DOI: 10.5958/2319-5886.2015.00095.8

International Journal of Medical Research & Health Sciences

www.ijmrhs.com Volume 4 Issue 3 Coden: IJMRHS Copyright @2015 ISSN: 2319-5886

Received: 27th Jan 2015 Revised: 25th March 2015 Accepted: 9th May 2015

Research article

PREVALENCE AND AT EARLY AGE ONSET OF HYPO AND HYPERTHYROIDISM IN POST-IODIZATION ERA: A HOSPITAL BASED STUDY FROM SOUTH INDIA

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ABSTRACT

Background: Thyroid dysfunction has been considered as one of the most common endocrine disorder in clinical practice throughout the world. Its increasing prevalence had led to the screening of general population in different parts of the world in order to investigate causes for rising incidence. A nationwide survey on epidemiology of thyroid dysfunction in selected cities of India suggested the need for further studies in order to have a more comprehensive analysis of epidemiological aspect for better awareness and control of this endocrine disorder. **Aim:** The major objective of the present study was to identify the prevalence and early age at onset of hypo and hyperthyroidism in post-iodization era based on a hospital based study. **Materials and Methods:** A total of 516 subjects visiting department of Medicine, Princess ESRA Hospital, Hyderabad, in age group of 10 to 75 years were included in the study from June 2013 to January 2014. Serum TSH, T3, and T4 assays were assessed by chemiluminescence method. Based on thyroid dysfunction test results, subjects were classified into Hypothyroidism, Subclinical Hypothyroidism and Hyperthyroidism. **Results:** The prevalence of hypothyroidism was highest in the females 33.52 % (n=173) as compared to males 2.32% (n=12) and hyperthyroidism in females 4.06% (n=21) and 0.19% (n=1) in males. Subclinical hypothyroidism in females was 7.55% (n=39). **Conclusions:** An inordinately high increase in the prevalence rate in women was observed particularly in the age group 21-30years. Monitoring of thyroid profile is necessary to prevent adverse outcome at clinical and subclinical levels related to infertility, pregnancies and other complications.

Keywords: Hypothyroidism, Hyperthyroidism, Subclinical hypothyroidism, T3 (Triiodothyronine), T4 (Thyroxin), TSH (Thyroid stimulating hormone)

INTRODUCTION

Thyroid dysfunction (TD) has been considered as one of the most common endocrine disorder in clinical practice throughout the world. [1] Its increasing prevalence had led to the screening of general population in different parts of the world in order to investigate causes for rising incidence. The world wide prevalence of hypothyroidism is estimated to be around 5% [2, 3] and that of subclinical hypothyroidism worldwide is 4-15%. [3, 4] In this scenario there is a need for further epidemiological studies in view of high prevalence reported by some initial studies both hospitals based as well as population surveys. Some recent reports from Europe have claimed that the non-toxic goiter

in the post-iodization era appears to be of auto-immune type i.e. hypothyroidism. The important signs and symptoms of hypothyroidism are fatigue, weight gain, constipation and cold intolerance whereas anxiety, palpitation, weight loss, increased appetite and sweating are important signs of hyperthyroidism. In a study by Doufas et al (1999)[5] it has been reported that apart from genetic and other environmental factors iodine excess in post-iodization era is considered to play an important role in the rising incidence of hypothyroidism of autoimmune type. Due to less awareness as well as less attention towards diagnostics of hypo and hyper thyroidism in India a considerable percentage of population, particularly women suffer from thyroid dysfunction which is considered as a common organ specific autoimmune disorder.[1]

A nation-wide study by Unnikrishnan et al. (2013)[6] on epidemiology of thyroid dysfunction in selected cities of India suggested the need for further studies in order to have a more comprehensive analysis of epidemiological aspects for better awareness and control of this endocrine disorder. Important factors that have been considered in such studies are age at onset, and gender ratio, and the relative prevalence rates of hypothyroidism and hyperthyroidism. In the present study emphasis has also been laid on the prevalence of subclinical hypothyroidism which may have various consequences such as increasing risk of cardiovascular disease, hyperlipidemia, somatic and neuromuscular symptoms, reproductive and other consequences as thyroid stimulating hormone (TSH) levels above the normal range can cause such ailments. In 1983 when India adopted the universal salt iodization programme it is noted that in post iodization period there was decline in goiter prevalence in several parts of the country. But the prevalence is estimated about that still 42 million people suffering from thyroid dysfunction. [7] There is a need for further studies on the prevalence of thyroid disorder in post iodization period in order to investigate the new emerging trends in the prevalence of TD.

MATERIALS AND METHODS

The study was conducted after taking approval from Institutional Review Board, Deccan college of Medical Sciences, Hyderabad.

This was a unicentric, prospective based study. A total of 516 subjects visiting Department of Medicine, Princess ESRA Hospital, Hyderabad for general health checkup in the age group of 10 to 75 years (those male cases who reported for thyroid profile checkup were also included) were screened after taking informed consent from them. Each subject was given a reference number for further reference. Only cases with primary thyroid disorders were considered to be included under inclusion criteria whereas cases suffering with secondary and tertiary hypothyroidism and chronic illness were excluded from the study.

Methodology: All the subjects underwent the assessment of physical examination, medical history and laboratory investigations. From each patient aseptically 2ml of blood was collected and serum was separated. The serum was used for the following thyroid profile biochemical analysis within 24 hours from collection. Serum TSH (Thyroid stimulating hormone), T3 (Triiodothyronine), and T4 (Thyroxin) assays were done by chemiluminescence method (Helfand et al) [8] (Biomerieux, France, 3rd Generation). Based on TD test results, subjects were classified as shown in Table 1. **Statistical analysis**: Statistical analysis was performed for all the subjects enrolled in the study as per the protocol. All statistical analysis was performed using Graph Pad Prism software Version 5.0 (San Diego, CA, USA). The prevalence of hypo, hyper and subclinical hypothyroid was expressed as counts and percentage. Distribution of various parameters such as age and gender among hypo, hyper and subclinical hypothyroidism was calculated using Fisher's exact test. P value ≤ 0.05 was considered statistically significant for the all variables.

RESULTS

A total of five hundred and sixteen (516) subjects were included in the study from June 2013 to January 2014. Out of these four hundred and eighty seven (487) subjects were females and the remaining 29 subjects were males falling in the age range of 10 to 75. However, the percentages of cases suffering from hypothyroidism were 185(35.85%), sub clinical hypothyroidism 39(7.55%), and hyperthyroidism 22(4.26%) (Table 2 and Fig. 1). The number of hypothyroid cases were significantly higher than hyperthyroid as well as subclinical hypothyroid cases ($p<0.05$).

Subjects who were already diagnosed as suffering from thyroid dysfunction and were on Levothyroxin/ Eltroxin/ Carbimazole etc constituted a total of 31.25% (n=145) with hypothyroidism and 1.93% (n=9) with hyperthyroidism (Table 3). The number of newly diagnosed hypo cases was 39 (7.55%) and that of hyperthyroid cases 13 (2.52%). The total number of already diagnosed hypothyroid cases were significantly higher than that of newly diagnosed hypothyroid cases (p<0.001). Gender-wise analysis total cases revealed that the total prevalence newly diagnosed and already known cases revealed the highest prevalence of hypothyroidism (36.99%) and hyperthyroidism (52.38%) was in the age group of 21-30years in females and 31-40 (50%) in males.

The prevalence of hypothyroidism was highest in the females 33.52 % (n=173) as compared to males 2.32% (n=12) and hyperthyroidism in females 4.06% (n=21) and 0.19% (n=1) in males. Subclinical hypothyroidism in females was 7.55% (n=39) and no male subclinical subjects were found. Details of prevalence rates of hypo and hyperthyroidism and subclinical thyroid condition are shown in table 4.The percentage distribution curves of hypothyroid as well as subclinical hypothyroid cases are shown in figure 2. However distribution for hyperthyroid cases is not shown here due to small number of cases (n=22). The statistical analysis revealed highest prevalence in age-group 21-30 years compared to other age groups (p<0.001).

Table1: Normal and elevated levels of thyroid profile to segregate disease type

	Normal Range	Hypo thyroidism	Subclinical Hypo-thyroidism	Hyper thyroidism
Serum TSH	0.3-5µIU/ml	≥7µIU/ml	5-7µIU/ml	≤0.2µIU/ml
Total T3	0.6-3.3 nmol/L	≥3.3 nmol/L	Normal	≤0.6nmol/L
Total T4	60-120nmol/L	≥120nmol/L	Normal	≤60nmol/L

Hypothyroidism versus hyperthyroidism and subclinical hypothyroidism cases were found statistically significant (p<0.05)

Table 2: Percentages of patients suffering from hypothyroid, subclinical hypothyroidism and hyperthyroid cases.

	Total number of subjects	Hypo thyroid	Hyper thyroid	Subclinical hypothyroidism
Number	516	185***	22	39
Percentage	100	35.85%	4.26%	7.5%

***p<0.0003

Table 3: The **number and percentage of newly and already diagnosed cases of hypo and hyperthyroidism**

	Hypothyroidism		Hyperthyroidism	
	Female	Male	Female	Male
Newly Diagnosed	37 (7.17%)	3 (0.38%)	12 (2.32%)	1(0.19%)
*Already Diagnosed	136 (26.35%)	9 (1.93%)	9(1.74%)	0
Total	173 (33.52%)	12 (2.32%)	21(4.06%)	1(0.19%)

*Already diagnosed hypothyroid cases versus newly diagnosed hypothyroid cases p<0.001

Table 4: Prevalence of hypo and hyperthyroidism in males and females in different age groups

Age group (Year)	Hypothyroidism		Subclinical hypothyroidism		Hyperthyroidism	
	F	**M**	**F**	**M**	**F**	**M**
10-20	27 (15.60%)	1(8.33 %)	2(5.12%)	0	3 (14.28%)	1
*21-30	64 (36.99%)	1(8.33%)	13(33.33%)	0	11 (52.38 %)	0
31-40	39 22.54%)	6(50.0%)	5(12.82%)	0	6 (28.57%)	0
41-50	20 11.56%)	2(16.6%)	9(23.07%)	0	0	0
51-60	10 (5.78%)	2(16.6%)	4(10.25%)	0	1 (4.76%)	0
61-70	12 (6.93%)	0	4(10.25%)	0	0	0
71-75	1 (0.57%)	0	2	0	0	0

*Number of cases in the age group of 21-30 was significantly higher than other age groups in females with hypothyroidism (p<0.001)

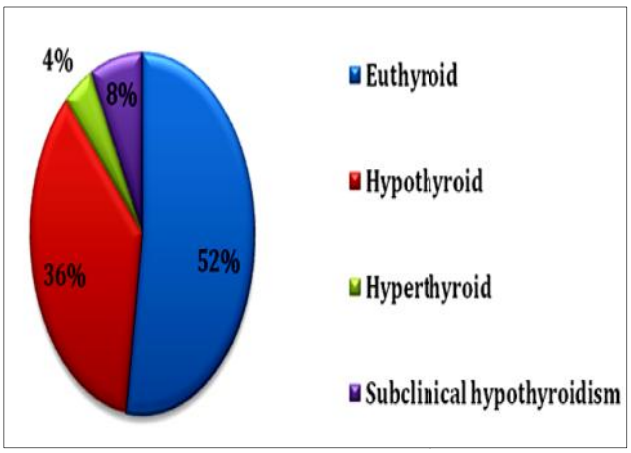

Fig 1: Percentage of hypothyroid, subclinical hypothyroid and hyperthyroid cases

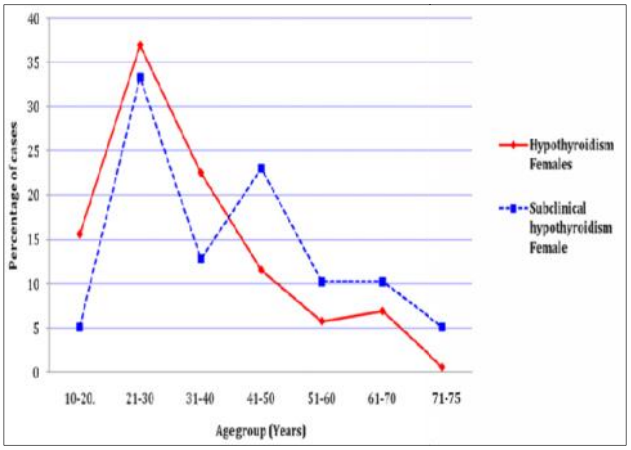

Fig2: Percentage distribution of overt and sub-clinical hypothyroidism cases (females only)

DISCUSSION

Post-iodization studies on the occurrence of thyroid disorders in different populations across the globe have indicated trends of increase in the prevalence rates of these disorders particularly in hypothyroidism and hyperthyroidism. [6] Even the incidence of anti-thyroid peroxidase (TPO) antibody positive subjects has been shown to be significantly increased. [9]

In the present study we report a prevalence rate of 35.84% of hypothyroidism (185/516) which is similar to another hospital based study published by Shekhar et al. (2012)[10] where the authors reported have found 31.3% cases with overt hypothyroidism in a cross sectional hospital based study from coastal Andhra Pradesh, India. In our study hypothyroidism cases (35.84%) included 7.55% (n=39) newly diagnosed and 28.29% (n=146) already diagnosed cases who were already on hormone replacement therapy (Table 3). The prevalence of subclinical hypothyroidism was 7.55% (n=39) and all these cases were females. The prevalence of Hypothyroidism and Hyperthyroidism was found to be highest in females (37.58%) which are similar to some previous studies. [10-12] The number of female cases was inordinately high with a ratio of 14 females versus 1 male. However, population based surveys have reported somewhat lesser rates of prevalence which show approximately a ratio of 3 females versus 1 male. [6] Female preponderance with variable female to male ratio has been reported in almost all epidemiological studies. [13] However, in post –Iodization period this ratio appears to be tilting more towards female cases due to increasing number of females getting affected with this disorder. Whereas endogenous environmental and genetic factors are being attributed to high vulnerability of females to these condition.

Age specific prevalence rate was found to be highest in the age range 21-30 years 36.99% with overt Hypothyroidism and 33.33% with subclinical Hypothyroidism (Table 4). The reason for highest incidence in the age range 21-30years in women may be attributed to problems related to infertility for which they report to the Gynecology and Obstetrics Department of the hospitals. In general our data represents that prevalence of thyroid dysfunction (TD) is highest in adults of age group 21-30 years(Fig2) specifically females, even in the subclinical group which constitutes all female cases. The peek incidence was noted in the third decade of life (21-30 years) (Table 4) both in overt and subclinical hypo cases.

In order to analyze incidence of hypothyroidism in younger and old age groups a cutoff age of 35 years was also considered. The incidence of the disorder in cases below the age of 35 years was 21.5% (n=111) while in those above 35 years of age it was 12% (n=62). These observations also clearly indicate the peek incidence is in younger age group.

Considerable women report to hospital for infertility problems with raised TSH levels which may be the reason for higher female to male ratio. In a report on prevalence of hypothyroidism in infertile women by Verma et al (2012), 395 women who reported for the first time; of these 25% were diagnosed as

hypothyroid and responded to the treatment with levothyroxin.[14]

Various endogenous factors are attributed to higher predisposition of females particularly in younger age; these include hormonal imbalance at puberty, pregnancy, higher level of estrogen which cause rise in TSH levels which in turn induces expression of major histo compatibility (MHC) class II molecules on cells including thyrocytes which may present self antigens released due to infection of the thyroid there by setting in motion the process of auto-immunity. [12]

The skewed X-chromosome inactivation (XCI) hypothesis for high susceptibility to hypo is also gaining more credence as it claims that the existence of XCI in females results in self antigen express ion in the thymus or in other peripheral sites which is involved in tolerance induction. Because of this reaction skewed XCI has been identified as a predisposition factor for the development of AITD. [15, 16]

Multiple genes are implicated in the causation of thyroid disorders which are mainly grouped into those that are responsible for coding thyroglobulin, TSH receptors etc and the other group comprises of those genes that are responsible for immunoregulatory molecules and cytokines. Single nucleotide polymorphisms in some of these have been reported to be associated with increased risk of thyroid dysfunction. [17]

In the present study the protocol did not include specific reasons for getting the thyroid profile tested. However it appears that a systematic analysis of thyroid profiles of patients visiting hospital appears to be of significant importance in identifying emerging trends in the prevalence of hypothyroidism.

These reports appear to represent emerging trends of high prevalence of both overt and subclinical hypo in women. These studies lend support to the results of high prevalence of hypothyroidism reported in this study, and indicate that the TSH levels are very crucial as they may have serious consequences, they may also affect cardiovascular and neuromuscular manifestations. [18]

It is suggested that iodine intake of a population should be kept within a relatively narrow range interval that prevents iodine disorders, but not higher. [12]

Limitations of our study are that it was performed on a modest sample size. Secondly no test was performed for screening for anti-TPO or antibodies. Finally, with regard to the significant cause of TD etiological factors may be one of the better explanations along with iodine sufficient status. It is suggested that further studies on similar lines may be carried out both at the population base as well as in the hospital with relatively larger sample size in order to draw more definitive conclusion.

CONCLUSION

This appears to be an increasing trend in the prevalence of thyroid disorders particularly hypothyroidism in the post-iodization era in India. An inordinately high increase in the prevalence rate in women is observed particularly in the age group 21-30years (Fig. 2) and indicating the need to explore possible molecular mechanisms underlying this trend. Monitoring thyroid profile and adopt to suitable measures to prevent adverse outcome as clinical, subclinical levels have been related to infertility, pregnancies and also cardiac problems particularly heart failure.

ACKNOWLEDGEMENTS: None

Conflict of Interest: Nil

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