally , a total of 51 hypothyroid patients were included in this study, comprising 8 male (15.68%) and 43 female (84.32%). The mean age was 18-65 years and mean BMI is 27.08±3.19. after that we find out the number of patient with overweight 36 and the percentage were 70.58%and the others were in normal weight those were in numbers 15 and percentage were 29.41 %. The etiology of hypothyroidism per case was 37 patients, 8 patients presented sub clinical hypothyroidism (TSH <10 µU/ ml) and 6 presented severe hypothyroidism (TSH 62.05 µU/ ml) and 53 µU/ ml respectively.

When comparing mean BMI, there were no significant differences were found between hypothyroid patients and hyperthyroidism 69.81±9.89 kg vs 65±10.94kg and BMI 27.10±3.21 kg/m2 vs 26.40±4.34 for hypothyroid and hyperthyroid patients respectively.

Conclusion:- In hypothyroid patients, after treatment and normalization of thyroid function have statistically significantly slight changes in BMI, but these are neither major changes nor show great (huge) relevance in clinical practice because the BMI remained in the overweight range.s

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INTRODUCTION

Obesity: - Obesity is an important risk factor for us. Its prevalence has increased worldwide since the mid 1970s. National health & National Examination survey presents that obesity affected 32.2% of adults in 2003-2004 and became the fifth cause of decade of life. [1]

Obesity is related with the risk of diabetes,dyslipidemia, kidney disease, cardiovascular disease etc.[1] Severe obesity may cause premature mortality in middle aged adults.[2]

Central obesity is associated with endocrine abnormalities. [3] & thyroid disorders [4]

There are some other diseases arising associated with thyroid dysfunction and autoimmune thyroid disease (ATTS) during these years. [5] There are two types of thyroid disorders like :- Hyperthyroidism & Hyperthyroidism. [5] In the developed countries obesity has become an epidemic. Its prevalence in USA has increased from 15.3 % in 1995 to 23.9 % in 2005. Obesity is defined as body mass index or BMI. If it is >30 kg/m2 that means a person is obese. [6] If BMI becomes >40 kg/m2 so it is known as morbid obesity nearly 5 % of all obese patients. [7] Obesity is complex & poorly understood. But it is concerned that it is

discuss the prevalence of obesity in USA. The newly investigated data represented in 2007 that the over. It is accounts for genetic, environmental, behavioral & psychological. [8] Most affecting factors is heredity because family study explain up to 67 % of the population variance in BMI.[9]

In the overall life there is increased obesity may lead to decline in developed countries . [10] So morbidity due to increased obesity economically damaging for society.

There are some obesity associated hormonal changes have been evaluated from the several clinical studies since last 10 years. [11]

In obese person thyroid dysfunction have been widely investigated. **[12]**

Excess obesity is related with adverse health consequences. Obesity and overweight are determined by the body mass index which is ratio of weight that is divided by height in meters squared. If BMI higher than 30 kg/m2 is indication of obesity.[13]

According to the centre for disease control BMI for age growth chart and value is equal or above the 95th percentile categorized as overweight.[14]

Prevalence of obesity is broad range from molecular biology to epidemiology.

National Health and Nutritional Examination Surveys (NHANES) represented by Centre for Disease Control that CDC directly measured height & weight as a sample to the last many years there has been a plateau in the prevalence in obesity in U.S. on the 72 million adults, who having more than 30 kg/m2.[15]

Adams and co-workers published in 2006 the relationship b/w mortality & weight. [16] Adams study reported during 10 years the mortality rate is more than 500000 Americans aged b/w 50-71 yrs , enrolled in National institutes of health –American Association of retired person. This population were neither smokers nor pre-existing ill. So this study established the relationship b/w mortality & weight. In this study, the population were divided in two groups (A) Men & (B) Women, Demonstrated that 20-40 % increase the mortality rate in both Men & Women, who were overweight in their midlife.

Obesity can reduce functional efficiency and produce more illness. Alley examined in their recent study that the relationship between obesity and disability in period of 1998-2004. [17]

Data for this study taken from the NHANES to examine the process of changes in the weight of the population affects the disability introduced as improper activities of functional impairment .In Alley study discovered in 1998-2004 period that disability in obese individuals grew relative to that seen in normal weight persons. After 2004, 42.2% of obese individuals reported . Some functional impairment compared with 26.6% in normal weight persons. This study expresses the increasing social costs related with the increasing prevalence of obesity in such serious obesity.

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There are so many health consequence arises due to obesity, both independently and in relation with other disease [18]

There are some examples of disease occurs due to obesity, development of type 2 diabetes mellitus, coronary heart disease (CHD), & may be an increased incidence of certain forms of cancer, respiratory problems & osteo - Arthritis of joints. Sometimes effects of obesity & overweight on the body. appear after 10 years or longer, this is presented in build & blood pressure study. [19]

Obesity predicts the decreased longevity, presented by the data of life insurance & epidemiological studies. [20]

According to the Framingham Heart study, only one pound of (.45kg) extra weight may increase 1% risk of death for 26-42 years individuals & 2% increased for 50-62 years of individuals .[21]

In developed countries, the conservative estimated cost obesity is b/w 2-7% of the total health costs & which represents a significant expenses of national health care budgets.[22]

The health problems of obesity are predictable from identifying the pathophysiology of increasing body fat. Obese persons who has extra fat in intra- abdominal part are at highly risky, with certain ethnic population carring risk on multiple levels. [23]

Thyroid:- Thyroid Hormone are most effective regulator of thermogenesis Thyroid hormone regulate the basal & total energy consumption , include the activity of several enzymes involved in lipid metabolism [24]

Hypothyroidism: - Hypothyroidism is a common endocrinal disorder , mostly occurs in women & elderly person [25]

In hypothyroidism , symptoms may influenced on severe levels ,as well as rapid onset . there autoimmune thyroiditis may occur due to slow failure of thyroid function [26]

There neck examination can be etiology & sign of hypothyroidism by performing the thyroidectomy scar , skin changes , specific autoimmune disease like (vitiligo).clinical presentation may exoress the unapparent disease to myxoedema coma , a rare endocrine emergency.[27]

Hypothyroidism is a disease of thyroid gland . if any person have hypothyroidism that means the thyroid gland is under active . the term hypothyroidism is made from the word “hypo” – means “under” or “ below the normal” & ” thyroidism “ – mean “thyroid function”.

In this condition , thyroid gland does not make sufficient thyroid hormone to keep the body runnimg normally . hypothyroidism may be due to some causes , are as – autoimmune disease , surgical removal of the thyroid and radiation treatment [28]

Fat cells produces leptin substance & thus considered an active endocrine organ & this leptin stabilized the correction b/w TSH & BMI , its production occurs in adipose tissue of fat cells . this laptin regulates the energy homeostasis by informing the CNS about the adipose tissue reserves.[29]

It improves Neuro-endocrine & behavior response to overfeeding , in this way , regulating food intake & energy expenditure. this leptin important Neuro-endocrine regulator of the hypothalamic pituitary-thyroid axis [30]

In obese children , adolescents & adults , TSH levels are at upper limit of normal range or may be slightly increased than the upper limit and are positively correlated with BMI .[31]

Means TSH seems to slightly related to the obesity [31] there has been stabilised the relationship .

A fact is noted that there is mildly increase in total T3 & FT3 levels in obese [32]

Fat accumulation was associated with increase in both TSH & FT3 levels irrespective of insulin sensitivity & metabolic parameters [32] & FT3 and T3 ratio has been reported positively associated .[32]

So this study expresses the conversion of T4 and T3 in patient with central fat obesity in case of increased de-Iodinase activity as a compensatory mechanism for fat accumulation to improve energy expenditure [32]

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Prevalence of thyroid disorders in population of span approx 10 %.

During low T4 levels in serum , the level of TSH may increase due to central hypothyroidism caused by pituitary or hypothalamic pathology. This situation also seen during recovery from severe illness. When the patient is well, then the repeat test is done for confirmation. There are some clinical clues given for hypothyroidism include other features of pituitary failure. Like – hypotension, abnormal-pallor, fine wrinkling of the skin, amenorrhoea, hyponatraemia or hypoglycemia or features suggestive of a pituitary mass lesion.such as –visual impairment or headache.(33)

The function of hypothalamic pituitary – adrenal axis should be tested and a magnetic resonance imaging (MRI) sean of pituitary gland obtained, if hypothyroidism is suspected.(34)

Subclinical hypothyroidism is a condition, when there is elevated serum thyrotropin level in combination with a serum FT4 level occurs in the population reference range. Occurance of subclinical hypothyroidism varies among population & its ranges 3-15 %, with a higher occurance related with increasing age, female, sex, & a suboptimal iodine status. (35)

Serum thyrotropin and FT4 relationship is such that a small decrease in FT4 can result large increase in serum thyrotropin, which is above the reference range while FT4 level is still within the reference range.

In hypothyroidism, the thyrotropin level continues to increases and FT4 level falls below the reference range. So this condition can be seen as a mild form of thyroid disorder, in most cases , this is caused by autoimmune thyroid disease. A thyrotropin cutoff level of 10 MIU/ ltr is distinguish b/w mild and severe subclinical hypothyroidism.
(36)

Most of the patient (75%) with subclinical hypothyroidism have lower level of thyrotropin, less than 10 MIU/ ltr. (35)

In healthy person, FT4 & serum thyrotropin shows substantial variability. Where as this variable range in individual healthy person tends to be relatively narrow. (37)

The risk of development of sub-clinical hypothyroidism to overt hypothyroidism is nearly 2-6 %/year; the risk is higher in women than men & persons with higher Thyrotropin levels, those who has higher levels of abs to thyroid peroxidase & those with low to normal FT4. (38)

Persons with increased thyrotropin measurement of lower than 7 MIU/ltr, it normalizes in upto 46 % within 2 years. (38)

SYMPTOMS OF HYPOTHYROIDISM:-

- Less energy
- Fatigue felling cold
- Loss of appetite
- New snoring
- Muscle cramp & joint aches
- New or worsening hoarse voice
- New or worsening hearing loss
- Goiter
- Slowing of heart rate. (28)

SYMPTOMS OF SUN-CLINICAL HYPOTHYROIDISM:-

Patients of subclinical hypothyroidism may not fells symptoms or can also be say. It is asymptomatic & patient may report the symptoms of overt hypothyroidism more often than age-matched control. In this condition symptoms are usually milder than in patient with overt hypothyroidism & goes to increase in severity with higher thyrotropin level.

In the patient of subclinical hypothyroidism, the study shows that the higher rate of depressive symptoms & can badly affects the cognitive function than normal thyroid function. (35)

In sub-clinical hypothyroidism the symptoms like – muscle weakness, constipation , cold intolerance , weight gain, fatigue are also reported.(35)

The symptoms are seen more in younger person than elder person. (39)

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SUB-CLINICAL HYPOTHYROIDISM:- In a study , the fact is reported that, patient older than 70 yrs of age even suggested that those who had sub-clinical hypothyroidism had a faster walking speed with good maintenance of physical exercise than did the Euthyroid control(39), but confirmed in a more recent study (40)

There are some difference related to symptoms reported by patient in different study & difference in the way that patient were identified for include in the study. The difference may vary due to different age of patients , severity of sub-clinical hypothyroidism may shows different symptoms in patient.

Causes of hypothyroidism:-

Autoimmune thyroiditis—Hashimoto's thyroiditis, atrophic autoimmune thyroiditis Iatrogenic—thyroidectomy, radioiodine therapy Thyroiditis—subacute thyroiditis (also known as De Quervain's thyroiditis), silent thyroiditis, postpartum thyroiditis Iodine deficiency Drugs—carbimazole, methimazole, propylthiouracil, iodine, amiodarone, lithium, interferons, thalidomide, sunitinib, rifampicin Congenital hypothyroidism—thyroid aplasia or hypoplasia, defective biosynthesis of thyroid hormones Disorders of the pituitary or hypothalamus (secondary hypothyroidism)

Raised thyroid stimulating hormone levels :-

:-Thyroid stimulating hormone level >10 mU/l with or without low free serum thyroxine

:-Thyroid stimulating hormone level 5-10 mU/l with low free serum thyroxine

:-Thyroid stimulating hormone level 5-10 mU/l with normal free serum thyroxine

Symptoms of hypothyroidism

Yes:- 3 months trial of thyroxine:-symptoms resolved? **- yes** :- treat with thyroxine life long

No **:-**Consider alternative diagnoses

No :-Check status of thyroid peroxidase antibody :-

Positive result :- diagnoses Recheck thyroid stimulating hormone level annually

Negative result:- Recheck thyroid stimulating hormone level every three years

Features of hypothyroidism :-

:- Exhaustion

:- Somnolence

:- Slow cognition

:- Intolerance to cold

:- Constipation

:- Depression

:- Weight gain

:- Calf stiffness

:- Menstrual disturbance

:- Carpal tunnel syndrome

:-Hearing impairment

:- Dry, thin and pale skin

:- Puffiness below the eyes

:- Bradycardia

:- Slow relaxing tendon reflexes

:- Coarsening of facial features

:- Pleural effusion

:- pericardial effusion

:- Ascites

:- Non-pitting oedema of lower leg

:- Hyponatraemia

;- Hypercholesterolaemia

: - Impaired consciousness (myxoedema coma)

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MANAGEMENT OF HYPOTHYROIDISM: - Method for the proper and effective management of hypothyroidism is as follow :-

:- Thyroid hormone replacement therapy:- it has been used for the treatment of hypothyroidism by levothyroxine and is usually lifelong ,the levothyroxine is commonly given to the patient s , in starting days only 25-50 µg daily dose efficient , but this is not a perfect approach for the treatment of hypothyroidism , according it is shown in randomized control trial and it is wasteful resources. [41] patient should started the full replacement dose of levothyroxine . its requirement based on the body mass of the patients. For the euthyroid patients it should be 1.6µg /kg body weight.[42] this dose is equals to the 100 µg of dose for the women with their weight approx 60 kg and 125µg dose for men with 75 kg weight (which is an average weight of men and women). For the treatment of subclinical hypothyroidism it started close to a full replacement dose approximately 75-100 µg daily

MATERIALS AND METHODS :-

We carried out a review and observational study on patients with thyroid dysfunction that were referred to the school of health sciences at C.S.J.M.U. and G.S.V.M. College Kanpur U.P. India Prevalence of hypothyroidism assessed by measurement of thyroid hormones. All male and by doctors of health sciences. In this study I collected the sample of those patients who have sign the informed consent and provide the blood sample for the laboratory investigation were included in this study. Participants were excluded if they were pregnant, mentally challenged , not signed the written informed consent form, recent surgery, and having meditation for affecting weigh and also hypertension patient were excluded from this study. The variables collected were thyroid dysfunction etiology, TSH levels and T3, T3 levels , BMI and weight at the time of referrals to the school of health sciences. This study carried out in accordance with the approved protocol , principle s of declaration of Helsinki and good clinical practices. All participants were required to provide written informed consent before study entry.

Result :- A total of 312 patients were referred to the School of health science (C.S.J.M. University , Kanpur) for the thyroid dysfunction measurement during the study. From this 220 patients were excluded from this study for further analysis due to some exclusion criteria. (Eg.:- due to pregnancy, weight loss , recent surgery, (96 patients had already initiated treatment for thyroid dysfunction, 38 were experiencing transient thyroid dysfunction , 47 excluded due to the hypertension, 39 were rejected due to lost to follow – up). 41 patients were excluded from this study due to hyperthyroidism. And then finally , a total of 51 hypothyroid patients were included in this study, comprising 8 male (15.68%) and 43 female (84.32%). The mean age was 18-65 years and mean BMI is 27.08±3.19. after that we find out the number of patient with overweight 36 and the percentage were 70.58%and the others were in normal weight those were in numbers 15 and percentage were 29.41 %. The etiology of hypothyroidism per case was 37 patients, 8 patients presented sub clinical hypothyroidism (TSH <10 µU/ ml) and 6 presented severe hypothyroidism (TSH 62.05 µU/ ml) and 53 µU/ ml respectively. When comparing mean BMI, there were no significant differences were found between hypothyroid patients and hyperthyroidism 69.81±9.89 kg vs 65±10.94kg and BMI 27.10±3.21 kg/m2 vs 26.40±4.34 for hypothyroid and hyperthyroid patients respectively.

After the treatment of hypothyroidism with the dose of levothyroxine for a month when the thyroid levels become normal, there were no statistically significant differences in the body weight of that population during pretest and post test 69.92±10.12 kg to 67.34±10.21 (mean difference weight (2.58±2.10)**.** statistically significant differences were also observed between patients BMI (PRETEST) 27.08±3.19 kg/m2 and POST TEST(26.32±3.42 kg/m2 (mean difference BMI (0.76±0.23)**.**

Discussion :- In this study, there were no statistically significant differences observed in the weight or the BMI of hypothyroid patients, neither pretest diagnosis , nor after normalization of hormone levels after treatment of the patients. At pretest , 51 hypothyroid and 41hyperthyroid patient groups demonstrated a non-significant weight difference of approximately 6 kg, and a very similar BMI, respectively, with both groups falling into the overweight range. Due to the treatment and normalization of Thyroidism, the difference in

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weight between the two groups was further slightly reduced. The BMI values also remained similar for both groups. During analyzing the thyroid function disorder (hypothyroidism) , we observed statistically significant differences between pretest and post-test after treatment body weight and BMI. Hypothyroid patients mean weight loss of(2.58±2.10) kg, which is less than the weight loss described in classic series. My result may have been influenced by the fact that 8 of the hypothyroid patients showed a subclinical hormone alteration (Thyroid stimulating hormone<10 µU/ ml). Those Patients who were with a greater degree of hypothyroidism (TSH 62.05 µU/ ml) and (53 µU/ ml) felt thew weight loss of less than 2.58kg. Some studies suggest that gaining of weight is most occurs in post-surgical hypothyroidism than in autoimmune hypothyroidism. In this study, there was no one case of post-surgical hypothyroidism. The relationship between obesity and hypothyroidism has historically been based on studies with a pretest population choosen from those obese patients whose thyroid hormone levels were assessed in the health sciences department of C.S.J.M.U. Kanpur. There are so many studies have proved. , higher incidences of hypothyroidism were found in obese patients than in the general non obese population.. according to these observations, there are some authors have suggested that minor thyroid dysfucnction might contribute to significant changes in body weight and Body Mass Index that could represent a risk factor for overweight and obesity and may be morbid obesity. However, these studies are uncertain for establishing a cause and effect relationship for the occurance of hypothyroidism in obese patients. Hypothyroidism in obese patients does not necessarily mean that, the obesity is caused by the disorder. The relationship of hypothyroidism with obesity looks to be weaker than previous study, even more in subjects with treated hypothyroidism. Hypothyroidism reduces an decreased basal energy expenditure that leads to weight gain as a result When sub clinical hypothyroidism is regained, weight gain occurs at the expense of both compartments. Another possible explanation for the tendency of hypothyroid patients to gain weight after achieving sub clinical hypothyroidism could be related to an increase in post-treatment TSH levels over pretest levels. Hence, this would represents the presence of associated hypothyroidism within the limits of analytic normality. In this study, we were able to test this hypothesis because of availability of patients of TSH levels prior to the onset of hypothyroidism. The nature of this study is observational , we had access of the information of patients' TSH level, but other chemistry data (for example glucose and cholesterol) were not available. Weight and BMI are variables that can be affected by multiple factors. Due to this, more than 60% of the patients initially included had to be excluded because of confounding variables that could affect weight eg :- (treatment , hyperthyroidism, thyroid surgery and specifically gestation and postpartum states, severe diseases and drugs with proven repercussion on weight. The reason for the high volume of pregnant women is that the study was conducted before having specific TSH ranges for pregnancy in our population, so we used the ATA (American thyroid association) ranges. Thereafter, the upper limit of TSH for pregnant women in our population was calculated resulting in 4.2µU/mL, with the consequent fewer referrals. Other those patients who were with mild or chronic disease excluded from this study (eg:- diabetic patients, hypertension).

Conclusion:- In hypothyroid patients, after treatment and normalization of thyroid function have statistically significantly slight changes in BMI, but these are neither major changes nor show great (huge) relevance in clinical practice because the BMI remained in the overweight range

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TABLES:-

Total collected	Total selected	Reason for selection	Total rejected	Reason for rejection
312 patients collected	37 8 6 **(Total 51)**	Hypothyroid Sub clinical hypothyroid Severe hypothyroid	96 38 47 39 **Total(220)** 41 Grand total(261)	Already initiated treatment Experiencing transient thyroid dysfunction Hypertension Lost to follow-up Hyperthyroidism

The demographic, anthropometric and biochemical characteristics for these patients are shown in a table which have been given below:-

PRETEST:-

Parameters	**Total**	
Number of patients	**51**	**Hypothyroid**

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Gender	**43 female** **12 male**	**84.32%** **15.68%**
Age	**18-65**	
Body Mass Index (pretest)	**27.08 ±3.19**	
No. of overweight patients	**36**	**70.58%**
No. of normal weight patients	**15**	**29.41%**
Pre test TSH Levels	**8.27±1.53 µU/ ml**	

POST TEST

Parameters		
Number of patients	**51**	**Hypothyroid**
Gender	**43 female** **12 male**	**84.32%** **15.68%**
Age	**18-65**	
Body mass index (post test)	**26.32±3.42**	
Post test TSH levels	**3.25±1.45µU/ ml**	