Original Article

Frequency of autoimmune disorders in patients of alopecia areata

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Abstract

ObjectiveTo determine the frequency of autoimmune disorders associated with alopecia areata in patients presenting in a tertiary care hospital.

MethodsThis study was conducted at the Dermatology Department, Unit II, KEMU/Mayo Hospital, Lahore.120 patients fulfilling the inclusion criteria were entered in the study during May 2013 to January 2014. After taking informed consent and recording demographic data, complete history was taken. Examination was performed and investigations were carried out where needed, for determination of factors associated with alopecia areata.

ResultsOut of 120 patients studied, 30.8% of patients had positive family history of alopecia areata. Atopic dermatitis was found in 29.2% of patients. Vitiligo and hypothyroidism were seen in 4.2% each. Diabetes mellitus was seen in 1.7% of the cases and 0.8% were hyperthyroid.

ConclusionPostive family history and atopic dermatitis were seen in one third of our patients with alopecia areata. Vitiligo and hypothyroidism were other important associations observed.

Key words
Alopecia areata, atopic dermatitis, family history, vitiligo, hypothyroidism, hyperthyroidism, diabetes mellitus

Introduction

Alopecia areata is a chronic inflammatory disease that involves the hair follicles and the nails.[1,2]At any given time, approximately 0.2% of the population has alopecia areata and approximately 1.7% of the population experiences an episode during their life time.

Alopecia areata peaks between the second and fourth decades with equal sex incidence.Clinical patterns of alopecia areata include patchy, confluent, diffuse, ophiasis, alopecia totalis and alopecia universalis.[1,2,3]It may occur as a single, self-limiting episode or may recur at varying intervals over many years.34-50% of patients will recover within one year and 14-25% will progress to alopecia totalis or universalis.[2]

The predisposition to alopecia areata is genetically determined.[1] Between 10% and 20% of patients give a family history of the disease. T cell-mediated autoimmune mechanism occurring in a genetically predisposed individual is responsible for hair follicle inflammation seen in alopecia areata.[4]The disease may get triggered by environmental factors.

Other factors associated with alopecia areata include atopic dermatitis, vitiligo, thyroid disorders, anaemia, diabetes mellitus and a positive family history of alopecia areata. The

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association with these disorders is because all of them are autoimmune disorders.

Chu *et al.*[3]found that alopecia areata had significant associations with psoriasis, atopic dermatitis and autoimmune thyroid disease. It was found that patients presenting with alopecia areata during childhood were most likely to have associated atopic dermatitis, those in their sixities to have comorbid thyroid disease while those in their second decade to have an elevated risk for psoriasis.

Atopic dermatitis was seen in 14.1%, vitiligo in 2.8%, diabetes mellitus in 7.1%, hyperthyroidism in 2.8% and hypothyroidism in 14%.[5]In a study, conducted by Ejaz *et al*.[6] personal and family history of atopy was found in 31.3% while a family history of alopecia areata in 12.1% patients. Two patients had thyroid disease and one patient had vitiligo.

Ahmed *et al.*[7]studied 112 patients. Majority of them were below 25 years. 8.9% patients revealed thyroid dysfunction, comprising 90% patients with hypothyroidism and 10% having hyperthyroidism (P<0.05).

International studies depict no large differences in the clinical features and associations of alopecia areata among various races. Till date two studies conducted in Pakistan have shown varied results and a lower incidence of positive family history. Moreover, there is variation regarding the frequency of outcomes in Indian and European population. We determined the frequency of autoimmune disorders in patients of alopecia areata in Pakistani population.

Methods

A cross-sectional survey was carried out atDermatology Department Unit II, Mayo Hospital, Lahore. Non-probability purposive sampling was the technique used. The study duration consisted of six months. Sample size of 120 cases was calculated with 95% confidence level, 3% margin of error and taking expected percentage of vitiligo i.e. 2.8%[5] (least among all) factors occurring in alopecia areata patients.Male or female patients, having alopecia areata, assessed clinically, were included in the study. Patients having scarring alopecia alone, showing any signs of inflammation on or around the affected area, having androgenetic alopecia, telogen effluvium or trichotillomania assessed clinically or patients taking any systemic or topical treatment for alopecia areata during last 4 weeks were excluded.

The purpose of the study was explained and an informed consent was taken. Demographic characteristics like age, sex and address were recorded. Detailed history and clinical examination was performed. Outcome variables recorded were, atopic dermatitis, vitiligo, family history of alopecia areata, hypothyroidism, hyperthyroidism and diabetes mellitus. Diagnosis of cutaneous diseases was made on history and clinical basis while labortary investigations like thyroid function test, fasting blood sugar level or any other relevant test e.g. skin biopsy was performed wherever required.

Data was entered and analyzed through SPSS (version 17). Data master sheet was generated for the variables under study. The quantitative data like age were presented as the mean and standard deviation. Qualitative data like, atopic dermatitis, vitiligo, thyroid disordersand diabetes mellitus were presented in the form of frequency and percentages.

Results

There were 120 patients in this study with the mean age of 22.28 ± 13.00 years, the youngest patient aged 2 years and the oldest 60 years of age. The gender ratio was almost equal with 1.1males for every female.

Table 1 Frequencies of autoimmune disorders in alopecia areata patients (n=120).

Factor	*Frequency*
Atopic dermatitis	29.2%
Vitiligo	4.2%
Hypothyroidism	4.2%
Diabetes mellitus	1.7%
Hyperthyroidism	0.8%

Autoimmunediseases associated with alopecia areata were observed in 55.8% of the study subjects.

A positive family history of alopecia areata was present in 30.8% of the cases.**Table 1** enlists the frequency of different autoimmune disorders observed in the study population. Atopic dermatitis constituted 29.2%.4.2% of patients had vitiligo. 4.2% of the patients were found to be hypothyroid.1.7% patients had diabetes mellitus and one was on antihyperglycemic medication at presentation while one new case of diabetes was identified during the study.Only 0.8% had hyperthyroidism.

Discussion

Alopeciaareata (AA)isoneofthemostcommonformsofhairlossin humans.It is typified by patchy hair loss on the scalpthat can progress to cover the entire scalp (alopecia totalis) and eventually the entire body (alopecia universalis). This disorder occurs inboth the sexes, at all ages.[8,9]

There are also lot of data concerning the contribution of autoimmune processes in the pathogenesis of AA.[9,10] The association of AA with other autoimmune processes, such as autoimmune thyroiditis and diabetes mellitus, has been widely reported and has been considered as a potent indicator of the contribution of autoimmunity in the pathogenesis.[9]There is a huge inconsistency regarding the prevalence of autoimmune diseases with alopecia areata. For example, in few studies on vitiligo, a very high association rate of almost 12.5% was noted, whereas other studies reported association rate as low as 0.3%.[11]There is paucity of clinical data in Asians regarding AA.[12]

AA may begin as early as the first month of life or as late as in the late seventies. The age of the youngest patient in our study group was 2 years and that of the oldest was 60 years which is almost similar to that found in study done by Thomas *et al.*[5]and Bhat *et al.*[13] in India.The mean age of the patients in our study was 22.28 ± 13.00 years, as was also found by Mane *et al.*[14] in India (26.85 years).

Our study showed almost equal sex predisposition, with very slight female predominance, female: male 1:1.1. The male: female ratio was 1.86:1 in a study done by Almutaiari *et al.*[15] in Kuwait. AA was seen equally in both genders in a study conducted by Yang*et al.*[16]in China.The female: male ratio was found to be 1.15: 1 in a study in Iran.[8] On the other hand in a study conducted by Ejaz *et al.*[12], 72% were males and 28% were females.The reason for male predominance in this study could be that the study was conducted in an army hospital. The majority of people, who consulted for their disease, belonged to outstation areas and were living away from their families and among them were mostlymales. In our tertiary care set up, on the other hand, the patients enrolled were from the civil society, representing the actual picture of the population demographics.

Reported figure of familial incidence vary from 10% to 50%.[15,17]Family history of alopecia areata was present in 30.8% of our patients. Family history was seen in about 32% by Goh*et al.*[18] in USA, in 24.4% of patients in Iran[10] and in 20% of patients by Almutaiari *et al.*[15] in Kuwait. Few studies show a much lower incidence of family history of alopecia areata. It was recorded in 12.1% patients in a study done by Ejaz*et al*.[12] in Pakistan.Study conducted by Sharma *et al.*[19] in

India showed family history to be positive in 9% of patients. There are certain genetic, ethnic and environmental factors operating, when it comes to the familial occurrence of diseases. This is suggested by theHLA studies which show that HLA-AI, HLA-DQ1 and HLA-DQ3 are significantly frequent in patients with alopecia areata than in controls. HLA-DR 16 is significantly less common in patients with alopecia areata than in the control group thus making us conclude that this allele might have a protective role for alopecia areata.[5] Various studies have shown increased prevalence of females and the familial tendency has been noted more so in such studies. Our study suggested the same fact.

Studies report frequency of atopy in AA patients ranging from 1% to 52%.[5]In the present study, atopy was associated with increased frequency in patients with alopecia areata, i.e., 29.2% cases. Personal and family history of atopy was found in 31.3% patients by Ejaz *et al.*[12]in Pakistan.In Ludhiana, atopy was seen to be associated with 22.5% cases of alopecia areata.[5]Definite evidence of atopy was obtained in 20% patients by Ahmed *et al.*[20] in Karachi, Pakistan.

Atopy was reported to be much higher, in greater than half of the patients studied, in a publication from USA, 56% of patients studied had atopy.[18]This difference may be because of the fact that the genetic, ethnic and environmental factors operating in various demographic areas are different. People in USA are of different origins, as they are immigrants from various areas of the world, belong to different races making it a country with a diversity of population data. Also the environmental factors are different including early exposure to various allergens, food preservatives, animal exposure, life style, eating habits, industrial pollutants etc.

Studies have ranged from 8% to 28%, when it comes to thyroid disorders in patients of alopecia areata.[5,7] In our study thyroid disorders were found to be present in 5% of patients. Among the thyroid disorders, hypothyroidism constituted 4.2% cases while hyperthyroidism was seen only in 0.8%. Similar results were seen in another study from Pakistan. 8.9% out of the patients revealed thyroid dysfunction, comprising 90% patients with hypothyroidism and 10% patients having hyperthyroidism.[7]Puavilai *et al.*[21] in Thailand also showed that the frequency of thyroid disease among the alopecia areata patients was low (7.2%) and they were not statistically different from patients with AA and control group.

In a study by Thomas*et al.*[5] in India, thyroid disorders showed the highest frequency, 18.3%, of the systemic diseases observed with alopecia areata.[5]This difference may be because of difference in genetic, autoimmune, environmental and infectious factors. Possibly, autoimmunity underlying thyroid disorders is strongly expressed, because of different genetic background, leading to clinically established disease. Iodine deficiency may be more in India and viral infections leading to thyroid disorders might have a higher incidence. The clinically evident expression of associated autoimmune diseases in AA is variable as is supported by the fact that in the 36% of the cases, it has revealed a silent pathology of organ.[22]Considering the possibility of silent organ pathology, thyroid disorders should be vigilantly looked for. It has been recommended that thyroid screening should be routinely performed in all children with long-standing AA.

In our study, vitiligo was seen in 4.2% of cases. One case had colocalised alopecia areata and vitiligo i.e. both disorders were present at the same site. To our knowledge, only 8 cases of colocalization have been reported so far in the world literature till

date.Regarding the colocalization, it is speculated that this coexistence in a single anatomic area could be due to localized co-stimulation of an immunological mechanism mediated either by helper T cells against both the melanocytes and the hair follicle antigens or polyclonal B-cell activation resulting in production of multiple autoantibodies. It has also been proposed that a structural similarity between circulating anti-endothelial antibody targeted against the endothelial cells of hair-bulb capillary plexus and anti melanocytic antibody might play a role. This concept is further supported by the pathogenesis underlying the perinevoid alopecia, which also shows antibodies against melanocytes.[11]

Vitiligo was found in 2.5% of the alopecia areata cases in USA.[18]Alopecia areata and vitiligo are also associated with various other autoimmune cutaneous disorders such as lichen planus, psoriasis and lupus erythematosus etc. Thus, it may be proposed that both these disorders share a common autoimmune mechanism and genetic susceptibility.

The association of alopecia areata with diabetes mellitushas been well reported in literature and has been considered as a potent indicator of the contribution of autoimmunity in the pathogenesis of the AA.[9]Diabetes mellitus was found in 1.7% of our cases. Ahmed *et al.*[7]in Karachi, Pakistan, found that 0.9% of alopecia areata patients were diabetic. Goh *et al.*[18] in USA showed a rate of 0.6%.

Conclusion

Autoimmune factors associated with alopecia areata were positive family history and atopic dermatitis seen in almost one third of patients. Vitiligo and hypothyroidism were other important factors. Whenever there is an autoimmune disorder present, the patient should be thoroughly examined and investigated, as indicated, to rule out any other autoimmune disease.

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