Association of other Autoimmune Diseases in Vitiligo Patients
Babar ZUM\textsuperscript{1}, Alam M\textsuperscript{2}, Khondker L\textsuperscript{3}, Siddiqua A\textsuperscript{4}, Alam MN\textsuperscript{5}, Imdad TI\textsuperscript{6}

Abstract

A cross sectional study of thirty eight vitiligo patients attending at the outpatients was conducted. The result revealed generalized presentation in 53.6\% cases followed by focal presentation, acro-facial and segmented presentation which were 26.3\% cases, 15.8\% cases and 5.3\% cases. Progressive type was found in majority of cases which were 71.1\% cases followed by stable case which was 39.9\% cases and positive family history was found in 36.8\% cases in our study. Among 38 vitiligo patients highest number of associated autoimmune disease was the thyroid abnormalities of which hypothyroidism was 15.8\% and hyperthyroidism was 7.9\% cases respectively. Diabetes mellitus was found in 2.6\% cases, Addison’s disease and SLE were found in 2.6\% case each. No autoimmune disease was found in the rest 68.5\% cases.

Key words: Vitiligo, autoimmune diseases.

Introduction

Vitiligo is an acquired, idiopathic, hypomelanotic disease characterized by circumscribed depigmented macules\textsuperscript{1}. It is a disfiguring disease with psychosocial stigma due to the chronic and progressive loss of melanocytes from the cutaneous epidermis \textsuperscript{2}. In India there is a stigma associated with vitiligo and affected persons and their families particularly girls are socially ostracized for marital purpose\textsuperscript{3}. Large population surveys have shown a world-wide incidence of 0.5–2\%, with the disease beginning before the age of 20 in 50\% of cases \textsuperscript{4}. About 6–38\% of patients have family members with the disease indicating hereditary factor \textsuperscript{5}. However, the inheritance pattern of the disorder is consistent with that of a polygenic trait not transmission by a simple Mendelian mechanism \textsuperscript{2}. Usually, vitiligo is viewed as a minor disease, but the impact on patients’ psychological well-being and social interactions should not be underestimated \textsuperscript{6}. Autoimmunity might arise as a secondary phenomenon following the self-destruction of pigment cells and this might then amplify the damage to melanocytes\textsuperscript{2}. Indeed, non-segmental vitiligo is characterized by an association with autoimmune disease and unstable results after autologous melanocytes grafting\textsuperscript{7}. Vitiligo is often associated with other autoimmune conditions \textsuperscript{2}.  

\textsuperscript{1} Dr Zahir Uddin Muhammad Babar, Specialist in Dermatology and Venereology. Bangabandhu Sheikh Mujib Medical University, Dhaka. Shahbag, Dhaka, Bangladesh.
\textsuperscript{2} Dr. Mansurul Alam, Associate Professor & Head, Department of Dermatology & Venereology Chittagong Medical College Hospital, Chittagong.
\textsuperscript{3} *Dr. Lubna Khondker, Assistant Professor, Department of Dermatology and Venereology. Bangabandhu Sheikh Mujib Medical University Dhaka.
\textsuperscript{4} Dr Ayesha Siddiqua, Specialist in Dermatology and Venereology. Bangabandhu Sheikh Mujib Medical University, Dhaka.
\textsuperscript{5} Dr Mohd Nurul Alam, Specialist in Dermatology and Venereology. Bangabandhu Sheikh Mujib Medical University, Dhaka.
\textsuperscript{6} Dr Tawhidul Islam Imdad, Junior Consultant, Department of Dermatology and Venereology. Jalalabad Ragib Rabeya Medical College Hospital, Sylhet.

* Address of correspondence
Mobile- 01552370429; E-mail: lubnaderma@gmail.com.
Moreover, in a survey of more than 2600 unselected Caucasian vitiligo patients, elevated frequencies of autoimmune thyroid disease, Addison’s disease, systemic lupus erythematosus and pernicious anaemia were found, with approximately 30% of patients being affected with at least one additional autoimmune disorder. Furthermore, these same autoimmune diseases occurred at an increased frequency in the first-degree relatives of the patients studied. Similarly, in multiplex generalized vitiligo families, higher frequencies of psoriasis, rheumatoid arthritis and type 1 diabetes mellitus were noted in addition to autoimmune thyroid disease, Addison’s disease, systemic lupus erythematosus and pernicious anaemia. Such data indicate that individuals can be genetically predisposed to a specific group of autoimmune diseases that includes generalized vitiligo. In contrast to the studies, one notable large-scale analysis of 321 vitiligo patients found associations with thyroid disease but not with any other autoimmune disease. The purpose of the present study was therefore destined to find out the association of vitiligo with any autoimmune diseases.
Methods
A cross sectional study was carried out in clinically diagnosed cases of vitiligo patients of any age and both sexes. The patients were voluntarily included in the study taking their consent and they were neither supported nor additionally burdened financially. A total number of 38 patients were enrolled for this study after fulfilling inclusion and exclusion criteria. Inclusion criteria: patients were with localized or generalized vitiligo confirmed clinically & by wood's lamp examination, at any age with both sex. Exclusion criteria: patients those suffering from systemic diseases like chronic arsenicosis, cirrhosis of liver or ectopic hormone secreting tumour, the cases showing white patches due to secondary causes, pregnant women and lactating mothers, severely ill patients and patients or attendants unwilling to take part in the study. The sampling technique was accidental or convenient type.

Study Procedure
An informed consent was taken from the patient who was taken part in this study. For data collection, structured questionnaire and case record proforma were used. At the base line visit, the questionnaire & case record proforma were used to collect data of the respondents, socio-economic factors, family and community status, personal history, disease type and length of time present including known autoimmune disorders. Patient were diagnosed clinically by assessing morphology of lesion, their distribution, percentage of skin involved and by doing woods lamp examination. All data were compiled and edited meticulously by thorough checking and rechecking. These were recorded systematically in preformed data collection form (questionnaire) and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS for windows version 12.0 and 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

Results
The demographic analysis showed among patients female sex is preponderant (52.6%) in comparison to males (47.4%). The distribution of patients according to marital status represented that the majority is unmarried (55.3%) and the rest are married (44.7%). The result of the questionnaire further revealed the socio-economic status of patients. It is remarkable that vitiligo patients mostly belong to middle class (60.5%) followed by lower and upper class statuses showing the distribution of patient 36.9% cases and 2.6% cases respectively. The analysis noticed further the distribution of patient according to occupation. It was ascribed to students which is 36.8% as majority of cases, followed by service holder, housewife, other occupations and business which are 23.7% cases, 15.8% cases, 15.8%cases and 7.9%cases respectively. Regarding smoking habit among 38 patients non-smokers were found more in numbers than smokers which are recorded as 84.2% and 15.8% cases respectively.

Table 1 represents the distribution of patients according to presentation of vitiligo. Generalized presentation is found in 53.6% cases followed by focal presentation, acrofacial and segmented presentation which is 26.3% cases, 15.8% cases and 5.3% cases. Table 1 shows the distribution of patient according to clinical progression also. Progressive type is found in majority of cases which is 71.1% cases followed by stable case which is 39.9% cases. This table also demonstrates the distribution of patients according to family history. Positive family history is found in 36.8% cases and the rest 63.2% cases are absent. Some photographs of patients under this study show the appearance of vitiligo at different sites.

Table 1: Distribution of patient according to presentation and clinical progression and Family History of vitiligo (n=38).
A total number of thirty eight vitiligo patients were selected in this study. The distribution of patient according to sex revealed male: female ratio as 1:1.1 which indicates that the vitiligo is more common in female. This finding is similar with Narita et al. The reason is thought to be due to estrogens driving the autoimmunity.

It has been found that the students are most commonly affected by vitiligo followed by service holders and house wife. This phenomenon is due to the fact that the students are more concern about such illness. The present study depicts the fact that vitiligo has little impact on smoking predominantly yielded vitiligo. There raises a question whether it proves the fact that females are more commonly affected with vitiligo than males, as they are mostly non-smokers. The distribution of patients according to family history is recorded. It is very common among those who have positive family history (36.8%). Poovaraj reported that increased frequency of autoimmune diseases has also been specifically described in family members of multiplex vitiligo families and families with multiple members having vitiligo which is similar with the present study. This indicates that the vitiligo is reflecting an inherited genetic component of autoimmune susceptibility in these families. Laberge et al also has also tried to find out the relationship between vitiligo and the history of family members and has found a similar result.

The association of other diseases with vitiligo is remarkable. Among all vitiligo patients highest number of associated autoimmune disease is the thyroid abnormalities of which hypothyroidism is more common than hyperthyroidism. Type 1 Diabetes mellitus is found among the study population. Addison's disease and SLE are found in 2.6% case each. Similarly Cunliffe et al found that there is a significant association between vitiligo and thyroid disease. The study also mentioned that thyroglobulin antibodies are significantly associated with vitiligo. Poovaraj reported...
that alopecia areata and diabetes mellitus are also significantly associated with vitiligo which is similar with the present study. In another study Alkhateeb et al reported that at least 30% of patients with vitiligo are to be affected with at least one additional autoimmune disorder. This agreement is analogous to the present study. The present study evidenced that the commonest association of vitiligo is with thyroid dysfunction. Dave et al. reported abnormal thyroid profile in vitiligo patients and also higher incidence of thyroid dysfunction in mucosal vitiligo. Studies by Zettining et al. reported subclinical thyroid disease and Betterle et al. reported only the presence of anti-thyroid peroxidase antibodies, thyroid microsomal antibodies and antithyroglobulin antibodies. All these findings when compared with other studies have shown that there is a strong relationship with the autoimmune diseases with vitiligo.

**Conclusion**

In conclusion, it may be drawn that the findings of this study clearly demonstrated and supported an association between autoimmune diseases with vitiligo of which thyroid diseases, Addison’s disease, systemic lupus erythematosus, alopecia areata, type 1 diabetes mellitus are worth mentioning. While examining a vitiligo patient the clinicians should give proper attention keeping in mind this above mentioned association for getting information prior to selecting a suitable therapy.

**Reference:**

1. Shajiil EM, Chatterjee S, Agrawal D, Bagchi T, Begum R. Vitiligo: Pathomechanisms and genetic polymorphism of susceptible genes. Indian J Exp Biol, 2006; 44:526-539
2. Rezaei N, Gavalas NG, Weetman AP, Kemp EH. Autoimmunity as an aetiological factor in vitiligo. JADV 2007;21:865–876
3. Mehta NR, Shah KC, Theodore C, Vyas V & Patel A. Epidemiological study of vitiligo in Surat area, South Gujarat. Indian J Med Res, 1973; 61: 145
4. Majumder PP, Nordlund JJ, Nath SK. Pattern of familial aggregation of vitiligo. Arch Dermatol 1993; 129: 994–998
5. Ortonne JP, Mosher DB, Fitzpatrick TB. Vitiligo and other hypomelanoses of hair and skin. In: Ortonne JP, Mosher DB, Fitzpatrick TB, eds. Topics in Dermatology, Plenum Medical Book Co: New York; 1983, 257–258
6. Kent G, Al-Abadle MSK. Psychologic effects of vitiligo: a critical incident analysis. J Am Acad Dermatol 1996; 35: 895–898
7. Taeib A. Intrinsic and extrinsic pathomechanisms in vitiligo. Pigment Cell Res 2000; 13 (Suppl): 41–47
8. Alkhateeb A, Fain PR, Thody A, Bennett DC, Spritz R. Epidemiology of vitiligo and associated autoimmune diseases in caucasian probands and their families. Pigment Cell Res. 2003;16:208–14
9. Laberge G, Mailoux CM, Gowan K, Holland P, Bennett DC, Fain PR, et al. Early disease onset and increased risk of other autoimmune diseases in familiar generalised vitiligo. Pigment Cell Res. 2005; 18:300-5
10. Schallreuter KU, Lemke R, Brandt O et al. Vitiligo and other diseases: coexistence or true association. Dermatology 1994; 188: 269–275
11. Narita T, Oiso N, Fukai K, Kabashima K, Kawada A, Suzuki T. Generalized Vitiligo and Associated Autoimmune Diseases in Japanese Patients and Their Families. Allergology International 2011; 60(4):505
12. Lockshin MD. Sex differences in autoimmune disease. Handbook of systemic autoimmune diseases 2005; 4:3-10
13. Shoerfeld Y. The decade of autoimmunity: Elsevier Science; 1999; 2:163
14. Poojary SA. Vitiligo and associated autoimmune disorders: A retrospective hospital-based study in Mumbai, India. Allergologia et Immunopathologia 2011;39(6):356
15. Cunliffe WJ, Hall R, Newell DJ, Stevenson CJ. Vitiligo, Thyroid Disease And Autoimmunity. British Journal of Dermatology 1968;80(3):135-139
16. 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.
17. Zettining G, Tanew A, Fischer G, Mayr W, Dudczak R, Weissel M. Autoimmune diseases in vitiligo: anti-nuclear antibodies decrease thyroid volume. Clin Exp Immunol. 2003;131:347-54
18. Betterle C, Caretto A, De Zio A, Pedini B, Veller-Fornasa C, Cecchetto A, et al. Incidence and significance of organ specific autoimmune disorders (clinical, latent or only autoantibodies) in patients with vitiligo. Dermatologica. 1985;171:419-23.