FREQUENCY OF UNDIAGNOSED HYPOTHYROIDISM IN OBESE FEMALES

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ABSTRACT

Objective: To determine the frequency of undiagnosed hypothyroidism in obese females.
***Study Design*:** Descriptive cross sectional study.
***Place and Duration of Study*:** Combined Military Hospital Peshawar, from Aug 2015 to Dec 2015.
Methodology: All individuals who were fulfilling the inclusion criteria were considered in the study after informed consent. The body mass index was calculated and their blood drawn for biochemical results. All the data was entered in SPSS-20 and results obtained.
Results: All participants were females, and their mean age (± SD) was 46.78 (± 11.272) years. The overall frequency of undiagnosed hypothyroidism was 5% (6 out of the 130 subjects).
Conclusion: Although, there is obvious linkage between (TSH) thyroid stimulating hormone and degree of obesity, however, the determined results/frequency of hypothyroidism in obese females are not high enough to recommend large scale/mass screening.

Keywords: Hypothyroidism, Mass screening, Obesity.

INTRODUCTION

Hypothyroidism is the commonest and curable endocrine disease which is characterized by insufficient levels of thyroid hormones[1]. Thyroid hormones are essential regulators of metabolism and transport, and thyroid hormone deficiencies of any cause result in hypothyroidism. The overall frequency/prevalence of acquired hypothyroidism is 1:500-1000 while that of Congenital Hypothyroidism (CH) is 1 per 4000[2]. Studies conducted in Pakistan to establish the incidence have been few and is on a smaller scale but predict a much higher incidence of 1:1000[2]. One male suffers from hypothyroidism in contrast to 5-10 females[3]. Hypothyroidism is more prevalent in obese than the lean population[4]. Given the "causal relationship between obesity and hypothyroidism, many studies have intended to establish the occurrence of hypothyroidism in obese people and vice versa.

In India Unnikrishnan *et al*[5], stated frequency of overt hypothyroidism to be 3.5%. In the recent times there has been a lot of interest in the relationship between hypothyroidism and obesity, however local data in this regard is limited though there is recent study conducted in multan show the cumulative frequency of undiagnosed hypothyroidism was 4.53. Another study was conducted in India concluded that the frequency of overt hypothyroidism and subclinical hypothyroidism in obese population was 33% and 11% respectively[5]. Thyroid function assays have indicated that a TSH concentration of 4.5 uIU/L is the upper limit of normal[6].

Primary hypothyroidism is due to failure of thyroid gland to produce thyroid hormones caused either by autoimmune disease (commonest) or post surgery, radiation, radioative iodine[7]. Secondary hypothyroidism is caused by a deficiency of thyroid stimulating hormone, occur as a result of lesion in pituitary gland or deficiency of thyrotropin releasing hormone, occur as a result of lesion in hypothalamus/pituitary stalk (also known as tertiary hypothyroidism). Causes include all pathologic processes that affect the hypothalamus or pituitary including tumors, Sheehan's syndrome, idiopathic hypopituitarism and infiltrative diseases, such as sarcoidosis,

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histiocytosis and lymphocytic hypophysitis radiation-induced central hypothyroidism.

The term subclinical hypothyroidism is used to describe the finding of a raised serum thyrotropin (TSH) above upper limit with a normal range free thyroxine (T4). In the community, the most common aetiology is chronic autoimmune thyroiditis[8]. In the original Whickham survey in Northeast England, 8% of women (10% of women over 55 years of age) and 3% of men had subclinical hypothyroidism[9]. In the Colorado study, 9.4% of the subjects had a high-serum TSH concentration, of whom 9.0% had subclinical hypothyroidism[10].

Hypothyroidism affects all major body systems and is associated with significant morbidity and mortality. Hypothyroidism is associated with metabolic disorders such as hyperlipidemia, Respiratory system dysfunction in the form of hypoventilation and obstructive sleep apnea, gastrointestinal disorders such as constipation or marked ileus, reproductive abnormalities, musculoskeletal disorders such as neuromucular junction disorder (autoimmune thyroiditis with Myasthenia Gravis), proximal myopathy, CVS dysfunction such as decrease cardiac output and cardiac contractility, reduction in heart rate, increase peripheral vascular resistance, pericardial effusion, dermatological changes and neuronal dysfunction ranges from headache, ataxia, movement disorders, dementia, Cranial and peripheral nerve abnormalities, Hashimoto's encephalopathy, myxedema coma.

These complications are reversible with timely initiation of treatment except for some neuromuscular and psychiatric features which may persist for several months. Studies have shown that there is no substantial increase in mortality of treated cases/patients of hypothyroidism compared to general population[11]. Hypothyroidism and obesity frequently co-exist in varying degree of severity. It is well known that hypothyroidism is associated with increase in lipid levels, endothelial dysfunction and increased risk of coronary artery disease[12]. Obesity is one of the most important health risks of our time. According to the National Health and Nutrition Examination Survey, obesity affected 32.2% of adults in 2003–2004 and reached a peak in subjects in the fifth decade of life 39.

Obesity is associated with an increased risk of diabetes, dyslipidemia, kidney disease, cardiovascular disease, all-cause mortality, and cancer[13]. Thus, severe obesity is an important cause of premature mortality among middle-aged adults[14]. 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. Subtle elevation of thyroid stimulating hormone (TSH) is associated with measurable deficiency in resting energy expenditure and increased body weight[15]. Obesity gene 'tub' is also regulated by thyroid hormone and its mutation causes obesity, insulin resistance and sensory deficits. The concentrations of thyroid hormone and TSH levels are mildly elevated in obese individuals[15]. Extreme obesity is associated with thyroid dysfunction due to hypothalamic-pituitary thyroid axis abnormality causing increased serum TSH. The finding that serum TSH, serum total T3, and leptin levels are increased in obese subjects and vise versa supports the hypothesis that the alteration in thyroid function observed in obese subjects is reversible by losing weight[16].

This fact highlights the importance of early identification and treatment of hypothyroidism Groups such as the American Academy of Family Physicians (AAFP) and the American Association of Clinical Endocrinologists (AACE) suggest periodic evaluation of thyroid function in older women[17]. In developing countries like Pakistan, the financial burden of the treatment of hypothyroidism and it complications amounts in billions of dollars. Adoption of an efficient way of screening and timely diagnosis will save both lives and money[18].

The aim of this study is to determine the prevalence of undiagnosed hypothyroidism in

obese females with secondary objective i.e. utility of BMI in screening of hypothyroidism. This study will help to identify the population groups which are at increased risk for developing hypothyroidism.

Operational Definitions

Undiagnosed hypothyroidism can manifest as any of the followings: Primary hypothyroidism: (all of the followings), TSH> 4m IU/l, Serum Total T3 <1.1n mol/l, Serum Free T4 <8.0 pmol/l.

Secondary hypothyroidism: (all of the followings), TSH <0.4m IU/l, Serum Total T3 <1.1 nmol/l,

Serum Free T4 <8.0 pmol/l.

Subclinical hypothyroidism: (all of the followings), TSH >4m IU/l, Serum Total T3 (1.1-2.7 nmol/l), Serum Free T4 (8.0-21.0 pmol/l).

Body mass index : weight in kilograms (BMI) (Height in meters)^2.

Obesity: Body Mass Index of >30 kg/m^2.

METHODOLOGY

This descriptive cross sectional study was carried out at the Department of General Medicine, Combined Military Hospital Peshawar on 130 patients. Obese/Body Mass Index of >30 Kg/m^2, age greater than 20 years and less than 65 years and female were included however, diagnosed cases of hypothyroidism, patients on anti thyroid medication patients on radio-iodine treatment, patients taking iodine tablets or any other drug that could affect thyroid function, pregnant obese females, patients with ongoing critical illnesses such as ischemic, heart disease, chronic renal failure and cirrhosis liver and patients suffering from other autoimmune diseases. All the female patients reporting to the family OPD and fulfilling the inclusion criteria were asked informed consent and enrolled here. A detailed history and a thorough clinical examination were undertaken by me in the presence of a female attendant. Patients with already diagnosed hypothyroidism, on anti thyroid iodine or medication was excluded. Pregnant obese females or with ongoing critical illnesses such as ischemic heart disease, chronic renal failure and cirrhosis liver, suffering from other autoimmune diseases was not be included. Height and the weight of the patients were measured and later their age and BMI was recorded in the proforma. They were underwent laboratory investigation including thyroid stimulating hormone, Total T3 levels, T4 levels which was free of cost as they are entitled patients. Selected patients data was noted and blood samples taken at laboratory counter made in Family OPD and results was verified by the pathologist. Data was collected as per the proforma annexed (Annex A).

All data was entered in SPSS version 20 and analysed. Descriptive statistics was used to calculate mean and SD for quantitative data like age, BMI and duration of obesity. Frequencies and percentages were calculated for qualitative data i.e hypothyroidism. Effect modifier like age, BMI and duration of obesity was controlled by stratification. Post-stratification chi-square test was applied. *p*-value ≤0.05 was significant.

RESULTS

This study was conducted on 130 patients (fulfilling the inclusion criteria) presented in out patients department of medicine in Combined Military Hospital Peshawar for total period of 6 months from August to December 2015. The aim of this study was to determine the frequency of undiagnosed hypothyroidism in obese females. Formal consent was taken from all patient included in this study. History and physical examination was carried out by trainee researcher which was followed by calculating their (BMI) body mass index and thyroid function tests was done and their results were entered in the proforma. The age of the study group ranged from 22-65 years. Mean age was 47.68 years with standard deviation of ± 11.382. As shown in table-I. The BMI of the study group ranged from 30 to 37 kg/m^2. The mean was 31 years with standard deviation of ± 2.110. As shown in table-II. The mean duration of obesity was 6 years with standard deviation of ± 3.476. as shown in table-

III. Out of the 130 patients in study population 124 (95%) did not have any hypothyroidism. While 6 patients (5%) had undiagnosed hypothyroidism. Shown in table-IV. Stratification of undiagnosed hypothyroidism with age BMI and duration of obesity is given in table-V,VI,VII.

Table -I: Age distribution (n=130).

Age (Years)	Frequency	Percentage
20-30	10	8
31-40	43	33
41-50	46	35
51-65	31	24
Total	130	100

Mean age was 47.68 years with SD ± 11.382.

Table-II: Distribution of BMI (n=130).

BMI	Frequency	Percentage
≤34	108	83
>34	22	17
Total	130	100

Mean BMI was 31 with standard deviation ± 2.110.

Table-III: Distribution of duration of obesity (n=130).

Duration	Frequency	Percentage
≤5 years	53	41
>5 years	77	59
Total	130	100

Mean duration was 6 years with SD ± 3.476.

Table-IV: Distribution of primary hypothyroidism (n=130).

Primary Hypothyroidism	Frequency	Percentage
Yes	6	5
No	124	95
Total	130	100

DISCUSSION

This was a cross-sectional study spread over six months with an aim to determine the frequency of undiagnosed hypothyroidism in obese females. Multiple studies have been conducted in order to determine the prevalence of hypothyroidism in obese population. However, the frequency of undiagnosed hypothyroidism in obese population has not been studied in detail. Local data in this regard is also limited.

The study was performed using a strict inclusion and exclusion criteria so as to enroll only those obese females who could not have thyroid illness due to any other cause. The study concluded that the frequency of undiagnosed hypothyroidism in obese females was 4.5%. Two (1.5%) patients were found to have subclinical hypothyroidism while four (3%) had biochemical evidence of primary hypothyroidism.

Hypothyroidism is a worldwide problem and is associated with significant co-morbidities.

Table-V: Stratification of primary hypothyroidism w.r.t age distribution (n=130).

Primary Hypothyroidism	20-30 years	31-40 years	41-50 years	51-65 years	Total
Yes	0	2	2	2	6
No	10	41	44	29	124
Total	10	43	46	31	130

Chi square test was applied in which *p*-value was 0.7814.

Table-IV: Stratification of primary hypothyroidism w.r.t BMI (n=130).

Primary Hypothyroidism	≤34	>34	Total
Yes	4	2	6
No	104	20	124
Total	108	22	130

Chi square test was applied in which *p*-value was 0.2723.

Table-VIII: Stratification of primary hypothyroidism w.r.t duration of obesity (n=130).

Primary Hypothyroidism	≤5 years	>5 years	Total
Yes	3	3	6
No	50	74	124
Total	53	77	130

Chi square test was applied in which *p*-value was 0.6375.

The overall prevalence of hypothyroidism is found to be 1 in 500 to 1 in 10002. Studies in Pakistan are limited. The reported prevalence of overt hypothyroidism is about 1 in 10002. Given the "cause and effect" related to hypothyroidism, various studies have been conducted to established the association/incidence of hypothyroidism in obese and vice versa. Unnikrishnan *et al* reported frequency of overt hypothyroidism in India to be 3.5%[12]. Verma *et al* studied the relationship between obesity and hypothyroidism[7]. They concluded that the prevalence of clinical hypothyroidism in obese population is 33% whereas of subclinical hypothyroidism in obese is 11%. Another study was conducted in USA in order to establish the frequency of thyroid disease in healthy population, which was found

to be 4.6%. This study however, was performed on general population and included both males and females. Our study targeted the obese female population but the frequency was not much different from that of the American study.

The study also showed an interesting relationship between thyroid status and degree of obesity. It was observed that with increasing body mass index (BMI), the thyroid status was changed from being normal to subclinical hypothyroidism and finally primary hypothyroidism. The mean BMI for patients with no hypothyroidism was 32.33 ± 2.043 kg/m², for patients with subclinical hypothyroidism was 33.65 ± 0.636 kg/m² and patients with hypothyroidism was 36.00 ± 1.414 kg/m². International studies also support this observation. Study shows that patients with morbid obesity have higher level of. Thyroid stimulating hormone (TSH). In our study thyroid status was not appear to be affected by age of patients. The mean/average age of patients with hypothyroidism was 47 ± 6.703 years whereas with no hypothyroidism was 47.83 years ± 11.358. And with subclinical hypothyroidism was 39 ± 22.627 years. Our results in this regard differ from international findings where the screening of thyroid disease is recommended in older people because of higher prevalence if thyroid disease in this age group[19].

The study had some limitations. The patients were selected from hospital setting where they had reported for some other illness. Better results can be expected from a general population based study. A strict inclusion and exclusion criteria was adopted but given the low literacy rate and socio economic status of most of our patients, it is possible that some females already had hypothyroidism who never sought medical help for that.

CONCLUSION

Although, there is obvious linkage between (TSH) thyroid stimulating hormone and degree of obesity, however, the determined results/ frequency of hypothyroidism in obese females are not high enough to recommend large scale/mass screening.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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