International Journal of Contemporary Pediatrics
Poornachand V et al. Int J Contemp Pediatr. 2017 Jan;4(1):43-47
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20164514

Original Research Article

Study of clinical and biochemical profile of subclinical hypothyroidism in children aged 2-12 years

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Received: 08 December 2016
Accepted: 13 December 2016

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ABSTRACT

Background: Subclinical hypothyroidism is quite a common clinical condition in pediatric population. Objective of this study was to understand the clinical and biochemical profile of Subclinical hypothyroidism in children attending endocrinology OPD at a tertiary care center in southern India.
Methods: In this study 62 children diagnosed with subclinical hypothyroidism. Clinical assessment and laboratorial evaluation was carried out in a systematic way. Symptomatology, anthropometry, measurement of vital parameters such as heart rate, blood pressure, tests for anti-thyroid antibody, lipid profile, estimation of bone age, USG neck, assessment of left ventricular function using M-mode echo were carried out at the time of diagnosis.
Results: Subclinical hypothyroidism is more common in female children, principle symptoms were neck swelling and weight gain, goitrous autoimmune thyroiditis is more common in female, significant number of children had positive anti-thyroid antibodies, mean TSH value of patients with positive anti-thyroid antibody was high, there was no delay in bone maturation in majority of children, both systolic and diastolic blood pressure were high, these children had abnormal lipid profile, heart rate and left ventricular function were normal.
Conclusions: Subclinical hypothyroid children have higher risk of hypertension and pro-atherogenic lipid abnormalities. As there is a risk of progression to overt hypothyroidism these children needs regular follow up.

Keywords: Autoimmune thyroid disease, Blood pressure, Cardiovascular morbidity, Lipid abnormalities

INTRODUCTION

Subclinical hypothyroidism can be defined as a "serum thyroid-stimulating hormone (TSH) concentration above statistically defined upper limit of normal range and serum free thyroxine within reference range".[1] Prevalence of SCH in adults ranges from 4 to 10%.[2] Prevalence in pediatric population is estimated to be less than 10%.[3] "Persistently elevated TSH over a period of time is one of the best indicator to assess true prevalence of SCH in pediatric population".

Most of the patients with SCH have no signs or symptoms, on the other hand a few patients have typical symptoms suggestive of hypothyroidism and number of other symptoms such as weight gain, cold intolerance, constipation, neck swelling which are similar in frequency and similarity to age matched euthyroid controls.[4]

In adult population subclinical hypothyroid disease is associated with marginally increased risk of progression to overt thyroid disease, abnormal lipid levels, increased risk for atherosclerosis which results in increased cardiovascular morbidity and mortality. Studies have shown that subclinical hypothyroidism in children is associated with pro-atherogenic abnormalities like low high-density lipoprotein, high triglyceride to high density-lipoprotein ratio and high homocysteine level.[5] No controlled studies are available in pediatric population

evaluating the outcomes in SCH children treated with L-thyroxine versus those children who received placebo.

Children differ from adults in etiology, the natural history of the thyroid dysfunction, as well as consequences of the disorder. Hence we cannot extrapolate available adult data to children. There are very few available pediatric randomized controlled trial data regarding treatment of subclinical hypothyroidism.

This study was conducted to study clinical symptomatology in children with subclinical hypothyroidism and the effect of subclinical hypothyroidism on growth, cardiac function and lipid profile among Indian children.

METHODS

This study was conducted between October 2015 and August 2016 at Institute of child health and hospital for children, Chennai which is a tertiary care centre for Pediatrics with referral from wide across the state and neighboring states. It is a prospective, descriptive observational study done on children attending endocrinology OPD of Institute of Child Health and Hospital for Children. These children were biochemically confirmed to have subclinical hypothyroidism. Symptomatology, growth, functional cardiac status and biochemical profile of these children in the age group 2-12 years was evaluated. A total of 62 children fulfilling the eligibility criteria were selected for the study over a period of 11 months. After obtaining informed written consent children were enrolled into the study. Height, weight, and BMI was measured and plotted in WHO growth charts.

Heart rate and blood pressure measurements were taken. Z-score for systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated separately. Thyroid function test, autoimmune anti-thyroid antibodies (anti-thyroid peroxidase - Anti TPO and anti-thyroglobulin - Anti TG), serum fasting lipid profile (high density lipoprotein - HDL, low density lipoprotein - LDL and triglycerides - TG) tests were carried out and compared with standard age and gender matched reference.[6]

X-ray bone age was estimated to assess skeletal maturation, ultra sonogram neck performed to look for changes in echogenicity in children with goiter. Left ventricular dimensions (left ventricular internal diameter systole- LVIDs, Left ventricular internal diameter diastole- LVIDd, Left ventricular posterior wall thickness diastole- LVPWd, interventricular septal thickness - IVS) and left ventricular systolic function (ejection fraction - EF and fractional shortening - FS) were assessed with the help of M-mode echo-cardiogram.

Z-scores for each left ventricular dimensions were calculated based on height and weight of the individual.

RESULTS

Among 62 children, 59.7% (n = 37) were girls and 40.3% (n = 25) were boys. Majority of children were in age group 8-11 years. Average age of presentation in this study is 8.42 years. Of this 62 children, 56.45% (n = 35) had sought medical advice for complaint of excessive weight gain, 45.16% (n = 28) had neck swelling as their principal symptom. 14.51% (n = 9) children had generalized weakness, 8% (n = 5) children had history of difficulty in swallowing, 4 had history of head ache. 1.6% children had decreased appetite, constipation, generalized swelling, these symptoms were mainly in association with above mentioned principal symptoms.

Table 1: HDL values of subclinical hypothyroid children in mg/dl.

		Mean	95% CI	Population mean[6]	p value
Male	5-9 years	38.25	34.53-41.96	55	<0.0001
	10-14 years	38.7	34.65-42.74	55	<0.0001
Female	5-9 years	37.33	34.58-40.07	52	<0.0001
	10-14 years	36	33.82-38.17	52	<0.0001

Table 2: Cholesterol values of subclinical hypothyroid children in mg/dl.

		Mean	95% CI	Population mean[6]	p value
Male	5-9 years	171.25	165.77-176.72	153	<0.0001
	10-14 years	171.4	164.36-178.43	161	0.008
Female	5-9 years	170.33	166.13-174.52	164	0.005
	10-14 years	173.64	169.18-178.7	159	<0.0001

Table 3: Triglyceride values of subclinical hypothyroid children in mg/dl.

		Mean	95% CI	Population mean[6]	p value
Male	5-9 years	69.91	61.7-78.12	48	0.0001
	10-14 years	85.9	68.89-102.9	58	0.005
Female	5-9 years	80.88	72.7-89.07	57	<0.0001
	10-14 years	73.77	66.85-80.7	68	0.096

Family history of thyroid disease was elicited in 11.3% (n = 7) of children, and family history of autoimmune disease was elicited in 4.84% (n = 3) of children. It was found that all children who had positive family history of thyroid disease and autoimmune disease were females. 11 (17.74%) children had goiter of which 9 (81.82%) were female and 2 (18.2%) were male. 7 (11.29%) children had features of thyroiditis in ultra-sonogram neck and all these children had elevated autoimmune antibodies.

Mean Z-score for height of the study group (-0.016) is lower than population mean which is not statistically significant (p = 0.832). Mean Z-score for weight (0.154) and mean BMI (0.216) of the study population is significantly higher with p values of 0.023 and 0.004 respectively. It implies that significant difference in height is not observed in SCH children. However these children had higher weight and BMI.

Heart rate of the study population is well within the reference range for all age groups. Mean Z-score for SBP (0.526) and mean Z-score for DBP (0.96) of the study population is significantly high with p<0.0001. This high value of Z-scores implies that these children are at higher risk of developing hypertension in future.

Among children with positive anti-thyroid antibodies Anti-TPO (n = 12) and anti-TG (n = 11), it was found that children positive titers anti-thyroid antibodies had high mean TSH when compared to children with normal titers of Anti-TPO and Anti-TG which was statistically significant (p = 0.036). It implies that SCH children due to autoimmune etiology tend to have high TSH when compared to other non-autoimmune etiology.

No significant discrepancy was observed between chronological age and bone age in 95.16% (n = 59) children. Significant delay of bone maturation (>2 years) was seen in 3 children which constituted <5% of study population.

While assessing left ventricular internal dimensions, three LVIDs values and one LVIDd value were found beyond 2SD in their respective population distributions. Mean Z-score for both LVIDs (0.2) and LVIDd (0.21) were positive, but statistically not significant (p value 0.093 and 0.067 respectively). It denotes that LV diameters were not significantly altered. Mean Z score for LVPWd (0.56) and IVS thickness (0.39) were above the population mean and statistically significant (p <0.0001 and p = 0.011 respectively). Left ventricular systolic function parameters like ejection fraction and Fractional shortening were found to be within reference range implying normal Left Ventricular systolic function in Subclinical hypothyroid children.

Mean HDL value is significantly lower in all children with p value of <0.0001. Mean total cholesterol is significantly high in all children. Though mean Triglycerides of 10-14 year old female children was high it was not statistically significant (p = 0.096), but remaining subjects had significantly high levels of Triglycerides. This implies that Subclinical hypothyroidism is associated with adverse pro-atherogenic lipid abnormalities.

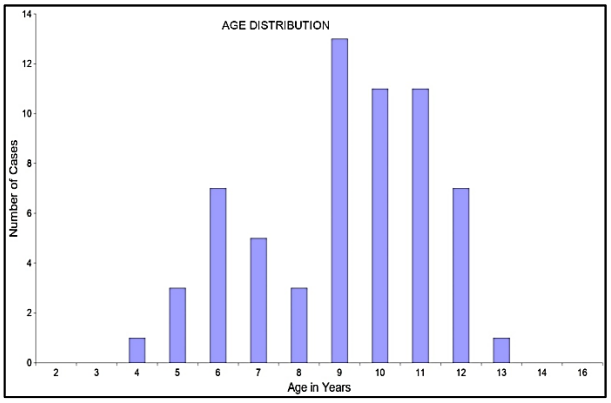

Figure 1: Age distribution.

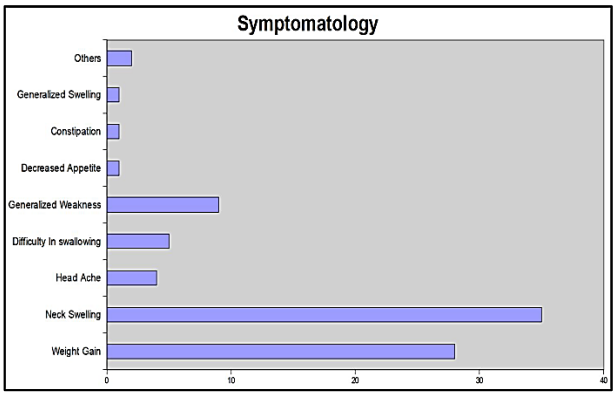

Figure 2: Symptomatic presentation of subclinical hypothyroid children.

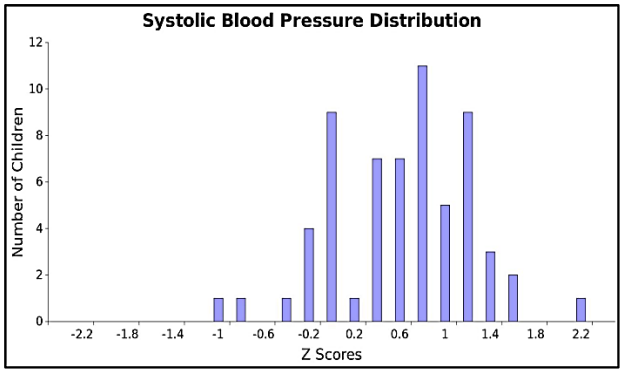

Figure 3: Systolic blood pressure distribution.

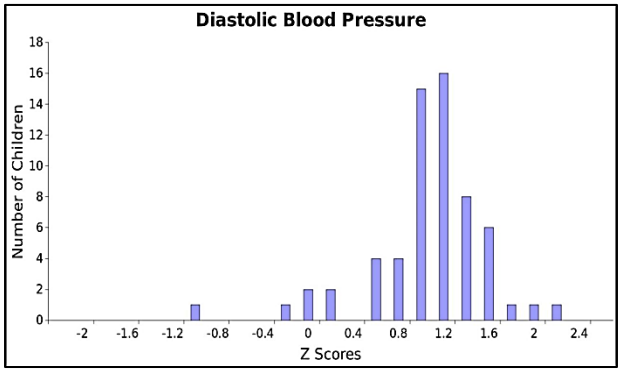

Figure 4: Diastolic blood pressure distribution.

DISCUSSION

The study sample is representative of Subclinical Hypothyroidism children attending endocrinology OPD in a tertiary care center in south India. In this study mean age of presentation was 8.42 years. Female children were largely affected (female: male ratio of 1.48:1). Major symptoms the children had were weight gain, neck swelling, and generalized weakness which are consistent with symptom description by David S Cooper4.

11.29% of children had family history of thyroid illness, 4.8% of children had family history of autoimmune disease. Goiter was noted in 17.74% of cases, majority of them being females (90.9%). Among the children with goiter, 81.8% had positive Anti-thyroid antibody implying goitrous autoimmune thyroid disease. It was found that only one male child had goitrous autoimmune thyroid disease. In our study 19.35% of children had positive Anti-TPO antibodies, 17.74% had positive Anti-TG antibodies. These Children had significantly higher mean level of TSH when compared to the children with normal titers. And these children must be followed up regularly with TSH monitoring as they have higher chance of future development of hypothyroidism. Radetti et al in their study had found that presence of goiter and elevated anti TG-Abs at presentation along with increase in anti TPO-Abs predicts future development of hypothyroidism.7 Similarly Zois et al also showed that elevated anti TPO-Abs can be considered as a predictive factor for impending thyroid failure.[8] Gopalakrishnan et al in their study had concluded that subjects with goitrous autoimmune thyroiditis needs periodic monitoring of thyroid function as development of thyroid dysfunction is insidious.[9]

All children had normal heart rate according to their age. Mean Z-scores of both SBP and DBP is high in the study group, implying these children are at increased risk of hypertension. Similar finding was obtained in a Chinese study by Chen et al where increase in BP was associated with high TSH without overt thyroid disease.[10] Ittermann et al also found positive relationship between serum TSH with SBP and DBP.[11]

95.16% of study subjects had no significant discrepancy in chronological age and bone age. It shows that majority of SCH children do not have significant delay in bone maturation. Similar observation was made by Di Mase et al where they had arrived at a conclusion that neither the duration of SCH nor TSH levels had significant impact on bone health.[12]

Mean left ventricular wall thickness (IVS and LVPW) of study patients as obtained by M-mode measurements were significantly higher when compared to population mean. Statistically significant increase in Left Ventricular wall thickness in our study group was obtained as a one point measurement. Serial monitoring of these children will be needed to ascertain the clinical and hemodynamic significance of this finding. Left ventricular dimensions during both phases of cardiac cycle were within normal limits. Left ventricular systolic functions which were measured by afterload dependent parameters like Ejection fraction and Fractional shortening were also within normal range.

Mean values of cholesterol and triglycerides were significantly elevated and mean value of HDL was significantly low in our study group. Implying these children had an abnormal lipid profile. Similar observation was made by Cerbone et al where SCH children had significantly high atherogenic index and triglyceride/HDL ratio indicating pro-atherogenic lipid abnormalities.[5]

This cross sectional study was done on a small sample of children (n = 62). Children with clinical symptoms were conveniently included in the study. Ideally sample should have been selected from population after screening. As the prospective follow up is missing natural course of the disease could not be studied. Diastolic function was not measured in study population. A large study with adequate controls would be needed to assess the impact of sub clinical hypothyroidism on growth, blood pressure, cardiac function, lipid profile and homocysteine level. A large randomized control study is needed to assess the beneficial effect of levothyroxine treatment on various morbidities associated with subclinical hypothyroidism.

CONCLUSION

Subclinical hypothyroidism is more common in female children. Principal complaints in these children are neck swelling and weight gain. Subclinical hypothyroidism children do not have significant alteration in bone maturation. Goitrous autoimmune disease presenting as subclinical hypothyroidism is more common in female children. Mean TSH value of patients with positive Anti-thyroid antibody is higher when compared to patients with negative titers. Subclinical hypothyroid children have normal cardiac functional indices despite showing ventricular thickness abnormalities. Both Systolic and diastolic blood pressures are high in these children. Subclinical hypothyroid children have adverse pro atherogenic lipid profile.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, et al. Subclinical thyroid disease. Scientific review and guidelines for diagnosis and management. JAMA. 2004;291(2);228-38.
2. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocrine Reviews. 2008;29(1):76-131.
3. Wu T, Flowers JW, Tudiver F, Wilson JL, Punyasavatsut N. Subclinical thyroid disorders and cognitive performance among adolescents in the United States. BMC Pediatrics. 2006;16(12):2006.
4. Cooper DS. Subclinical hypothyroidism. Thyroid Res Pract. 2013;10:9-11.
5. Cerbone M, Capalbo D, Wasniewska M, Mattace Raso G, Alfano S, Meli R, et al. Cardiovascular risk factors in children with long-standing untreated idiopathic subclinical hypothyroidism. Clin Endocrinol Metab. 2014;99(8):2697-703.
6. Daniels SR, Greer FR. Lipid screening and cardiovascular health in childhood. Pediatrics. 2008;122(1):198-208.
7. Radetti G, Gottardi E, Bona G, Corrias A, Salardi S, Loche S. Natural history of euthyroid Hashimoto's thyroiditis in children. J Pediatr. 2006;149:827-32.
8. Zois C, Stavrou I, Svarna E, Seferiadis K, Tsatsoulis A. Natural course of autoimmune thyroiditis after elimination of iodine deficiency in northwestern Greece. Thyroid. 2016;16:289-93.
9. Gopalakrishnan S, Chugh PK, Chhillar M, Ambardar VK, Sahoo M, Sankar R. Goitrous autoimmune thyroiditis in a pediatric population: a longitudinal study. Pediatrics. 2008;122:670-74.
10. Chen H, Xi Q, Zhang H, Song B, Liu X, Mao X, et al. Investigation of thyroid function and blood pressure in school aged subjects without overt thyroid disease. Endocrine. 2012;41(1):122-9.
11. Ittermann T, Thamm M, Wallaschofski H, Rettig R, Volzke H. Serum thyroid stimulating hormone levels is associated with blood pressure in children and adolescents. J Clin Endocrinol Metabol. 2012;97(3):828-34.
12. Di Mase R, Cerbone M, Improda N, Esposito A, Capalbo D, Mainolfi C, et al. Bone health in children with long-term idiopathic subclinical hypothyroidism. Ital J Pediatr. 2012;38(1):56.

Cite this article as: Poornachand V, Kumarasamy K, Seenivasan V, Karamath SP. Study of clinical and biochemical profile of subclinical hypothyroidism in children aged 2-12 years. Int J Contemp Pediatr 2017;4:43-7.