THYROIDITIS IN A JORDANIAN COHORT WITH GOITRE: RESULTS OF FINE NEEDLE THYROID ASPIRATE

Fares Haddad MD*, Ahmad Omari MD*, Wijdan Ajour BSc MT**, William Haddadin MD**, Anwar Masri MD*, Omar Malkawi MD*, Haytham El-Khushman MD^, Alia Issat BSc DSN^^, Abdelkarim Khawaldeh MD*

ABSTRACT

Objective: To determine the prevalence of cytologically proven thyroiditis among patients with goiter referred to Endocrine clinic at King Hussein Medical Center using fine needle thyroid aspirate and to assess thyroid status among those patients.

Methods: Case study of patients who underwent fine needle aspirate thyroid biopsy for different types of goiter from January 1995 to June 2004 was conducted. Fine needle aspirate thyroid biopsy was taken using a 20cc syringe on a pistol gun apparatus under aseptic technique. All reports including the diagnoses of thyroiditis, autoimmune thyroiditis (Hashimoto's thyroiditis), lymphocytic thyroiditis, and focal thyroiditis were included. Thyroid function tests and thyroid antibodies were also reported in some patients.

Results: A total of 1934 patients underwent fine needle aspirate thyroid biopsy during the study period, 279 cases were excluded because of inadequacy of the sample, missing reports and repeated sample in some patients with the same diagnosis. Those actually included in the study were 1655 (females 1475, males 180, male: female ratio was 8:1). Thyroiditis was reported in 323 patients (females 93.5%), giving a total prevalence of 19.5%; 11.7% for males and 20.5% for females. Hashimoto', lymphocytic and unclassified thyroiditis were found in 66.25%, 22.6% and 8.6% of the patients respectively.

Conclusion: Hashimoto' and lymphocytic thyroiditis are the commonest causes of thyroiditis in Jordanian patients with goiter, females being affected more commonly than males. Fine needle aspirate thyroid biopsy of thyroid gland is an important tool of investigation for thyroid disorders in general and thyroiditis in patients with goiter. Long term follow up of patients with thyroiditis should be adopted.

Key words: Prevalence, Thyroiditis, Fine needle aspirate, Jordan

JRMS August 2007; 14(2): 5-9

Introduction

Thyroiditis is a term that encompasses many relatively common disorders. It includes Hashimoto's thyroiditis (HT), painless postpartum thyroiditis, sporadic thyroiditis and others.[1]

The prevalence of thyroiditis varies depending on the region, iodine status of the area, ethnicity, sex and correlates with increasing age.[2,3] The prevalence of thyroiditis tested by thyroid auto-antibodies in USA is 14.3% in whites, 10.9% in Mexican Americans and 5.3% in blacks.[4] The prevalence of thyroiditis ranges from 3.4% in iodine deficient areas to 18.8% in some iodine replete areas.[5-10]

The prevalence is higher in association with other autoimmune and non immune disorders; such as type 2 diabetes,[11,12] type 1 diabetes,[13,14] in association with anti-glomerular basement membrane antibodies,[15] multiple sclerosis[16] and polycystic ovary syndrome.[17]

From the Departments of:
* Internal Medicine, Endocrine Division, King Hussein Medical Center (KHMC), Amman-Jordan
**Histopathology, Cytology Division, Princes Iman Laboratory and Research Center (KHMC),
^ Internal Medicine, Respiratory Medicine Division (KHMC)
^^Nursing (KHMC)
Correspondence should be addressed to Dr. F. Haddad, P. O. Box 967 Amman 11118 Jordan, E-mail: Haddf@hotmail.com
Manuscript received October 2, 2005. Accepted December 15, 2005.

Hashimoto thyroiditis constitutes 40-50% of patients with hypothyroidism.[1,18,19]

Clinically, the prevalence of goiter in Jordan in school children was 37.5% in the 1993 which has dropped to 33.5% in 2000 after implementing iodinization program.[20,21] Using ultrasonography in adults the prevalence of goiter is 32.1%.[22]

In this study we aimed to determine firstly the frequency of cytologically proven different types of thyroiditis using fine needle aspirate of the thyroid among patients with goiter and secondly to assess the rate of thyroid dysfunction and auto-antibodies status among those patients with thyroiditis.

Methods

A retrospective study of fine needle thyroid aspirates done on patients with various types of goiter who were referred to the Endocrine clinic and the Cytopathology section of Histopathology Department at KHMC between January 1995 and end of June 2004 was conducted.

The aspirates were done using a 20cc syringe with 23 gauge needle mounted on a pistol gun grip apparatus under aseptic technique. Multiple aspirates from the lesion were done after obtaining verbal consent. The aspirates were spread on 3-4 slides and were air dried and fixed in 96% alcohol for Papanicolou and Diff Quick Stain. The slides were examined under light microscope by an experienced cyto-pathologist.

All reports from thyroid registry and computer data base with the diagnosis of thyroiditis, autoimmune (Hashimoto's), lymphocytic, and focal thyroiditis were included in this study. Patients with clinical Grave's disease were excluded.

The cytological diagnosis of Hashimoto' thyroiditis (autoimmune thyroiditis) was based on the finding of reactive lymphoid cells with multinucleated and epithelioid histocytes in addition to the presence of numerous hurthle cells, lymphocytic thyroiditis was diagnosed by the findings of polymorphic population of reactive lymphoid cells admixed with follicular cells in all passes and smears and lacking hurthle cells and background granulomatous inflammation. Focal thyroiditis was suggested when some but not all passes and smears contained reactive lymphoid cells mixed with follicular cells while the diagnosis of unclassified thyroiditis was made when some but not all the criteria mentioned above were met.

Blood tests for free thyroxin (f T4, normal range 0.7-1.9 µg/dl), free tri-iodotyronine (f T3, 3.5-5.5 mcg/dl) thyroid stimulating hormone (TSH, 0.4-4.4 miU/ml) using Immulite 2000 of DPC by immuno-cheimolumincent assay, thyroid peroxidase (TPO) and anti-thyroglobulin antibodies (ATA) were analyzed.

Statistical analysis using windows XP excel program to perform mean ± Standard Deviation (SD), for difference between two percentages and t test for differences between means was done.

Results

An initial number of 1934 aspirates were included, 279 aspirates were excluded because of inadequate sampling (n=103), missing reports (n=13) and repeated tests in same patient with same final diagnosis. This gives an inadequacy rate of 5.3% and drop rate for all causes listed of 14.4%.

A total of 1655 patients with thyroid Fine Needle Aspirate Thyroid Biopsy (FNAB) were finally included. There were 1475 females and 180 males with a mean (±SD) age of 38.8 ±14.18 years (range 12-84). No hemorrhage or infection was encountered, vaso-vegal attacks was seen in 10 patients only.

Thyroiditis

Thyroiditis was found in 323 patients, mean age 34.5±12.48 years (range 12-70years). The female:male ratio was 15:1. The prevalence of thyroiditis in females was 20.5% while in males was 11.11% (p=0.00639) this gives an overall prevalence of 19.5%. Hashimoto' thyroiditis (autoimmune thyroiditis) was found in 214 (66.25%) patients, Lymphocytic thyroiditis in 73 (22.6%), focal thyroiditis in a background of benign colloid nodule in 8 (2.5%) patients and unclassified thyroiditis in 28 (8.6%) patients. The demographic features, thyroid function test and thyroid antibody status are shown in Table I. There was no statistical significant difference in the age of different groups.

Thyroid status

The mean TSH for the thyroiditis group (n=220) was 14.5±20 miU/ml ranging from 0.01-123, mean fT4 is 1.07±0.55 (range 0.08-4.5, n=219) and for fT3 is 3.17 ±1.5 (range 0.8-11, n=75). TSH was statistically higher in patients with Hashimoto' thyroiditis and unclassified thyroiditis vs. focal or lymphocytoic thyroiditis (as shown in Table I)

There are 18 (8.2%) patients with a suppressed TSH (10% in lymphocytic thyroiditis, 16.6% in focal thyroiditis and 5.6% in Hashimoto's thyroiditis) and 88 (40%) subjects with a normal TSH. One hundred and fourteen patients (51.8%) had high TSH; 49 of them with subclinical hypothyroidism and 65 patients with overt hypothyroidism. There were 40.2% with high TSH in Hashimoto's thyroiditis, 36% in lymphocytic thyroiditis, 64.3% and 16.7% in unclassified and focal thyroiditis respectively.

Table I. The cytological diagnoses, thyroid status, gender distribution and thyroid antibodies

	Autoimmune thyroiditis (Hashimoto's thyroiditis) n=214(66.25%)	**Lymphocytic thyroiditis n=73(22.6%)**	**Focal thyroiditis n=8(2.5%)**	**Unclassified thyroiditis n=28(8.6%)**	**Total n= 323**
Mean age ± SD years	34.75±12.1	32.7±12.5	36±9.9	37±14.1	34.5±12.48
Males Females	12 202	5 67	2 6	1 17	20(6.2%) 303(93.8%)
Mean TSH±SD miU/ml	16.66±25.5*	9.3±19.7#	2.3±4**	18.6±23.6&	*N=220* 14.5±20
Mean T4±SD ng/ml	1.1±0.99	1.1±0.5	1.7±1.1	1.0±.4	*N=219* 1.07±0.55
TSH n= 0-0.4 0.41-4.4 4.5-10 >10	150 12 52 34 52	50 5 27 11 7	6 1 4 - 1	14 5 4 5	220 18(8.2%) 88(40%) 49(22.3%) 65(29.5%)
Positive thyroid antibodies	N = 23 16	N = 6 5	N= 1 0	N= 2 1	N=31 22(70.1%)

* p=0.037 vs. Lymphocytic thyroiditis, p<0.0004 vs. Focal thyroiditis. / #p =0.0368 vs. focal thyroiditis. / ** p=0.0248 vs. unclassified thyroiditis. & p=0.024 vs. focal thyroiditis

Thyroid antibodies

Thyroid antibodies were only tested in 31 patients with thyroiditis, 70.1% of patients had positive one or both thyroid antibodies; 66.7% had positive TPO, 14.3% with positive ATA and 19 % had both auto-antibodies positive. Positive TPO and/or ATA was found in 76.2% of patients with TSH $\geq$ 4.4, 19% of patients with a normal TSH and only in 4.8% of subjects with suppressed TSH<0.4.

Discussion

In this cohort of 1655 patients underwent Thyroid FNAB for different types of goiter at King Hussein Medical Center which is a tertiary referral military hospital with a catchment area of 1.5 million people. Thyroiditis occurred in 19.5% of the sample. This rate being higher in females (20.5%) compared with males (11.11%). This is a relatively high prevalence rate when compared to other studies from different countries (see Table II).

The prevalence of thyroiditis is dependent on the area studied, ethnicity, iodine intake, associated conditions, population size and methodology and ranges from 3.4-21.5%.[2-9]

The explanation of this high prevalence of thyroiditis is the high prevalence of goiter.[20-22] The prevalence of goiter was indeed reduced after six years of implementing this program.[21] The rate of thyroiditis in countries with iodine deficiency has been reported to be low. [24, 26-30]

In our cohort with goiter the predominant cytological diagnosis was Hashimoto's (autoimmune) thyroiditis followed by lymphocytic, unclassified and focal thyroiditis respectively; all of the focal thyroiditis were diagnosed on a background of benign colloid nodules.

In this study, clinical and sub clinical hyperthyroidism is found in 8.2% of the patients all of them being females. Almost fifty two percent of the cohort were having overt or sub clinical hypothyroidism out of whom 91.1% were females and 59% needed thyroxin therapy. The natural history and follow up of these patients' thyroid status was not stated as most of them were referred back to their treating physicians in the referring hospitals for follow up.

Thyroid antibodies are a useful marker of thyroiditis and their presence suggest the diagnosis. Positive anti TG antibodies and /or anti TPO antibodies was found in 70.1% of patients tested with thyroiditis which is slightly lower than other reports.[2-9,24,27,28,31-34] This is explained by the small number tested and the trend toward cytotological diagnosis by FNA rather than performing these tests. The highest rate of positive antibodies were found in patients with High TSH > 4.4 mIU/ml than those with lower TSH readings.

Radaideh *et al*.[12] in a group of type II diabetes patients in Jordan has reported a thyroiditis rate of 8.3% vs. 10.3% in a control group tested for anti TPO antibodies. When both TPO and TG were positive the prevalence was 2.5% in diabetics vs. 6% in controls. Another study by the same author[14] in type I diabetes showed a 9.2% thyroiditis rate in diabetics vs. 6.3% in controls. The higher rate of thyroiditis compared with these results is due to the selection of patients with goiter for FNA in this study.

The limitation of this study lies in the absence of a control cohort of subjects without goiter and the small number of patients who had thyroid antibodies tested.

We conclude that thyroiditis is quite common disorder in Jordanian patients with goiter, females being affected

Table II. Prevalence of thyroiditis in different studies using thyroid antibodies or FNAB

	Year	Number of cases	Thyroid Ab +ve		FNAB proved
			Control	Study	
Current Study	2004	1655		-	19.52%
Abu Esbeih T *South Jordan*[18]	2003	46		-	6.85%
Okamura K *et al*. Hisayama-Japan[31]	1987	1251		22.7%	
Niederwieser G *Multiple Sclerosis /Austria*[16]	2003	353	11.1%	18.1%	-
Slowinska-Klencka d *et al. Poland*[8]	2002	3572			5.7%
Hanasat *et al.* / *Bangladesh*[28]	2000	397		AMcA=26.7% ATA =34%	-
Al-Hureibi K/*Yamen*[23]	2003	234		-	2.9%
Radaideh AR / *T1DM/ Jordan*[13]	2003	79 127	6.3%	9.2%	-
Radaideh AR/ *T2DM/ Jordan*[14]	2004	908/ 282	10.3% 6%	TPO=8.3% TPO+ATA=2.5%	-
Kabelitz M/ *Berlin*[5]	2003	660		3.4%	
Pedersen IB /*Denemark*[6]	2003	4649		18.8%	-
Matejkova-Behanova M T2DM/*Prague Czech Republic*[11]	2003	118		19.0%	-
Roti E *et al. /Italy*[9]	1992	342		Men=2.3% Women=10.2%	-
Tunbridge WMG *Whickham survey /UK*[27]	1977	2779		Females= 10-13% Males= 3%	
Mariotti S[3]	1992			Females >70 yr= 3%	
El Haj IA/ *Saudi Arabia*[33]	2003	303			17. 6%
Mahmood S/ *Bangladesh*[34]	2004	221		57.01%	
Mitra RB/ *Calcutta-India*[26]	2002	100			10%
Marwaha RK/ *New Delhi-India*[24]	1998	94		9.6%	13.8%
Kaerak AK/*India*[30]	2003	1312			6.3%
Mazziotti G/ Seri Lanka[8]	2001 1998	282 401		23.4% 49.9%	
Jaksic J/*Croatia*[32]	1994	5492			0.35%
Gharib MD/ USA[35]	1995	31			29%

more commonly than males. It has also showed that FNAB of thyroid gland is useful and safe tool of investigation of goiter. Long term follow up of patients with thyroiditis should be adapted.

References

1. **Pearce EN, Farwell AP, Braverman L.** Thyroiditis. *NEJM* 2003; 348(26):2646-2655.
2. **Dayan CM, Daniels GH.** Chronic Autoimmune Thyroiditis. *NEJM* 1996; 335(2):99-107.
3. **Mariotti S, Sonsoni P, Borbesino G, *et al.*** Thyroid and other organ-specific auto antibodies in healthy centenarians. *Lancet* 1992; 339(8808):1506-1508.
4. **Hollowell JG, Staehling NW, Flanders WD, *et al.*** Serum TSH, T(4) and thyroid antibodies in the United States population(1988-1994): National Health and Nutrition Examination Survey (NHANESIII). *J Clin Endocrinol Metab* 2002; 87(2): 489-499.
5. **Kabelitz M, Liesenkotter KP, Stach B, *et al.*** The prevalence of anti-thyroid peroxidase antibodies and autoimmune thyroiditis in children and adolescents in an iodine replete area. *Eur J Endocrinol* 2003; 148(3):301-307.
6. **Pedersen IB, Knudsen N, Jorgensen T, *et al.*** Thyroid peroxidase and thyroglobulin autoantibodies in a large survey of population with mild and moderate iodine deficiency. *Clin Endocrinol* (Oxf) 2003; 58(1):36-42.
7. **Hurach HR, Escalante DA, Onativia A, *et al.*** Thyroid carcinoma and thyroiditis in an endemic goiter region before and after iodine prophylaxis. *Acta Endocrinol* (Copenh) 1985; 108:55-60.
8. **Slowinska-Klencka D, Klencki M, Sporny S, Lewinski A.** Fine needle aspiration biopsy of the thyroid in an area of endemic goiter: influence of restored sufficient iodine supplementation on the clinical significance of cytological results. *Eur J Endocrinol* 2002; 46(1):19-26.
9. **Mazziotti G, Premawardhana LD, Parkes AB, *et al.*** Evaluation of thyroid autoimmunity during iodine prophylaxis, the Seri Lankan experience. *Eur J Endocrinol* 2003; 149(2):103-110.
10. **Roti E, Gardini E, Minelli R, *et al.*** Prevalence of antithyroid peroxidase antibodies in serum in the elderly: comparison with other tests for antithyroid antibodies. *Clinical Chemistry* 1992; 38(1):88-92.
11. **Matejkova-Behanova M, Zamrazil V, *et al.*** Autoimmune Thyroiditis in non obese subjects with initial diagnosis of type 2 diabetes mellitus. *Endocrinol Invest* 2002; 25(9):779-784.
12. **Radaideh AM, Nusier MK, Amari FL, *et al.*** Thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. *Saudi Medical Journal* 2004; 25(8):1046-1050.

13. **Kordonouri O, Klinghammer A, Lang EB, *et al.*** Thyroid autoimmunity in children with type 1 diabetes mellitus. A multi-center survey. Diabetes Care 2002; 25(8):1346-50.
14. **Radaideh AM, El-Khateeb MS, Batieha AM, *et al.*** Thyroid function and thyroid autoimmunity in patients with type 1 diabetes mellitus. *Saudi Medical Journal* 2003; 24(4):352-355.
15. **Ara J, Robert J, Mirapeix E, *et al.*** High prevalence of antithyroid antibodies in anti-glomerular basement membrane antibody- mediated disease. *J Nephrol* 2000; 13(1):65-67.
16. **Niederwieser G, Buchinger W, Bonelli RM, *et al.*** Prevalence of autoimmune thyroiditis and non-immune thyroid disease in multiple sclerosis. *J Neurol* 2003; 250(6):672-675.
17. **Janssen OE, Mehlmauer N, Hahn S, *et al.*** High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. *Eur J Endocrinol* 2004; 150(3):363-369.
18. **Abu-Esbeih T.** Hashimoto's thyroiditis, a retrospective study in southern Jordan. *JRMS* 2004; 11(1):67-70.
19. **Diez JJ.** Hypothyroidism in patients older than 55 years. Analysis of the etiology and assessment of the effectiveness of therapy. *J Gerontol A Biol Sci Med Sci* 2002; 57(5):M315-320.
20. **Study of Iodine Deficiency in Jordan.** Jordan Ministry of Health, in collaboration with WHO and UNICEF.1993.
21. JDN 2000/004, Kharabsheh S, Belbesi A, Qarqash W. Assessment of iodine deficiency status among Jordanian children after introduction of iodized salt. WHO and UNICEF 2000.
22. **Khulaifat S.** Thyroid incidentalomas at King Hussein Medical Center. *Jordan Medical Journal* 2001; 35(1):47-50.
23. **Al-Hureibi KA, Al-Hureibi AA, Abdulmughni YA, *et al.*** The diagnostic value of fine needle aspiration cytology in thyroid swelling in a university hospital in Yemen. *Saudi Medical Journal* 2003; 24(5): 499-503.
24. **Marwaha RK, Garg MK, Nijhavan VS, *et al.*** Prevalence of chronic lymphocytic thyroiditis in adolescent girls. *J Assoc Physicians India* 1998; 46(7): 606-608.
25. **Hanukoglu A, Mizrachi A, Dalal I, *et al.*** Extra pancreatic autoimmune manifestations in type 1 diabetes patients and their first degree relatives. *Diabetes Care* 2003; 26(4): 1235-1240.
26. **Aghini –Lombardi F, Antonangeli L, Martino E, *et al.*** The spectrum of thyroid disorders in an iodine-deficient community. The Pescopagano survey. *J Clin Endocrinol Metab* 1999; 84(2): 561-566.
27. **Mitra RB, Pathak S, Guha D, Petra SP, *et al.*** Fine needle aspiration cytology of thyroid gland and histopathological correlation-revisited. *J Indian Med Assoc* 2002; 100(6):382-384.
28. **Tunbridge WM, Evered DC, Hall R, *et al.*** The spectrum of thyroid disease in a community: the Wickham survey. *Clin Endocrinol* (Oxf) 1977; 7(7):481-493.
29. **Hasanat MA, Rumi MA, Aalam MN.** Status of antithyroid antibodies in Bangladesh. *Postgraduate Med J* 2000; 76(896):345-349.
30. **Karak AK, Marwaha RK, Tandon N, *et al.*** Cytologic characterization of post iodization residual goiter in school children by fine needle biopsy. *Acta Cytologica* 2003; 47(2):227-38.
31. **Okamura K, Nakashima T, Ueda K, *et al.*** Thyroid disorders in the general population of Hisayama Japan, with special reference to prevalence and sex differences. *International Journal of Epidemiology* 1987; 16:545-549.
32. **Jaksic J, Dumic M, Filipovic B, *et al.*** Thyroid disease in a school population with thyromegaly. *Archives of Disease in Childhood* 1994; 70:103-106.
33. **El Hag IA, Kollur SM, Chiedozi LC.** The role of FNA in the initial management of thyroid lesions: 7 year experience in a district general hospital. *Cytopathology* 2003; 14(3):126-130.
34. **Mahmood S, Islam MM, Siddiqui NI, *et al.*** Prevalence of anti thyroid microsomal antibody in thyroid patients of endemic goiter area. *Mymensingh Med J* 2004; 13(1): 4-10.
35. **Gharib H, Zimmerman D, Goellner MD, *et al.*** Fine needle aspiration biopsy: use in diagnosis and management of pediatric thyroid disease. *Endocrine Practice* 1995; 1(1):9-13.