

Detection of autoimmune thyroiditis in children with goitre attending the pediatric department of a tertiary care hospital in Chennai.

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Abstract

Introduction: Goitre is a common problem among children. The incidence of autoimmune thyroiditis is on the rise. This study is intended to evaluate all goitrous children with Thyroid profile and to look for autoimmunity. **AIM** To detect autoimmune thyroiditis in children less than 15 years of age with goitre.

Objectives: To screen for thyroid dysfunction. To detect autoimmunity by antithyroid antibodies and FNAC. **Materials and methods** 107 Children with goitre attending the Paediatric Department of ESIC Medical College and PGIMSRS were included. Relevant history and physical examination findings were documented in a preset proforma. Thyroid function tests, anti TPO antibody and FNAC of the thyroid gland were done. The results were analysed statistically.

Observations and Results: Out of 107 children, 10 had evidence of hypothyroidism. Anti TPO antibodies were detected in 11, while 8 had FNAC evidence of autoimmune thyroiditis. While all the FNAC positive cases had hypothyroidism only 8/11 antibody positive cases had evidence of thyroid dysfunction. Three cases with neither evidence of hypothyroidism nor FNAC positivity had antibody positivity. On comparing antibody positivity with FNAC in the detection of autoimmunity, we inferred that antibody positivity can be used as a diagnostic tool.

Conclusion: Prevalence of autoimmunity was 7.5% by FNAC and 10.3% by anti TPO antibodies. Hypothyroidism was detected in 9.34% of goitres. Few cases of AIT may not have hypothyroidism, may require serial TFT. Anti TPO antibody positivity is an effective, less invasive indicator for detecting AIT in children, compared to FNAC which is the gold standard.

Keywords: Goitre, Hypothyroidism, Hashimoto's Thyroiditis, Thyroid function test, Free Triiodothyroxine, Free thyroxine, Thyroid peroxidase antibody, Fine needle aspiration cytology.

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Introduction

Thyroid hormone in optimal quantities is essential for neurodevelopment and growth in children [1]. The development of thyroid dysfunction is insidious and may not be accompanied by typical symptoms or clinical signs. Diseases result from both under- and over activity of thyroid gland. Chronic autoimmune thyroiditis, a major cause of goitre in iodine repleted areas which results in thyroid dysfunction that is rather difficult to identify clinically in children. [2]

In the past, goitre in adolescent children were brushed aside as physiological puberty goitre and were not investigated further. But with the increased incidence of autoimmunity following iodized salt consumption all goitres have to be evaluated to rule out thyroid dysfunction and autoimmunity [2]. AIT may not always present with thyroid dysfunction and hence we are likely to miss this entity if autoimmune evaluation is not included in the panel of tests for goitre. Since AIT can have a variety of thyroid dysfunction at different points in time scale, only repeated evaluation with TFTs can pick up hyper or hypothyroidism to enable us to treat them appropriately. In a child with goitre if hypothyroidism is not documented we generally do not repeat the evaluation frequently. But if the antibodies are positive it becomes mandatory to do TFTs

repeatedly. This study is intended to evaluate all goitrous children with thyroid profile and to look for autoimmunity.

Aim of the study

To detect autoimmune thyroiditis in children under 15 years of age presenting with goitre.

Objectives

1. To screen all children with goitre for thyroid dysfunction.
2. To detect autoimmunity in these children by anti-thyroid antibodies and FNAC.

Materials and Methods

This observational study was conducted in the Paediatric Department of Paediatrics, ESIC medical college KK Nagar Chennai, from October 2014 to August 2016. The study population comprised of 107 children less than 15 years with goitre. Informed consent was obtained for inclusion in the study.

Detailed history and clinical examination was done and documented on a predesigned proforma. Goitres were graded as per WHO guidelines. TSH, Free T3, Free T4, TPO

antibodies, Lipid profile, CBC, ESR, and FNAC were done in all the cases.

The goitrous children were screened for autoimmunity after a thorough clinical examination with Thyroid function tests, thyroid peroxidase auto antibodies, and Fine needle aspiration cytology.

The efficacy of autoimmune antibodies in detecting autoimmunity was compared with the Gold standard, namely FNAC of thyroid. Data entry form was filled, data was analysed and statistical significance of the result was determined.

Observation and Results

Out of the 107 children studied, 43% (n=46) were between 10 to 15 years age group, 56.1% (n=60) of them aged between 5 to 10 years and one child (0.9%) aged less than 5 years.

The mean age was 10.13 ± 1.84 years. We observed that 68.2% (n=73) of the study population were girls and 31.8% (n=34) were boys. WHO grading of goitre was made. Grade 1 (A&B) goitre was found in 59 (55.1%), grade 2 in 45 (42.1%) and grade 3 in 3 cases (2.8%). The consistency of goitre was firm in 18 (16.8%) children.

Thyroid profile of the study population shows that 7.5% (n=8) had overt hypothyroidism, 1.9% (n=2) had sub clinical hypothyroidism and rest 90.6% (n=97) were euthyroid.

There were 11 (10.3%) cases with TPO antibody positivity and 8 cases (7.5%) had FNAC evidence of Autoimmunity. Among the 8 FNAC proved cases of AIT, 87.5% were girls, 12.5% were boys and 37.5% (n=3) had family history of hypothyroidism.

In this study, Grade of goitre was highly significantly associated with positive FNAC (P=0.0001). Out of 8 cases of FNAC positivity, 2 cases had grade 3 goitre and 6 cases had grade 2 goitre.

In our study, all FNAC positive cases had firm consistency highly significant statistically (p value=0.0001). Among 11 TPO Positive cases, 7 (63.6%) had firm goitre.

Discussion

Incidence of autoimmune thyroiditis has been on the increase in the post iodisation era since iodised salt is known to unmask the thyroid antigens and induce autoantibody production. Studies have quoted the prevalence of AIT in children ranging from 10.2% to 28.6% [3,2]. Kabelitz et al., in their Berlin study also concluded autoimmune thyroiditis as the major cause of thyroid disorder in children and adolescents in iodine sufficient areas [4].

We attempted to detect autoimmunity in children presenting with goitre and screened them for thyroid dysfunction and autoimmunity. Anti-thyroid peroxidase antibody positivity and Fine needle aspiration cytology suggestive of lymphocytic thyroiditis were considered as evidence of autoimmunity.

An attempt was also made to compare the relative efficacy of TPO to detect autoimmunity as compared to the gold standard namely FNAC.

We also looked into the possibility of using a few clinical and laboratory data as a combination of parameters which could be used to predict autoimmunity so that resources are not wasted in future on indiscriminate screening of all goitrous children for AIT.

We recruited a total of 107 children with goitre. Majority of them belonged to 5-10 yrs. (56.1%) and 10 to 15 years (43%) age group. As observed in other studies, our study too had female (68%) preponderance.

We also found the presence of autoimmunity was much higher in girls. Our study reveals that 87.5% of FNAC proven cases and 81.8% of anti TPO antibody positive cases were girls.

Similar observation of greater prevalence of goitre in girls compared to boys was made by Samid Das et al., Siriwerera et al. and Singh et al.

Thyroid dysfunction was also observed more in girl children than boys with Female:Male ratio of 9:1 in our study. This was similar to studies by Siriweera et al. where there was a female preponderance with Female:Male ratio of 10.3:1 [5-7].

Autoimmune thyroid diseases have strong genetic association and in our study too we found 37.5% of the children with AIT having family history of thyroid dysfunction especially in the mother (Table 1).

Since this association is statistically significant, we recommend that adolescent girls of mothers with thyroid dysfunction should be screened for autoimmunity.

		FNAC		Total	
		Positive	Negative		
Family history	Positive	Count	3	9	12
		% within family history	25%	75%	100%
		%within FNAC	37.50%	9.20%	11.30%
	Negative	Count	5	89	94
		% within family history	5.30%	94.70%	100%
		% within FNAC	62.50%	90.80%	88.70%
Total	Count	8	98	106	
	%within family history	7.50%	92.50%	100%	
	% within FNAC	100%	100%	100%	

Table 1. Association of positive family history with FNAC positivity. Pearson–Chi square test, P=0.015 significant out of

12 cases those who had positive family history, 3 cases (25%) had FNAC positivity. Among the 8 FNA positive cases 37.5% (n=3) had family history of hypothyroidism.

In our study we found a greater correlation of autoimmunity with larger size of goitres. All the 8 (100%) FNAC proved AIT and 8/11 cases (72.7%) of antibody positivity belonged to higher grades (II and III) of goitre (Table 2).

Hence we would infer that in resource poor settings the need for screening of autoimmunity can be limited only to girl children presenting with grade II and grade III goitre.

GRADE	FNAC		Total
	Positive (n=8)	Negative	
1a	0	4	4
% within Grade	0.00%	100.00%	100%
% within FNAC	0.00%	4.10%	3.80%
1b	0	54	54
% within Grade	0.00%	100.00%	100.00%
% within FNAC	0.00%	55.10%	50.90%
2	6	39	45
% within Grade	13.30%	86.70%	100.00%
% within FNAC	75.00%	39.80%	43%
3	2	1	3
% within Grade	66.70%	33.30%	100.00%
% within FNAC	25.00%	1.00%	2.80%
Total	8	98	106
% within Grade	7.50%	92.50%	100.00%
% within FNAC	100.00%	100.00%	100.00%
Pearson Chi square test value	21.921,3		
P value	0.0001****		

Table 2. Association of WHO Grades of Goitre with FNAC (n=107). Out of 8 cases of FNAC positivity, 2 cases had grade 3 goitre and 6 cases had grade 2 goitre. In this study grade was highly significant associated with FNAC at P=0.0001. 1a: Goitre detected on palpation; 1b: Goitre palpable and visible and neck extended.

From our study we found that besides the larger size firmer consistency of goitre could also be used as an indicator of autoimmunity.

Out of 18 cases of goitre with firm consistency, 8 of them (44.4%) had FNAC evidence of autoimmunity, 7(38.9%) had TPO positivity and 9 (50%) had evidence of hypothyroidism.

All the FNAC positive cases had firm goitres which is found to have statistical significance (Table 3).

Thus we conclude that in contrast to soft goitre, firm goitre would definitely require further investigations for autoimmunity.

		FNAC		Total	
		1	2		
Consistency	Firm	Count	8	10	18
		% within consistency	44%	56%	100%
		% within FNAC	100.00%	10.20%	17.00%
	Soft	Count	0	88	88
		% within consistency	0.00%	100.00%	100%
		% within FNAC	0.00%	89.80%	83.00%
Count		8	98	106	
	% within consistency	7.50%	92.50%	100%	
	% within FNAC	100%	100%	100%	
Pearson chi square test			36.174,1		
P value			0.0001****		

Table 3. Association of consistency with FNAC positivity. In our study, all FNAC positive cases had firm consistency highly significant statistically (P=0.0001).

In the spectrum of autoimmunity, thyroid dysfunction can range from hypothyroidism to euthyroidism or even hyperthyroidism. In our study 10 out of 107 children (9.3%) had hypothyroidism (Table 4). Interestingly majority of them (8/10) also had clinical evidence of hypothyroidism (80%) in the form of lethargy, poor school performance and constipation. This is in contrast to Gopalakrishnan et al. study where, in a series of 112 children with AIT, majority were euthyroid and only 7.2% had hypothyroidism [8].

		No of patients	%	Mean ± SD
		(N=107)		
TSH	<5.5	97	90.7	5.00 ± 8.15
	>5.5	1000.00%	930%	
T4	<0.9	2100.00%	1960.00%	1.40 ± 1.02
	>0.9	86	80.4	

Table 4. Thyroid profile of the study population (n=107). Based on the thyroid profile, 10 children (9.3%) were found to be biochemically hypothyroid, 97 children were Euthyroid.

Out of these 10 cases in our study, 7 cases had definite AIT as evidenced by positivity of both FNAC and anti TPO antibody (Figures 1 and 2), while one case had TPO positivity alone as an indicator of autoimmunity. However one case of hypothyroidism had neither TPO nor FNAC positivity in which other aetiologies for thyroid dysfunction rather than AIT was considered.

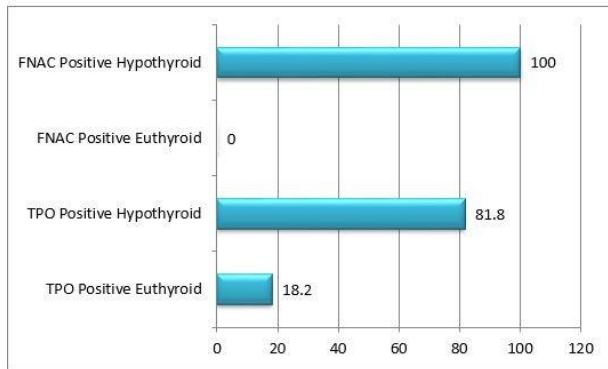


Figure 1. Association of Hypothyroidism with FNAC & TPO (n=10).

On analysing the thyroid profile with evidence of autoimmunity, 100% of FNAC positive cases and 81.8% of anti-TPO antibody positive cases were hypothyroid.

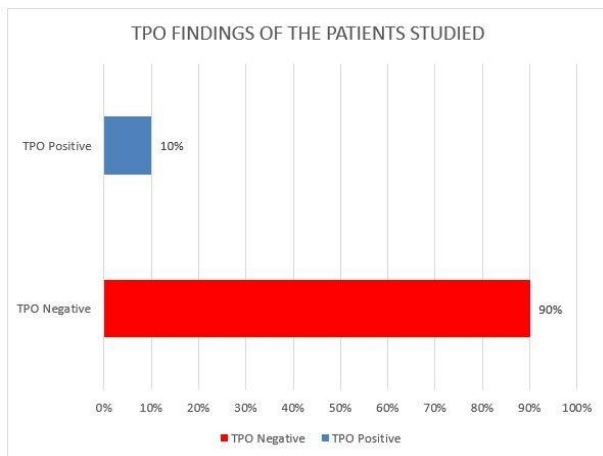


Figure 2. TPO findings of the patients studied. Among 107 children with goitre, 11 children (10.3%) had TPO positivity and 96 children (89.7%) were TPO Negative.

Anti TPO antibody is a sensitive indicator of autoimmunity, being much less invasive than FNAC. In our study 11/107 cases had anti TPO antibody positivity (10.3%) while only 8 (7.5%) cases had definite cytological features of autoimmune thyroiditis. Among these 11 cases of antibody positivity 72.7% children had hypothyroidism and 27.3% had euthyroidism (Figure 3) which was similar to Shinto et al. study¹ who in their series also found majority of children of AIT to have hypothyroidism. Our observations were in contrast to Filippo De Luca et al. study [9] where euthyroidism was the predominant finding in AIT.

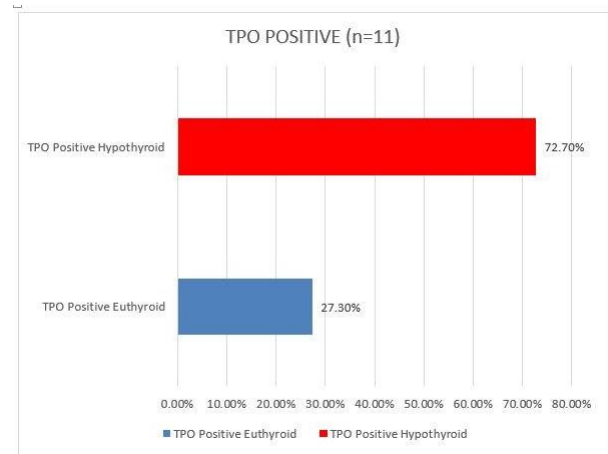


Figure 3. Thyroid dysfunction in anti-TPO antibody positive cases. Among the 11 TPO positive cases, 8 children of them had hypothyroidism (72.7%) while 3 children (27.3%) had no thyroid dysfunction.

In our series, among the 4 cases of antibody positivity with no cytological evidence suggestive of AIT, only one had hypothyroidism and the other 3 were euthyroid. We plan to follow up these 3 children both clinically and by repeated TFT estimation as studies have stated that nearly 20% of children with autoimmune thyroiditis develop hypothyroidism ultimately [10]. This fact is also supported by Bijoro et al. study [11], where the authors report that TPO antibodies appear in the circulation long before thyroid dysfunction or histological changes appear. Thus this study has helped us to detect these 3 cases of AIT very early even before the derangement of thyroid function.

From our study we found the prevalence of autoimmune thyroiditis among the goitrous children to be 7.5% by FNAC (Figure 4) and 10.3% by anti TPO antibodies (Figure 2). Though FNAC is considered the gold standard for diagnosis of AIT, it is an invasive procedure, difficult in non-cooperative children and may not be available in most centres. In our study also among the FNAC positive cases there was 100% biochemical hypothyroidism (Figure 5). Hence we made an attempt to compare the efficacy of Anti TPO antibody with FNAC in the diagnosis of AIT (Table 5).

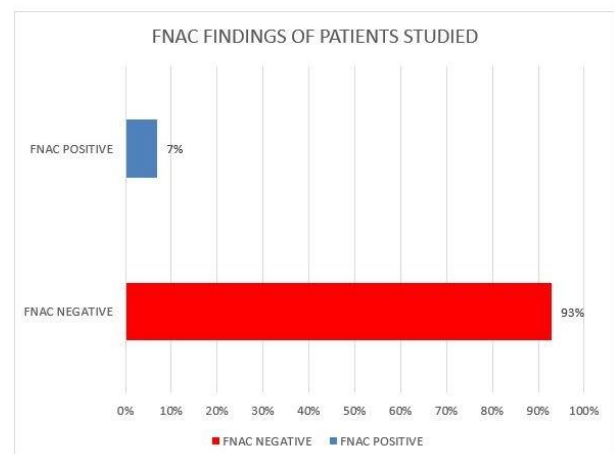


Figure 4. FNAC Findings of the patients studied. Among 107 children with goitre, 8 children (7.5%) had autoimmune thyroiditis by FNAC and 99 children (93%) were FNAC Negative.

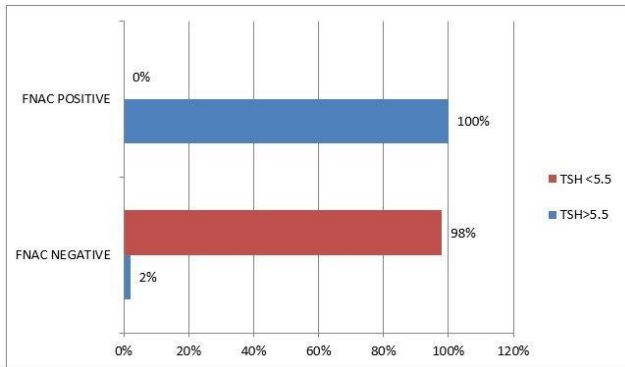


Figure 5. FNAC findings in hypothyroid children with goitre: P<0.001**, Significant, Fisher Exact test. Among the FNAC positive cases that showed evidence of lymphocytic thyroiditis, there was 100% biochemical hypothyroidism.

TPO	FNAC		
	Positive	Negative	Total
Positive	7	4	11
Negative	1	95	96
Total	8	99	107

Table 5. Comparing anti-TPO antibody positivity with FNAC positivity. Among the 8 FNAC positive cases, 7 of them were also anti-TPO antibody positive.

Statistical analysis showed that anti- TPO antibody had a high specificity (95.96%) and also had a high negative predictive (98.96%) value (Table 6). Thus the absence of this antibody can reasonably rule out autoimmunity. Its diagnostic accuracy is also quite high (95.33%), thus making this less invasive test a useful diagnostic tool for AIT in children. This fact is also supported by Tina Thomas’s [12] retrospective analysis of 144 cases of FNAC proved AIT in which she found 92.3% of the cases had TPO positivity.

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	87.50%	(52.91, 97.76)
Specificity	95.96%	(90.07, 98.42)
Positive Predictive Value	63.64%	(35.38, 84.83)
Negative Predictive Value	98.96%	(94.33, 99.82)
Diagnostic Accuracy	95.33%	(89.52, 97.99)

Table 6. Evaluation of TPO as a screening tool for AIT. Anti TPO antibodies have a high diagnostic accuracy.

In a resource poor setting, it is unreasonable to perform the entire battery of tests in all goitrous children to detect autoimmunity. From our data we made an attempt to find out

whether a combination of parameters could effectively predict autoimmunity. On analysis we found that larger size of goitre with firmness in consistency and presence of thyroid dysfunction can together be taken as a combination to predict autoimmunity (Tables 7 and 8).

Combination of goitre of grade ≥ 2, Firmness&Hypothyroidism	TPO		
	Positive	Negative	Total
Positive	7	2	9
Negative	4	94	98
Total	11	96	107

In children with all three parameters of higher grade of goitre, firm consistency and hypothyroidism 7 out of 9 had TPO positivity.

Table 7. Combination of size, consistency and thyroid dysfunction as a tool in predicting TPO Positivity.

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	63.64%	(35.38 , 84.83)
Specificity	97.92%	(92.72, 99.43)
Positive Predictive Value	77.78%	(45.26, 93.68)
Negative Predictive Value	95.92%	(89.97, 98.4)
Diagnostic Accuracy	94.39%	(88.3, 97.4)

Table 8. Evaluation of the combination as a screening tool to detect autoimmunity. As a screening tool the diagnostic accuracy of the combination is 94.39%.

On comparing these three parameters with anti TPO antibody positivity, we found that though the sensitivity was not very high (63.64%) the negative predictive value was rather high (95.92%) with the diagnostic accuracy of 94.39%.

In contrast the same combination of parameters when compared with FNAC positivity, both sensitivity and negative predictive value were 100% with the diagnostic accuracy of 99.07% (Tables 9 and 10).

Thus we would like to infer that all cases of firm goitre with WHO grade 2 or higher with accompanying thyroid dysfunction should definitely be screened for autoimmunity.

Grade >2, Firmness & Hypothyroidism	FNAC		
	Positive	Negative	Total
Positive	8	1	9
Negative	0	98	98
Total	8	99	107

Table 9. Combination of size, consistency and thyroid dysfunction as a tool in predicting FNAC Positivity.

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	100%	(67.56, 100)
Specificity	98.99%	(94.5, 99.82)
Positive Predictive Value	88.89%	(56.5, 98.01)
Negative Predictive Value	100%	(96.23, 100)
Diagnostic Accuracy	99.07%	(94.89, 99.83)

Table 10. Evaluation of the combination as a screening tool to detect AIT.

Conclusion

1. Prevalence of autoimmunity among goitrous children was found to be 7.5% by FNAC and 10.3% by anti TPO antibodies.
2. Hypothyroidism was detected in 9.34% of goitres.
3. Though majority of cases of AIT have thyroid dysfunction, in a few cases, antibody positivity may be the only evidence of AIT. Such cases would require regular follow up with serial TFT estimation to detect and treat hypothyroidism early.
4. In a resource poor set up, the screening for autoimmunity could be limited to large goitres of grade 2 or more, which are firm in consistency along with accompanying hypothyroidism
5. Anti TPO antibody positivity is an effective, less invasive and more feasible indicator for detecting AIT in children as compared to FNAC which is considered the gold standard.

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