Hypothyroidism and obesity

Cause or Effect?

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ABSTRACT

الأهداف: من أجل إنشاء علاقة بين البدانة ونقص إفراز الدرق. قمنا بتحليل تكرار نقص الدرق الأولي لدى المرضى المصابين بالسمنة، وتكرار السمنة لدى المرضى المصابين بنقص إفراز الدرق.

الطريقة: أجريت دراسة إستعادية بقسم السمنة والغدد الصماء – مستشفى مدوين –حيدر آباد – الهند، في مارس 2008م. خلال الثمانية عشرة شهراً الماضية (من سبتمبر 2006م وحتى فبراير 2008م)، تم تحليل بيانات 625 مريض مصاب بنقص إفراز الدرق الأولي، (المجموعة الأولى) و450 مريض من عيادة البدانة (المجموعة الثانية). تم تقييم الفروقات المتكررة بين المجموعتين حسب اختبار تشي– سكوير.

النتائج: في المجموعة الأولى، 625/278 (44%) كان مدخل كتلة الجسم لديهم (BMI) (>25 kg/m²). كانت البدانة أعلى (46% مقابل 34%)، في نقص إفراز الدرق الواضح من نقص إفراز الدرق شبه السريري (p=0.21). كان عدد المرضى المصابين بالسمنة أكثر لدى المجموعة التي تعاني من نقص إفراز الدرق الواضح من المجموعة التي تعاني من نقص إفراز الدرق شبه السريري (p=0.02). في المرضى المصابين بالبدانة، كانت نسبة الإصابة بنقص إفراز الدرقية الواضح (33%) ونقص إفراز الدرق شبه السريري (11%) من المرضى.

خاتمة: تبين وجود توقف وظيفة الدرق الشامل بشكل أكثر لدى الأفراد المصابين بالسمنة مع درجة متفاوتة من الوضوح. الدراسات المفصلة مطلوبة لتقييم السبب والتأثير ذي الصلة بين البدانة ونقص إفراز الدرق.

Objectives: To establish relationship between obesity and hypothyroidism and to analyze the frequency the frequency of primary hypothyroidism in obese patients and frequency of obesity in primary hypothyroidism patients.

Methods: We conducted this retrospective, observational study in the Department of Endocrinology and Obesity Clinic, Medwin Hospital, Hyderabad, India in Mar 2008. In the last 18 months (between September 2006 to February 2008), data on 625 consecutive primary hypothyroidism patients (Group I) and 450 patients from obesity clinic (Group II) were analyzed. Frequency difference between the 2 groups was assessed by Chi-square test.

Results: In Group I, 278/625 (44%) had body mass index (BMI) >25 kg/m^2. Obesity was higher (46% versus 34%) in overt hypothyroidism than in subclinical hypothyroidism (p=0.21). More patients were overweight in overt hypothyroidism group than in subclinical hypothyroidism group (p=0.02). In obesity patients, overt hypothyroidism was present in 33% and subclinical hypothyroidism in 11% patients.

Conclusion: Overall thyroid dysfunction was found more in obese individuals with varying degree of significance. Detailed studies are required to assess the cause and effect relation between obesity and hypothyroidism.

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Thyroid hormones are potent modulators of adaptive thermogenesis. Overt hypothyroidism leads to increased body weight by increasing mucin deposits and by salt and water retention.[1] Extreme obesity also leads to increased thyroid stimulating hormone (TSH) due to hypothalamic-pituitary-thyroid axis abnormality. Leptin produced by adipocytes directly stimulates thyrotropin releasing hormone (TRH) neurons in the paraventricular nucleus, thus increasing TSH.[2] Thyroid function tests form an important component of the clinical studies on the relationship between thyroid function and obesity. Few studies found that weight gain increases serum thyroid stimulating hormone levels; yet, others showed no relationship between TSH and body weight.[3-5] Therefore, we planned to analyze the frequency of obesity in patients with primary hypothyroidism and frequency of primary hypothyroidism in obese patients in our clinic. We also studied the frequency of these disorders in subgroups of subclinical versus overt hypothyroidism and moderate versus extreme obesity.

Methods. A total of 1075 consecutive patients (primary hypothyroidism n=625, obesity n=450) from September 2006 to February 2008 were studied in the Department of Endocrinology and Obesity Clinic, Medwin Hospitals, Hyderabad and approved by the Institutional Ethics Committee. Individuals between 18-70 years (mean age 34.7 ± 10.2years) of age were included. All the patients underwent thorough physical examination including height, weight, waist circumference, presence of goiter, acanthosis nigricans or peripheral stigmata of dyslipidemia and blood pressure measurement. Body mass index (BMI) was calculated as weight (kg) divided by height (meter)^2. They were subclassified as per BMI. Patients with BMI 25- 29.9 kg/m^2 were labeled over weight. Moderate obesity was defined as BMI 30-39.9 kg/m^2 and extreme obesity when BMI was >40 kg/m^2. All the patients were studied in 2 subgroups: Group I (primary hypothyroidism) and Group II (obese). In Group I, patients who presented with primary hypothyroidism were analyzed. Both pre-existing and newly detected cases were included. Further, these patients with primary hypothyroidism were subdivided into subclinical (raised TSH with normal total triiodothyronine [T3] and thyroxine [T4]) and overt hypothyroidism (elevated serum TSH with low serum T3 and serum T4). Anthropometry, lipid profile and blood glucose levels were carried out. Pregnant women, patients with secondary hypothyroidism, thyroid carcinoma, thyroid nodule and sick euthyroid disease were excluded. Thyroid function test (Serum total T3, total T4 and TSH) was performed in all the patients. Thyroid function tests were carried out by enzyme linked immunosorbant assay and the reference values in our laboratory were TSH : 0.25-4.3 mIU/L, T3: 0.7-2.0 ng/ml and T4: 5-12 µg/dl. Thyroid cytology and thyroid peroxidase antibody was performed in selected patients. In Group II patients presenting with obesity were analyzed. All patients enrolled in our obesity clinic with BMI of >30 kg/m^2 were included in this group. Family history of hypothyroidism, hypertension, diabetes, dyslipidemia and thyroid disorders was noted. They were assessed for associated primary hypothyroidism (subclinical or overt hypothyroidism). Thyroid function test (serum total T3, total T4 and TSH) was performed in all patients. These patients were further subdivided into overt (raised TSH with low T3, T4) and subclinical hypothyroidism (raised TSH with normal T3, T4). Patients with secondary obesity due to endocrinopathy (other than hypothyroidism), genetic syndromes and hypothalamic obesity were excluded.

Chi square analysis with Fisher's exact test (2 by 2 tables) was used to compare frequency of variables among different groups. P value of <0.05 was taken as statistically significant.

Results. In Group 1, female to male ratio was 542/83 (7:1). Subclinical hypothyroidism was present in 77/625 (12%) patients while 548/625 (88%) had overt hypothyroidism. Of all 625 cases, 347 (56%) were non-obese (BMI <25 kg/m^2), while 278 (44%) were obese (BMI >25 kg/m^2). Among all 278 obese patients, 5 (2%) patients were extreme obese, 113 (41%) were moderately obese and 160 (57%) were overweight. Among 548 overt hypothyroidism cases, 252 (46%) had BMI >25 kg/m^2 while 296 (56%) were non-obese (BMI <25 kg/m^2). Among 77 patients with subclinical hypothyroidism, 26 (34%) had BMI >25 kg/m^2 and 51 (66%) patients were non-obese. This difference of obesity among overt and subclinical hypothyroidism was not statistically significant on Chi-square analysis (p=0.21) (**Table 1**). We analyzed 450 consecutive obese individuals (Group II) enrolled in our obesity clinic for hypothyroidism. Female to male ratio was 378/72 (8:2). Mean BMI was 33.6 kg/m^2 (range 30-57kg/m^2). Of them, 352 (78%) were moderately obese and 98 (22%) were extreme obese. Overt hypothyroidism was present in 148/450 (33%) cases while 50/450 (11%) patients had subclinical hypothyroidism. Mean TSH among euthyroid obese and hypothyroid obese individuals were 1.92 mIu/L (range 0.3-4.3 mIu/L) and 6.3 mIu/L (range 4.31-15.8 mIU/L) respectively. Among moderately obese individuals 143 (41%) had primary hypothyroidism. Out of them, 107/352 (31%) had overt hypothyroidism and 36/352 (10%) had subclinical hypothyroidism. In individuals with extreme obesity, 55 out of 98 (56%) patients had thyroid profile

Table 1 - Prevalence of obesity in patients with primary hypothyroidism (n=625).

Parameters	Primary hypothyroidism (n=625)		*P* value
	Subclinical hypothyroidism (n=77)	Overt hypothyroidism (n=548)	
Overweight (BMI 25-29.9 kg/m^2)	10 (13)	153 (28)	0.0245
Moderately Obese (BMI 30-39.9 kg/m^2)	15 (19)	93 (17)	0.6381
Extremely Obese (BMI >40 kg/m^2)	1 (1)	4 (1)	-
Total	**26 (34)**	**252 (46)**	**0.2134**

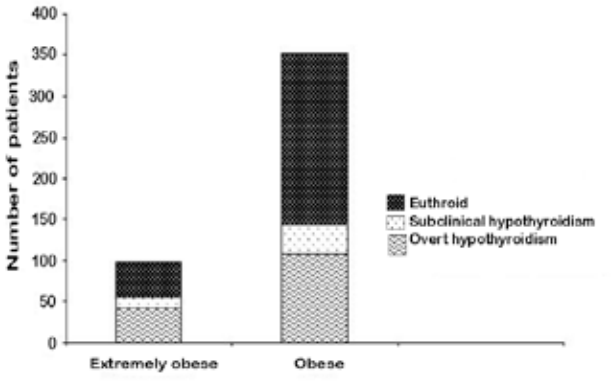

Figure 1 - Prevalence of hypothyroidism in obese individual (n=450).

suggestive of primary hypothyroidism. Among them 41/98 (42%) had overt hypothyroidism and 14/98 (14%) had subclinical hypothyroidism. Prevalence of overt and sub clinical hypothyroidism was higher in extreme obesity group as compared to obese group but difference was not statistically significant (p=0.10). (**Figure 1**).

Discussion. Thyroid hormones are potent regulator of thermogenesis. They regulate basal and total energy consumption, and also modulate the activity of several enzymes involved in lipid metabolism.[6] Hypothyroidism and obesity frequently co-exist in varying degree of severity. Overt hypothyroidism leads to increased body weight by increasing mucin deposits in skin and other organs and by salt and water retention.[1] Subtle elevation of thyroid stimulating hormone (TSH) is associated with measurable deficiency in resting energy expenditure and increased body weight.[7] Obesity gene 'tub' is also regulated by thyroid hormone and its mutation causes obesity, insulin resistance and sensory deficits.[8] Association of obesity and thyroid dysfunction is shown in recent studies.[4,9,10] The concentrations of thyroid hormone and TSH levels are mildly elevated in obese individuals.[7] Extreme obesity is associated with thyroid dysfunction due to hypothalamic-pituitary-thyroid axis abnormality causing increased serum TSH. The association between serum TSH and body weight is caused by signals from adipose tissue. Leptin produced by adipocytes directly stimulates TRH (thyrotropin releasing hormone) neurons in the paraventricular nucleus increasing TSH level.[2] In obesity, T3 receptors are decreased and the negative feedback between TSH is decreased.[11] Neuro-transmitters and hormones that regulate body weight and satiety are also involved indirectly in regulation of thyroid stimulating hormone (TSH) production. An increased level of leptin and increased pro-opiomelanocortin (POMC) down regulates agouti related peptide (AgRP) causing activation of melanocyte stimulating hormone (α-MSH) and stimulation of thyrotropin releasing hormone neurons resulting in increase of TSH.[12,13] It is well known that subclinical hypothyroidism is associated with increase in lipid levels, endothelial dysfunction and increased risk of coronary artery disease.[14] Obese individuals are at higher risk of these complications and subclinical hypothyroidism will add to it. There is growing evidence that obese individuals with mild increase in thyrotropin levels should be treated with levothyroxine. In this study, we analyzed the frequency of obesity in primary hypothyroidism patients and frequency of primary hypothyroidism in obese individuals. We divided them into sub groups of subclinical versus overt hypothyroidism and moderate versus extreme obese and studied further. We compared our data with existing literature and briefly discussed the association between these 2 disorders. In Group I with primary hypothyroidism, 44% (278/625) individuals were obese. This is in line with the existing literature (40-50%).[15,16] Whereas, the prevalence of overweight or obesity in population from our geographical region is approximately 17-22%.[17] They were subdivided into subclinical and overt hypothyroidism patients. In subclinical hypothyroidism patients, 34% (26/77) had obesity whereas among overt hypothyroidism patients,

46% (252/548) were obese. Even though obesity was more common in overt hypothyroidism patients as compared to that in subclinical hypothyroidism (46% versus 34%), this difference was not statistically significant (p=0.21). In Group II with obesity patients, 44% (198/450) had primary hypothyroidism. Of them 75% (148/198) had overt hypothyroidism and 25% (50/198) had subclinical hypothyroidism. Prevalence of hypothyroidism in normal population is approximately 1-9%.[18] Frequency of hypothyroidism among obese patients is more in our series (44%) than mentioned in literature (19.5%).[7] Indian data on this prevalence rate are very sparse. As per an Indian study, hypothyroidism was quoted 14% among obese individuals.[9] Hypothyroidism was reported more in obese individuals as compared to overweight individuals. However, the patient cohort in this study was only 50 patients. Recently, a Turkish study concluded that serum TSH levels are positively correlated with degree of adiposity.[5] In our study, primary hypothyroidism was more prevalent in individuals with extreme obesity as compared to moderate obesity patients (56% versus 41%). However this difference was not statistically significant (p=0.1083). This higher prevalence of hypothyroidism in obese patients in our study may be due to referral bias. Our center being a tertiary care endocrine clinic, thyroid disorders make up a significant pool of our clinical practice.

The limitations of this study are its retrospective design and it may not represent common pool since it was conducted in a specialist endocrine clinic. Higher female proportion in both the groups may be due to higher prevalence of thyroid disorders in females and greater concern for weight gain among women. To conclude the association between hypothyroidism and obesity is well established and our study also confirms the same. On the other side, obesity also contributes to thyroid dysfunction in form of mildly elevated TSH levels. All individuals with obesity should be screened for thyroid dysfunctions and optimum control of hypothyroidism should be considered an integral part of obesity management. Further studies are required in appropriate design to assess the cause and effect relationship between obesity and thyroid dysfunction.

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