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Evaluation of thyroid function and presence of anti-thyroid peroxidase antibodies in patients with vitiligo

Hinah Altaf *, Iffat Hassan Shah, Qazi Masood Ahmad*****

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*postgraduate scholar, **assistant professor, ***professor and head department of Dermatology, STD and Leprosy; Government Medical College and associated hospitals, Srinagar, Jammu and Kashmir, India

e-mail: hinah.altaf@gmail.com

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Abstract:

Background and Objectives:

Vitiligo is a fairly common disorder with tremendous psycho-social impact. The association of vitiligo with a number of autoimmune diseases especially involving the thyroid gland, is of considerable interest since early detection can lead to proper management of patients. We aim at studying the thyroid profile and the presence of anti-thyroid antibodies in patients with vitiligo.

Methods:

One hundred and ninety two patients attending the outpatient department were included in this case controlled study. Thyroid profile (free T3, free T4 and TSH) and ELISA for anti-TPO antibodies was done in cases as well as controls.

Results:

Thirty one patients (16.1%) with vitiligo had an abnormal thyroid profile (2 were hyperthyroid and the rest hypothyroid). Twenty one patients (11%) were positive for anti-TPO antibodies as against 5 (2.6%) controls (p value=0.001).

Conclusion:

Patients with vitiligo have an increased incidence of anti-TPO antibodies. Female patients are affected to a greater extent.

Introduction:

Vitiligo is a primary, acquired disorder characterized by the presence of well-circumscribed, milky-white or chalk-white macules on the skin and mucous membranes as a result of loss of functioning melanocytes from the involved areas. Hair overlying a vitiligo lesion may also become white (leucotrichia) [1-4]. Vitiligo is relatively common, incidence varying from 1-2%. All races are affected and both sexes are affected equally.

Vitiligo is a fairly common skin disorder in the Kashmir valley. The valley of Kashmir, known to its inhabitants as 'Kashir', is situated in the extreme north of India and is perched securely among the Himalayas at an average height of about 6000 feet above sea level. The prevalence of vitiligo has been found to be about 2.3% in patients attending the outpatient department in Kashmir [5].

Vitiligo can be classified into generalized and localized types. Vitiligo vulgaris, acrofacial and vitiligo universalis are included in the generalized type and segmental and focal vitiligo in the localised type. Vitiligo is also classified as segmental, non-segmental and mixed types. The segmental type is localized to a segment of the integument; the segment might be composed of several, or parts of several adjacent dermatomes, or have no relation to dermatomes at all. It does not generally cross the midline and shows a relatively stable course after its early rapid-spreading phase. The non-segmental type presents as bilateral, usually symmetrical macules [6-8].

Numerous studies have demonstrated the significant increase in frequency of various autoimmune disorders including autoimmune thyroid disease, pernicious anaemia, Addison's disease and systemic lupus erythematosus in patients with vitiligo [9-11]. Organ specific antibodies to thyroid (anti-thyroid peroxidase, anti-thyroglobulin), gastric parietal cell, and adrenal tissue are found more frequently in the serum of patients with vitiligo than in the general population [12-17].

Various thyroid antibodies including thyroid stimulating antibody, anti-thyroglobulin antibody and anti-thyroid peroxidase antibody (TPO) have been detected in patients with vitiligo at an increased frequency [18-22]. These antibodies are detectable in autoimmune thyroid disorders, anti-TPO being the most sensitive for the diagnosis and follow-up for these disorders. Antithyroid peroxidase antibody, historically referred to as the anti-microsomal antibody is an established, sensitive tool for the detection of early subclinical autoimmune thyroid disease. Thyroid peroxidase enzyme is involved in thyroid hormone synthesis. After iodine enters the thyroid gland, it is trapped and oxidized in an organification reaction that

involves thyroid peroxidase (TPO) and hydrogen peroxide [23].

This study was designed keeping in mind the high prevalence of vitiligo in our state, to assess associated thyroid disease in vitiligo.

Material And Methods:

The study was conducted on 192 patients with vitiligo and an equal number of age and sex matched controls. The cases were recruited from the out-patient wing of the department of Dermatology, STD and Leprosy, SMHS hospital (associated teaching hospital of Government Medical College, Srinagar).

The inclusion criteria included patients in the 6-60 years age group with vitiligo, without any associated medical or cutaneous disease related to the thyroid gland directly or indirectly. Children less than 6 years of age, patients with known thyroid disease on replacement therapy, thyroid surgery and those on anti-thyroid medication, and patients with other causes of leukoderma were excluded.

A complete medical history especially information pertaining to vitiligo like age at onset, duration of disease, family history, any was taken from each patient. Age of onset was defined as the age at which the first spot was noticed.

In each patient a thorough general physical and systemic examination including examination of the thyroid gland was done. A detailed cutaneous examination was done to determine the site of involvement, morphology, type and the percentage of body surface area involved by vitiligo. A note was made of the hair involvement and mucosal involvement. Diagnostic criteria for vitiligo were those of the Vitiligo European Task Force [24]. The extent of involvement was determined by the "Wallace rule of nines". Clinical photographs were taken in selected patients.

Controls were selected among patients in the age group of 6-60 years who attended the out-patient department for minor unrelated dermatological problem. Children less than 6 years of age and patients with known thyroid disorders or autoimmune disorders were not included in the controls.

Apart from routine investigations, thyroid function tests (free T3, freeT4 and TSH) were done by electro-chemiluminesense assay (ECLIA) in both cases and controls. Subclinical hypothyroidism was diagnosed on the basis of a raised TSH and a normal T3 and T4 values, the diagnosis of overt hypothyroidism required a low T3 and T4 as well. The diagnosis of subclinical hyperthyroidism was based on a low TSH and a normal T3 and T4; overt hyperthyroidism was diagnosed by a low TSH and a raised T3 and T4 value. The following values were taken as normal:

TSH 0.2-4.3 µIU/ml
fT3 0.8-2.1 ng/ml
fT4 5-14.1 ng/dl

Anti-thyroid peroxidase (anti-TPO) antibodies were determined by means of Microplate Enzyme Immunoassay using Accubind Elisa Microwells (Monobind Inc USA). Values in excess of 40 IU were considered to be positive.

Statistical methods:

The statistical analysis of the data was done using student's t-test for difference of means and chi-square test. These tests were referenced for p values and a p value less than 0.05 was taken as significant. Fischer's exact test was also used. The analysis of the data was performed by using SPSS computer program (Statistical Package for Social Sciences, SPSS Inc. Chicago, USA) version 10.0.

Results:

One hundred ninety two (192) patients with vitiligo in the age range of 6-60 years were studied. The study group comprised of 101 females and 91 males. The mean age in females was 19.61±11.054 years and the mean age in males was 20.89±9.909 years. Generalized type of vitiligo was present in 140 (72.9%) patients and localized vitiligo was present in 52 patients (27.1%). Of these, 134 (69.8%) patients had vitiligo vulgaris, 28 (14.6%) had focal vitiligo, 24 (12.5%) had segmental vitiligo, 5 (2.6%) had acrofacial vitiligo and 1 (0.5%) patient had vitiligo universalis. Classical presentation of vitiligo was seen in 177 (92.2%) patients; followed by trichrome vitiligo in 15 (7.8%) patients. Cases of quadrichrome vitiligo, inflammatory vitiligo or confetti-like macules were not seen in any of the patients included in our study.

The age of onset of vitiligo varied from 6-60 years. In 172 (89.3%) patients with vitiligo, age of onset was ? 30 years. The mean age of onset was 17.58±9.811 years for females and 19.03±9.215 years for males. The mean age of onset in males and females was not significantly different. Onset before 30 years of age was seen in a statistically significant number of patients ($p < 0.0001$).

Involvement of the mucosa was seen in 6 (3.1%) patients of which oral mucosa was involved in 5 (2.6%) and genital mucosa in 1 (0.5%) patient. Among patients with mucosal involvement, 5 (2.6%) had generalized vitiligo and 1 (0.5%) had localized vitiligo. Leucotrichia was found in 34 (17.7%) patients. Of these 27 (14.1%) had generalized vitiligo and 7 (3.6%) had localized vitiligo. The difference in hair involvement in localized and generalized types of vitiligo was not significant ($p = 0.67$). Koebner phenomenon was seen in 23 (11.9%) patients out of which 9 (4.6%) were males and 14 (7.3%) females. All these cases had generalized vitiligo.

A family history of vitiligo was present in 34 (17.7 %) patients of whom 26 (13.5%) had generalized vitiligo and 8 (4.2%) had localized vitiligo. No difference in the family history was seen in males and females ($p = 0.666$). Only 30 patients (15.6%) with vitiligo had a stable course, of whom 11 had generalized vitiligo and 19 had localized vitiligo. 162 patients (84.4%) had an unstable course.

Results of thyroid assessment in the study group:

Among patients with vitiligo, 161 (84%) were found to be euthyroid, 29 (15%) were hypothyroid and 2 (1%) were hyperthyroid. The difference in thyroid profile between generalized and localized types was not significant ($p = 0.761$).

Among the 29 hypothyroid patients, 22 were females and 7 were males. The higher number of females with thyroid dysfunction was statistically significant ($p = 0.008$).

In the hypothyroid group, 24 (83%) patients had subclinical hypothyroidism and 5 (17%) patients had clinical hypothyroidism.

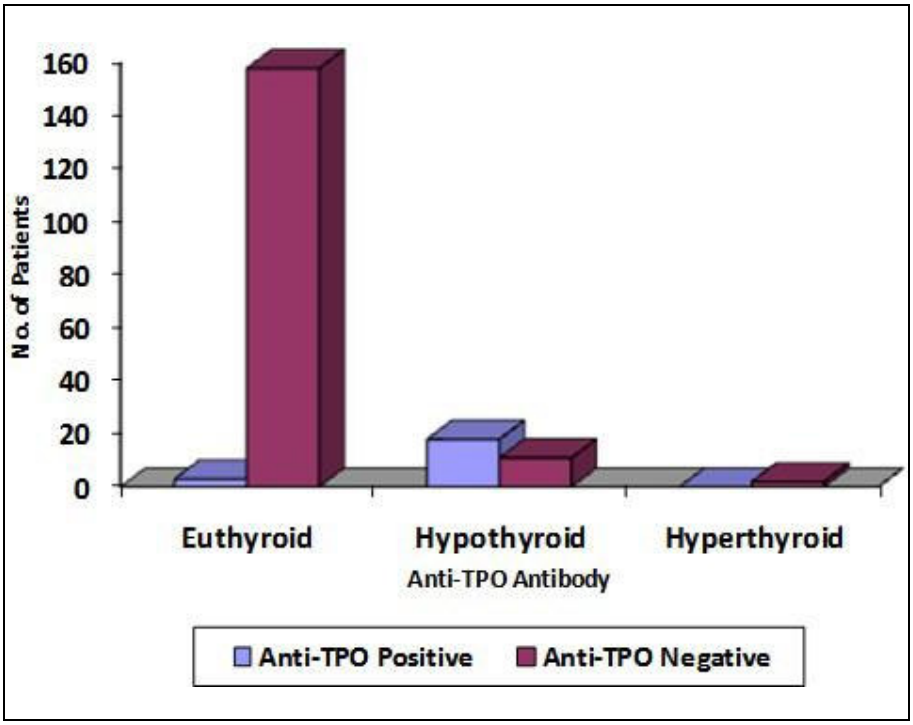
Anti-TPO antibodies were present in 21 (11%) patients of vitiligo. Of these, 17 (81%) had generalized vitiligo and 4 (29%) had localized vitiligo. Nineteen (90.5%) patients were females and 2 (9.5%) patients were males. The higher incidence in females was statistically significant ($p < 0.0001$). Out of the 21 patients with anti-TPO antibody 18 (86%) had early onset vitiligo. No association was found between age of onset and the presence of anti-TPO antibody ($p = 0.602$). Seventeen (81%) patients with a positive anti-TPO antibody had vitiligo vulgaris, 2 (9.5%) had segmental and 2 (9.5%) had focal vitiligo. The difference among the various types was found to be non-significant ($p = 0.506$). Mucosal involvement was not seen in any patient with a positive anti-TPO antibody. Five (24%) of the 21 patients with positive anti-TPO antibodies had leukotrichia. The association was not statistically significant ($p = 0.438$). Out of the 21 patients with positive anti-TPO antibodies, 4 (19%) patients had a positive family history.

Eighteen (86%) of the patients with positive anti-TPO antibodies were hypothyroid and 3 (14%) patients were euthyroid **(Table 1)**. The presence of anti-TPO antibodies had a significant association with the thyroid profile of the patient ($p < 0.0001$).

The control group comprised of 101 females and 91 males. The mean age in the control group was 20.42±9.604 years.

Anti-TPO Antibody	Thyroid Function			Total
	Hypothyroid	Euthyroid	Hyperthyroid	
Absent	11	158	2	171
	6.40%	92.30%	1.30%	100.00%
Present	18	3	0	21
	85.70%	14.30%	0%	100.00%
Total	29	161	2	192
	15.10%	83.90%	1.00%	100.00%
$\chi^2 = 91.687$		p value < 0.0001 (Significant)		

Table 1: Anti-tpo Antibody And Thyroid Profile In Vitiligo

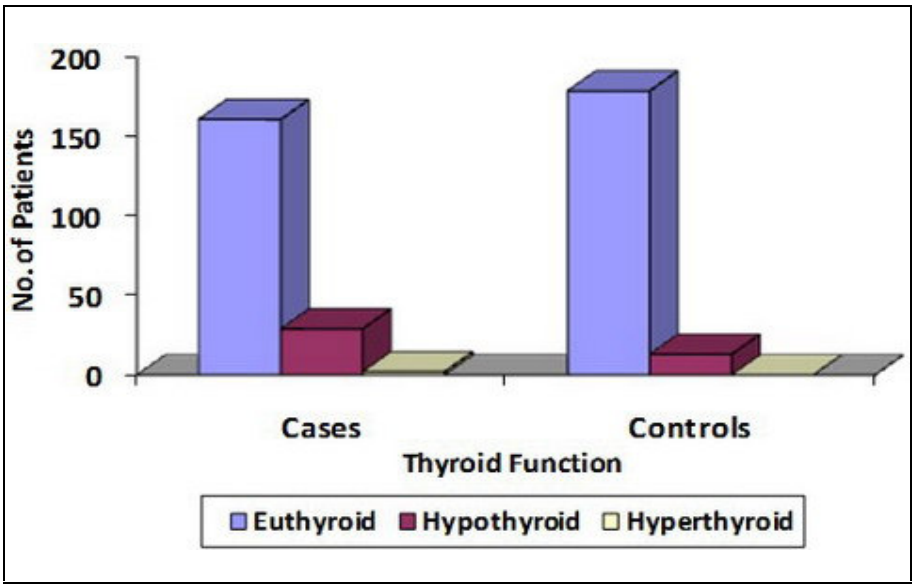


Comparison between cases and controls:

One hundred and sixty two (83.9%) cases with vitiligo were euthyroid, 29 (15.1%) were hypothyroid and 2 (1%) were hyperthyroid. Among the controls 179 (93.2%) were euthyroid and 13 (6.8%) were hypothyroid **(Table 2)**. The difference between thyroid profile in cases and controls was not significant (p = 0.011). Anti-TPO antibody was positive in 21 (11%) of the cases and 5 (2.6%) controls **(Table 3)**. The association between the presence of anti-TPO antibody and vitiligo was statistically significant (p = 0.001).

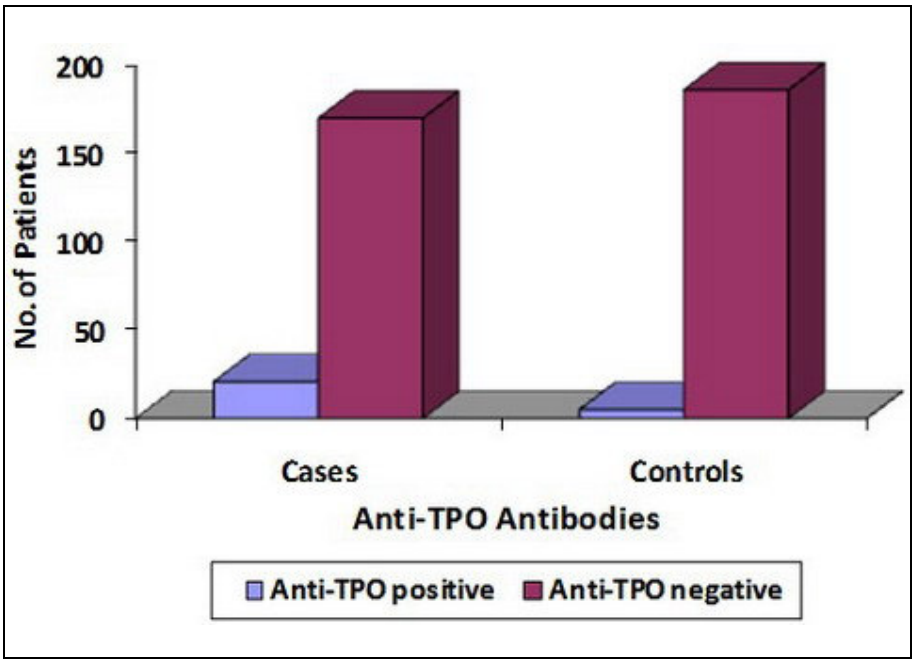
Group	Thyroid Function			Total
	Hypothyroid	Euthyroid	Hyperthyroid	
Cases	29	161	2	192
	15.10%	83.90%	1.00%	100.00%
Controls	13	179	0	192
	6.80%	93.20%	0.00%	100.00%
Total	42	340	2	384
	10.90%	88.50%	0.50%	100.00%
$\chi^2 = 9.048$			p value = 0.011 (NS)	

Table 2: Comparison Of Thyroid Function In Cases And Controls



Group	Anti-TPO antibody		Total
	Negative	Positive	
Cases	171	21	192
	89%	11%	100.00%
Controls	187	5	192
	97.40%	2.60%	100.00%
Total	358	26	384
	93.20%	6.80%	100.00%
$\chi^2 = 10.56$	p value = 0.001 (Significant)	Fischer's exact test 0.002	

Table 3: Comparison of Anti-TPO Antibody among cases and controls



Discussion And Conclusions:

Vitiligo is known to be associated with a number of systemic disorders most of them of autoimmune aetiology; whether these occur prior to or after the onset of vitiligo is not known.

Our study was planned to evaluate the association of thyroid disease and presence of anti-TPO antibody in patients with vitiligo keeping in mind that both vitiligo and thyroid disorders are fairly common in this part of the world and no studies of this kind, to the best of our knowledge, have been done previously in our population.

About 5 to 15% of euthyroid women and up to 2% men have thyroid antibodies and such individuals are at an increased risk of developing thyroid dysfunction. Almost all patients with autoimmune hypothyroidism and up to 80% of those with Graves' disease, have TPO antibodies, usually at high levels [23].

Most of the studies available on this subject have shown a significant association between thyroid disease especially anti-thyroid antibodies and vitiligo [18-22]. Not many studies pertaining to this subcontinent are available. The largest study from India involving 1436 patients did not reveal any significant association between thyroid disorders and vitiligo [25].

In our study of 192 patients with vitiligo 31 (16.1%) patients, had an abnormal thyroid function of which 24 (77%) were females. 1% patients were hyperthyroid and the majority 29 (15%) were hypothyroid. Among the hypothyroid patients, 24 (83%) had subclinical disease. No difference was observed in the thyroid profile among patients with generalized or

localised vitiligo (p = 0.761). Our study did not reveal a significant difference in the thyroid profile in cases and control (p = 0.011). This could in part be due to the fairly high prevalence of iodine deficiency disorders in our state accounting for the high level of thyroid dysfunction among controls.

Anti-thyroid peroxidase antibodies (anti-TPO) were detected in a statistically significant 21 (11%) patients with vitiligo (p = 0.001). This number, even though significant, is lower than that in studies involving mostly Caucasians. The significance of this is as yet, unknown. It could be due to a number of unknown confounding factors in our population which needs further evaluation.

The presence of anti-thyroid antibodies in various studies ranges from 7 to 58% of vitiligo patients (17% in the large study on Caucasians by Alkhateeb et al), in studies from the developed world. Studies from India reveal a very low percentage (0.5%) of patients with vitiligo, have thyroid disease. Even though it has been attributed to lower detection rates in this part of the world, an actual difference between the two populations in the prevalence of autoimmune disorders could also be contributor [25].

Our study has demonstrated an increased incidence of anti-thyroid antibodies in patients with vitiligo. This is in concordance with the results obtained in various studies [25-41].

Among the 21 patients with positive anti-TPO antibodies, 18 (86%) patients had hypothyroidism and about 3 (14%) patients had no detectable abnormality in their routine thyroid function.

It has been suggested that if anti-TPO antibodies are present with a normal thyroid function, thyroid ultrasonography should be carried out to detect any changes compatible with autoimmune thyroiditis. This helps detect subclinical autoimmune disease, so that monitoring and possible replacement can be done. If anti-TPO antibody is positive along with increased TSH levels (after two tests 4 weeks apart) patient should be referred for an endocrinology evaluation as these patients have a high risk of progression to clinical hypothyroidism. In fact it has been proposed that patients with vitiligo should be annually screened for thyroid function (TSH, anti-TPO antibody, anti-thyroglobulin antibody [34].

Most of our patients with a positive anti-TPO antibody 17 (81%) had generalized vitiligo and 4 (19%) had localized vitiligo. The difference between the two types of vitiligo was not significant (p = 0.38). Hair involvement was seen in 24% and none of the patients with a positive anti-TPO antibody had mucosal involvement.

In our study, females were found to have higher incidence of anti-TPO antibody positivity. Of the 21 patients with a positive anti-TPO antibody 90% were females. This is in conformity with the observation that autoimmune disease is more common in females [23].

A family history of vitiligo was seen 19% patients with anti-TPO antibody, however this was not found to be significant (p = 0.865). Among the anti-TPO antibody positive patients, 85.7% patients had developed vitiligo before the age of 30 years but since the majority of patients develop vitiligo before 30 years of age this association was not found to be significant (p = 0.602).

Morgan et al., [29] in his study found auto-antibodies were especially raised in generalized vitiligo. In another study, patients with late onset and higher mean age were found to have a higher incidence of anti-TPO antibodies [14]. Various other studies have described the association of long lasting vitiligo, mucosal involvement or early onset vitiligo with the presence of anti-TPO antibodies [12-23]. No such association between the presence of anti-TPO antibody and any of these factors was found in our study.

Our findings have important implications for evaluation and surveillance of patients with vitiligo. As is corroborated by other studies autoimmune thyroid screening should become standard medical practice in patients with vitiligo for early detection and appropriate management.

References

1. Ortonne JP, Bahadoran P, Fitzpatrick TB, Moscher DB, Hori Y. Hypomelanoses and hypermelanoses. In Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI., eds, Fitzpatrick's dermatology in general medicine, 6th ed., McGraw Hill Co: New York 2003; 1: 839- 847

2. Lee SJ, Cho SB, Hann SK. Classification of vitiligo. In Gupta S, Olsson MJ, Kanwar AJ, Ortonne JP., eds, Surgical management of vitiligo Blackwell Publishing Delhi 2007; 3: 20- 29

3. Bleehan SS, Anstey AV. Disorders of skin colour. In: Burns T, Breathnach S, Cox N, Griffiths C. eds Rook's Textbook of Dermatology, 7th ed., Blackwell Science: UK 2004; 2: 39.53-39.57

4. Spielvogel RL, Kantor GR. Pigmentary disorders of the skin. In Elder DE, Elenitsas R, Johnson BL, Murphy GF. eds, Lever's histopathology of the skin, 9th ed., Lippincott Williams and Wilkins Philadelphia 2005:705-711

5. Masood Q, Hassan I. Pattern of skin disorder in Kashmir valley. Indian J Dermatol 2002; 47(3): 147- 148

6. Grimes PE: White patches and bruised souls: Advances in the pathogenesis and treatment of vitiligo. J Am Acad Dermatol 2004; 51(1): 55- 57

7. Fargnoli MC, Bolognia JL. Pentachrome vitiligo. J Am Acad Dermatol

1995; 33: 853- 856

8. Koga M, Tango T. Clinical features and course of type A and type B vitiligo. Br J Dermatol 1988; 118: 223- 228

9. Dawber RP Clinical associations of vitiligo. Postgrad Med J 1970; 46(535): 276- 277

10. Gopal KV, Ramarao GR, Kumar YH, Appa Rao MV, Vasudev P, Srikant. Vitiligo: a part of systemic autoimmune process. Indian J Dermatol Venereol Leprol 2007; 73(3): 162- 165

11. Kovacs SO. Vitiligo. J Am Acad Dermatol 1998; 38(5): 647-666.

12. Bystryn JC. Theories in the pathogenesis of depigmentation: Immune hypothesis. In Hann SK, Norlund JJ eds. Vitiligo. Blackwell Science, London, 2000: 21

13. Ongenae K, Van Geel N, Naeyaert JM. Evidence for an autoimmune pathogenesis of vitiligo. Pigment Cell Res 2003; 16(2): 90-100

14. Brostoff J. Autoantibodies in patients with vitiligo. Lancet 1969; 2(7613): 177- 178

15. Kemp EH. Autoantibodies as diagnostic and predictive markers of vitiligo. Autoimmunity 2004; 37: 287- 290

16. Grimes PE, Halder RM, Jones C, Chakrabarti SG, Enterline J, Minus HR, Kenney JA. Autoantibodies and their clinical significance in a black vitiligo population. Arch Dermatol 1983; 119(4): 300- 303

17. Rezaei N, Gavalas N, Weetman A, Kemp E.Autoimmunity as an aetiological factor in vitiligo. J Eur Acad Dermatol Venereol 2007; 21(7): 865- 876

18. Cunliffe WJ, Hall R, Newell DJ, Stevenson CJ. Vitiligo, thyroid disease and autoimmunity. Br J Dermatol 1968; 80(3): 135- 139

19. Kurtev A, Dourmishev AL. Thyroid function and autoimmunity in children and adolescents with vitiligo. J Eur Acad Dermatol Venereol 2004; 18: 109- 111

20. Pal SK, Ghosh KK, Banerjee PK. Thyroid function in vitiligo. Clin Chim Acta 1980; 106(3): 331- 332

21. Ai J, Leonhardt MJ, Heymann RW. Autoimmune thyroid disease. Etiology, pathogenesis and dermatological manifestations. J Am Acad Dermatol 2003; 48: 641- 659

22. Koppers LE, Palumbo PJ. Pigmentation and the endocrinologist. Med

Clin North Am 1972; 56(4): 1041- 1049

23. Jameson JL, Weetman AP. Disorders of the thyroid gland. In Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL and Jameson JL. eds Harrison's Textbook of Internal Medicine 15th ed McGraw Hill New York 2001; 2: 2060- 2078

24. Taieb A, Picardo M, VETF Members. The definition and assessment of vitiligo: a consensus report of the Vitiligo European Task Force. Pigment Cell Res 2007; 20(1): 27- 35

25. Handa S, Kaur I. Vitiligo: clinical findings in 1436 patients. J Dermatol 1999; 26(10): 653- 657

26. Alkhateeb A, Fain PR, Thody A, Bennett DC, Spritz RA. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their families. Pigment Cell Res 2003; 2003: 208- 214

27. Hegedüs L, Heidenheim M, Gervil M, Hjalgrim H, H?ier- Madsen M. High frequency of thyroid dysfunction in patients with vitiligo. Acta Derm Venereol 1994; 74(2): 120- 123

28. Kumar V, Shankar V, Chaudhary S, Bhatia KK, Mehta LK, Arora N, Arora DR. Radio-active iodine uptake in vitiligo. J Dermatol 1990; 17(1): 41- 43

29. Morgan M, Castells A, Ramirez A. Autoantibodies in vitiligo: clinical significance. Med Cutan Ibero Lat Am 1986; 14: 139- 142

30. Betterle C, Caretto A, De Zio A, Pedini B, Veller-Fornasa C, Cecchetto A, Accordi F, Peserico A. Incidence and significance of organ-specific autoimmune disorders (clinical, latent or only autoantibodies) in patients with vitiligo. Dermatologica 1985; 171(6): 419- 423

31. Boisseau-Garsaud AM, Garsaud P, Calès-Quist D, Hélénon R, Quénéhervé C, Claire RC. Epidemiology of vitiligo in the French West Indies (Isle of Martinique). Int J Dermatol 2000; 39(1): 18- 20

32. Mandry RC, Ortiz LJ, Lugo-Somolinos A, Sanchez JL. Organ specific antibodies in vitiligo patients and their relatives. Int J Dermatol 1996; 35: 18- 21

33. Iacovelli P, Sinagra JL, Vidolin AP, Marenda S, Capitanio B, Leone G et al. Relevance of thyroiditis and of other autoimmune diseases in children with vitiligo. Dermatology 2005; 210: 26- 30

34. Kakourou T, Kanaka-Gatenbein C, Papadopoulou A, Kaloumenou E, Chrousos GP. Increased prevalence of chronic autoimmune thyroiditis in children and adolescents with vitiligo. J Am Acad Dermatol 2005; 53(2): 220- 223

35. Daneshpazhooh M, Mostofizadeh M, Javad Behjati, Akhyani M, Robati R. Antithyroid peroxidase antibody and vitiligo: a controlled study.BMC Dermatol 2006; 6: 3

36. Birlea SA, Fain PR, Spritz RA. A Romanian population isolate with high frequency of vitiligo and associated autoimmune diseases. Arch Dermatol 2008; 144(3): 310- 316

37. Laberge G, Mailloux CM, Gowan K, Holland P, Bennett DC, Fain PR and Spritz RA. Early disease onset and increased risk of other autoimmune diseases in familial generalized vitiligo. Pigment Cell Res 18; 300- 305

38. Zettinig A, Tanew A, Fischer G, Mayr W, Dudczak R and Weissel M. Autoimmune diseases in vitiligo: do anti-nuclear antibodies decrease thyroid volume. Clin Exp Immunol 2003; 131: 347- 354

39. Shong YK, Kim JA. Vitiligo in autoimmune thyroid disease. Thyroidology 1991; 3: 89- 91

40. Korkij W, Soltani K, Simjee S, Marcincin PG, Chuang TY. Tissue-specific autoantibodies and autoimmune disorders in vitiligo and alopecia areata: a retrospective study. J Cutan Pathol 1984; 11(6): 522- 530

41. Dave S,D'Souza M, Thappa DM, Reddy KS, Bobby Z. High frequency of thyroid dysfunction in Indian patients with vitiligo. Indian J Dermatol 2003; 48: 68- 72