Journal of Scientific Research ISSN 0555-7674
Vol. XXXX No. 2, December, 2010

Serum Concentration of Thyroxin and Thyroid Stimulating Hormone in Children Suspected of Thyroid Dysfunction

Shan Elahi[1], Humaira Rasheed[2], Zulqurnain syed[1], Zainab Aman[3], Riffat Yasmeen[3]
[1]Centre for Nuclear Medicine (CENUM), Mayo Hospital, Lahore
[2]Department of Chemistry, University of Engineering & Technology, Lahore
[3]Institute of Chemistry, University of The Punjab, Lahore

Summary: This study was planned to investigate serum concentration of free thyroxin (FT_4) and thyroid stimulating hormone (TSH) as well as thyroid dysfunctions in children attending CENUM, Mayo Hospital Lahore. A total of 227 children (131 female and 96 male) were selected for this study. Their age range was 1 to 12 years (mean 7.6 ± 3.4 years). 45 (19.8%) children had goiter with significantly more frequency in female as compared to male children (28.2% Vs 8.3%; $p<0.05$). More than 70% of the children had F_4 and TSH within their respective normal ranges (euthyroid). Thyroid dysfunctions were detected in 11.0% children (7.5% hypothyroidism; 3.5% hyperthyroidism). Only the incidence of hyperthyroidism was significantly more in goiterous children. There was no significant difference in the incidence of hyperthyroidism but hypothyroidism was significant ($p<0.05$) more common in female children.

Key Words: Thyroid hormone, Children, Hyperthyroidism, Hyperthyroidism, Goiter

Introduction

Thyroid is an important endocrine gland in human body that synthesizes thyroid hormone-thyroxin (T_4) and triiodothyronine (T_3) under the influence of thyroid stimulating hormone (TSH). The secretion and release of TSH is stimulated by the hypothalamic thyrotropin releasing hormone (TRH), which in turn is controlled by the serum concentration of T_4 and T_3 through a negative feedback mechanism (Stockigt 2003). Iodine is the essential component of the thyroid hormone, T_4 and T_3, contributing 65% and 59% of their respective molecular weight (Dunn 1998). Thyroid hormone plays essential role for the regulation cellular metabolism, growth and development. In children it is imperative to detect and correct thyroid dysfunction to achieve optimal growth and development (Bettendorf 2002).

Disorders of thyroid glands like goiter, nodules, hyperthyroidism or hypothyroidism are amongst the most common endocrine problems of childhood (Desai 1997). Low or high iodine intake, thyroid autoimmunity, nutritional status and ingestion of goitrogens are the most common etiologies of thyroid dysfunctions in children (Desai 1997, Larson et al 2000). Iodine deficiency markedly alters thyroid metabolism resulting in low circulating T_4 and increased TSH secretion by the pituitary. This enhanced TSH stimulation alters the morphology of the thyroid and produces hyperplasia and goiter. Goiter may also occur as a result of inflammation of the thyroid gland and it may be diffuse or nodular, symmetric or asymmetric (Langer 1999). Isolated thyroid nodules are uncommon in childhood (Hung et al 1992). Hyperthyroidism is very rare in children and its frequency increases with age. The most common cause of childhood hyperthyroidism is autoimmune, diffuse

1-For Proof and Correspondence: **Shan Elahi**

goiter, Grave's disease or Basedow disease. Grave's disease is extremely rare before 5 years and only 10% of patients are below 10 years of age (Dreimane & Varma 1997). Hypothyroidism is most common among children and autoimmune thyroiditis is often the cause of acquired hypothyroidism in older children (Rallison et al 1975). Thyroid cancer is very rare in children (Dreimane & Varma 1997).

This study was planned to know the biochemical thyroid dysfunctions among children attending Centre for Nuclear Medicine (CENUM), Mayo Hospital Lahore.

Material and Methods

All referred male and female children, aged 1-12 yrs, attending CENUM during March to June 2010 were initially selected for the study. A careful history of patient was taken by the qualified physician included age, sex, use of medication, surgery and past incidence of thyroid dysfunction. For this study the children already diagnosed for thyroid diseases and taking thyroid medication or had past history of thyroid surgery were excluded.

A 5.0 ml blood sample was taken from each child for laboratory determinations. The serum was separated by low-speed centrifugation (2000×g) for 5 minutes at room temperature. Serum samples were stored at -20°C until analysis. Serum FT_4 was estimated by radioimmunoassay (RIA) and TSH by IRMA techniques using commercial kits of Immunotech Inc. (Beckman, Czech Republic). RIA & IRMA batches were run with commercially derived control sera at low, medium and high concentrations. Measurement of radioactivity, fitting of the standard curve and analysis of samples was carried out using a computerized gamma counter (Cap-RIA 16, CAPINTEC; Inc. USA). Assay reliability was determined by the use of commercially derived control sera of low, medium and high concentrations which were included in every run. All assays were carried out in duplicate. RIA and IRMA results were expressed at less than 10%CV of imprecision profile. Normal ranges for FT_4 and TSH, as standardized in our laboratory were 11 - 22 pmol/L and 0.3 - 4.0 mIU/L respectively. Hyperthyroidism was diagnosed if serum TSH was < 0.3 mIU/L and FT_4 > 22 pmol/L. Hypothyroidism was considered if serum TSH was > 4.0 mIU/L and FT_4 < 11.0 pmol/L. A patient with TSH > 10.0 mIU/L irrespective of FT_4 concentration was also considered hypothyroid (Hoogendoorn et al 2006).
The analysis of thyroid hormones levels distribution was carried out using Microsoft Excel program on a personal computer. Chi-Square test was applied to test the significance of difference between two arbitrary groups. Student t-test was applied to test the significance of difference between mean values. A value of $p<0.05$ was considered significant.

Results

A total of 227 children fulfill the selection criteria and were selected for this study. There were 131 female and 96 male children. Their mean (± SD) age was 7.6 ± 3.4 years with age range between 1 to 12 years. Among selected children 45 (19.8%) had goiter with significantly more frequency among female as compared to male children (28.2% versus 8.3%; $p<0.05$).

Analysis of thyroid function tests showed that 162 (71.4%) and 191 (84.1%) children respectively had within normal range values of TSH (0.3-4.0 mIU/L) and FT4 (11.0-22.0 pmol/L). The distribution of abnormal serum concentration of FT_4 and TSH in male and female children is shown in Table 1.

Although female children had increased ratio of abnormal FT_4 and TSH levels but the difference in this respect between male and female children was non-significant.

Biochemical thyroid dysfunction (hyperthyroidism and hypothyroidism) was detected in 25(11.0%) children. Among them 17(7.5%) children had hypothyroidism while 8(3.5%) had hyperthyroidism. Thus incidence of hypothyroidism was almost double as compared to hyperthyroidism.

Table 1: Distribution of abnormal concentration of FT_4 and TSH in male and female children

Thyroid Hormone	Male (%)	Female (%)	p -Value
FT_4 (pmol/L)			
< 11.0	04 (4.2)	11 (8.4)	0.461
> 22	07 (7.3)	14 (10.7)	0.678
TSH (mIU/L)			
≤0 3	03 (3.1)	10 (7.6)	0.352
> 4.0	20 (20.8)	32 (24.4)	0.815

Table 2 showed the incidence of hyperthyroidism and hypothyroidism in male and female children. Female children exhibited many a time increased incidence of both hyper and hypothyroidism as compared to male children. Statistical analysis showed that there was no significant difference in the incidence of hyperthyroidism between male and female children. However, this difference was statistically significant ($p<0.05$) for hypothyroidism.

Table 2: Incidence of thyroid dysfunction in male and female patients

Group of Patient	Hyperthyroidism	Hypothyroidism
Female (131)	07 (5.3 %)	15 (11.4%)
Male (96)	01 (1.0%)	02 (2.1%)
P-Value	0.217	0.001

To test whether the significant difference in incidence of hypothyroidism is associated with presence of goiter, we computed incidence of hyperthyroidism and hypothyroidism in goiterous and non-goiterous children. Results are shown in Table 3. The incidence of hyperthyroidism was significantly more in goiterous children but hypothyroidism was not effected by presence of goiter.

Table 3: Thyroid dysfunction in goiterous and non-goiterous children

Group of Patient	Hyperthyroidism	Hypothyroidism
Goiterous (n=45)	06 (13.3%)	06 (13.5%)
Non-Goiterous (n=182)	02 (1.1%)	11 (12.5%)
P-Value	0.0003	0.260

Discussion

Disorders affecting the thyroid gland represent the most common endocrinopathies during childhood. The etiology and clinical presentation of thyroid disorders in children substantially differ from that in adults (Bettendorf 2002). The objective of this study was to analyze serum FT_4 and TSH as well as the incidence of biochemical thyroid dysfunctions among children attending Centre for Nuclear Medicine (CENUM), Mayo Hospital Lahore. Our aim was the appreciation of distinct characteristics of thyroid function and dysfunction in childhood in our area. We investigated thyroid hormone profile of 227 children (131 female and 96 male) of 1 to 12 years age. According to our result 45 (19.8%) children presented with goiter. The reason for high incidence of goiter in our study is that our children were the referred ones that already had signs and symptoms of thyroid dysfunction. Desai (1997) in India reported the same incidence of goiter in 800 children referred for thyroid problems. The dominant reason for goiter in children is the low iodine content of subcontinent diets (Geelhoed 2004, Akhtar et al 2004). Our incidence of goiter is very high when compared to a study of Jaksic et al (1994) who reported goiter incidence in 2.8% living in area of Croatia where salt was regularly iodized. However, in severe iodine deficiency areas like Sudan, the reported incidence of goiter in children aged 1–6 y is 22.3% (Elnour et al 2000). We found that incidence of goiter was significantly more among female as compared to male children (28.2% Vs 8.3%; $p<0.05$). This result is in accordance to other studies (Jaksic et al 1994; Desai 1997).

Analysis of thyroid function tests showed that most of the study children had normal serum concentrations of FT_4 and TSH (euthyroid). Clinical thyroid dysfunction (hyperthyroidism and hypothyroidism) was detected in 11.0% of the children. The incidence of hypothyroidism (7.5%) was almost double as compared to hyperthyroidism (3.5%). This observation is in accordance to that of Desai (1997) in India who reported that clinical presentation in children was most commonly for goiters and hypothyroidism while hyperthyroidism was infrequent. In a study carried out in nearly 800 children referred for thyroid problems, it was

found that 79% had hypothyroidism while only 2% had hyperthyroidism. Hyperthyroidism is infrequent before age of 5 and increases in frequency with age, reaching peak in adolescence (Mokhashi et al 2000).

In this study we found that female children had increased ratio of abnormal FT_4 and TSH levels as compared to male children. Though this difference was non-significant but female children exhibited many a time increased incidence of both hyperthyroidism as well as hypothyroidism as compared to male children. Further analysis showed that there was no significant difference in the incidence of hyperthyroidism but incidence of hypothyroidism was significanty ($p<0.05$) more in female as compared to male children. This observation is again in accordance to other studies (Desai 1997; Hunter et al 2000). The reason may the increased prevalence of autoimmune thyroiditis (ATA) in female children (Loviselli et al 2001; Setian 2007). Hashemipour et al (2007) in Iran had reported a 7.3% incidence of positive anti-thyroid antibodies in children aged 7-13 year-old. ATA prevalence is more frequently detected in female children (Loviselli et al 2001, Hashemipour et al 2007). The presence of ATA is not age-dependent in males, whereas a significant increase of ATA is observed in females older than 11 years of age (Loviselli et al 2001).

According to our results the presence of goiter in this study was associated with increased incidence of hyperthyroidism but not hypothyroidism in children. The reason for this phenomenon may be the nodular development due to iodine deficiency or other factors in children (Wiersinga 2007). Loviselli et al (2001) and Hashemipour et al (2007) had reported increased frequency of ATA in children with enlarged glands implying more incidence of hypothyroidism but our results do not seems to support this observation. A limitation of our study is the low number of children presenting with goiter. Moreover, we have not determined serum thyroid autoantibodies.

In summary, thyroid dysfunctions were detected in 11% of the referred children. Further large studies are warranted to explore the etiology and management of thyroid diseases in this vulnerable group of population.

References

1. Stockigt J Assessment of thyroid function: towards an integrated laboratory - clinical approach. *Clin Biochem Rev* 24:110-23, 2003

2. Dunn JT. What's happening to our iodine? *J Clin Endocrinol Metabol*. 83(10):3398-3400,1998.

3. Bettendrof M Thyroid disorders in children from birth to adolescence *Eur J Nucl Med* 29 (Suppl. 2):S439–S446, 2002

4. Desai M. Disorders of thyroid gland in India. *Indian J Pediatr*. 64:11-20,1997.

5. Larson J, Koslawy M, Andreson E. Thyroid disease: a review for primary care. J *Am Acad Nurse Pract*. 12 (6):226-32, 2000.

6. Langer P. Discussion about the limit between normal thyroid and goiter: minireview. *Endocrine Regulation* 33:39-45,1999.

7. Hung W, Anderson KD, Chandra RS, et al. Solitary thyroid nodules in 71 children and adolescents. *J Pediatr Surg* 27(11):1407-9, 1992

8. Dreimane D and Varma. Common childhood thyroid disorders. *Indian J Pediatr*. 64:3-10,1997.

9. Rallison ML, Dobyns BM, Keating FR, Rall JE, Tyler FH. Occurrence and natural history of chronic lymphocytic thyroiditis in childhood. *J Pediatr* 86(5):675-82, 1975

10. Hoogendoorn EH, Hermus AR, de Vegt F, Ross HA, Verbeek ALM, Kiemeney LALM, Swinkels DW, Sweep FCGJ and den Heijer M. Thyroid function and prevalence of anti-thyroperoxidase antibodies in a population with borderline sufficient iodine intake: influences of age and sex. *Clin Chem*. 52(1):104-111,2006.

11. Geelhoed GW Marginal micronutrients: iodine insufficiency in subcontinental diets-cultural, biological and humanitarian implications. *Nutrition* 20:334 –335, 2004

12. Akhter P, ur-Rehman K, Orfi SD, Ahmad N. Assessment of iodine levels in the Pakistani diet. *Nutrition* 20:783-87, 2004

13. Jaksic J, Dumic M, Filipovic B, Ille J, Cvijetic M, Gjuric G. Thyroid diseases in a school population with thyromegaly. *Arch Dis Child*. 70():103-106, 1994.

14. Elnour A, Hambraeus L, Eltom M, Dramaix M, Bourdoux P. Endemic goiter with iodine sufficiency: a possible role for the consumption of pearl millet in the etiology of endemic goiter[1–3]. *Am J Clin Nutr* 71:59–66, 2000.

15. Mokashi MH, Desai U, Desai M. Hyperthyroidism in children. *Indian J Pediatr* 67(9):653-656, 2000.

16. Hunter I, Greene S, MacDonald TM and Morris AD. Prevalence and aetiology of hypothyroidism in the young. *Arch Dis Child* 83;207-210, 2000.

17. Loviselli A, Velluzzi F, Mossa P, Cambosu MA, Secci G, Atzeni F, Taberlet A, Balestrieri A, Martino E, Grasso L, Songini M, Bottazzo GF, Mariotti S; Sardinian Schoolchildren Study Group The Sardinian Autoimmunity Study: 3. Studies on circulating antithyroid antibodies in Sardinian schoolchildren: relationship to goiter prevalence and thyroid function. *Thyroid* 11(9):849-57, 2001

18. Setian N. Hyperthyroidism in children. *J Pediatr* 83(5):209-206,2007.

19. Hashemipour M, Amini M, Aminorroaya A, Dastjerdi MS, Rezvanian H, Kachoei A, Moaddab MH, Mohammadi M, Kelishadi R, Amini Z, Haghighi S and Fariba S. High prevalence of goiter in an iodine replete area: do thyroid auto-antibodies play a role? *Asia Pac J Clin Nutr*. 16(3):403-410,2007.

20. Wiersinga Management of thyroid nodules in children and adolescents. *Hormones* 6(3):194-199, 2007.