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ASSOCIATION OF THYROID DYSFUNCTION AMONG PEOPLE WITH ALOPECIA AREATA IN DIFFERENT AGE GROUPS

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ABSTRACT

Introduction: Alopecia Areata (AA) is a common hair loss condition having non-scary patchy hair loss. It frequently occurs in association with autoimmune diseases like vitiligo, lichen planus and others, more common association is seen with thyroid disorders. **Aim and Objectives:** To find the correlation between Alopecia Areata and thyroid related disorders. To assess the severity and duration of Alopecia Areata in varied age groups of patients visiting the dermatology OPD. To determine the levels of serum T3, T4, TSH and anti-TPO antibodies in patients with Alopecia Areata. **Materials and methods:** The study population included 100 patients aged between 7 to 70 years with clinically diagnosed AA. Clinical history of AA was taken and blood tested for T3, T4, TSH and Anti-Thyroid Peroxidase and Anti thyroglobulin antibodies. T3, T4, TSH, Anti-Thyroid peroxidase and Antithyroglobulin antibody levels were assessed by chemiluminescence immunoassay and association between alopecia areata and thyroid dysfunction was evaluated. **Results:** The commonest age group was 21-30 yrs (31%) with male preponderance (69%.) Positive family history of AA was noted in 83% cases. Association with other autoimmune disorders was seen in 54%.Patchy type was the commonest (69%) with nail involvement was in 13%. Commonest area was scalp (76%) with parietal region. Three patients (3%) had hypothyroidism as defined by low T3 & T4 levels. None of our patients had deranged TSH levels. Anti TPO antibody positivity was observed in 43% and anti-thyroglobulin antibody positivity in 31 %.No correlation was found between Alopecia Areata and thyroid disorder. **Conclusion:** Longer follow ups are needed to observe if AA patients develop clinical thyroid dysfunction in the future. Studies involving large sample size with control group and with long term follow up to determine the association between alopecia areata and thyroid dysfunction are required. Thyroid autoantibodies may be detected in euthyroid AA subjects. These should be followed up for early detection of thyroid dysfunction.

KEYWORDS: Alopecia areata, thyroid, autoimmune.

INTRODUCTION

Alopecia Areata (AA) is a common hair loss condition with a lifetime prevalence of approximately 2%[1] characterized by acute onset of non-scarring hair loss in usually sharply defined areas.[2] Any hair-bearing area can be affected, but the most noticeable are the scalp, the beard area and the eyebrows.[3] The most frequent clinical presentation of AA is in the form of single or multiple patches. The characteristic patch of AA is usually round or oval, and is completely bald and smooth. By the nature of its autoimmune origin, AA tends to be a chronic and recurrent disease. A large surface area, a long disease duration and associated nail abnormalities have a negative impact on prognosis, as well as co-morbidities and other atopic diseases.[4]

AA may be related to stress, excessive anxiety, autoimmune disorders and genetic factors.[5] It is often associated with lupus erythematosus, vitiligo, autoimmune hemolytic anaemia, allergic rhinitis, asthma, and atopic dermatitis. Among various autoimmune disorders AA is most commonly associated with vitiligo, atopy, Hashimoto's thyroiditis, diabetes mellitus, psoriasis, celiac disease and lupus erythematosus.[6] Among all these, thyroid disorders, especially hypothyroidism and vitiligo have the strongest association.[7]

Thyroid hormones have been shown to be necessary for the initiation and maintenance of hair growth as well as normal secretion of sebum. It is an important organizer of epidermal homeostasis.[8] In tissue culture studies

using replacement for DNA expression, T3 has been shown to catalyze growth of both epidermal keratinocytes and dermal fibroblasts, also thyroid hormone is vital for both maintenance and initiation of hair growth and normal secretion of sebum.[9] The prevalence of thyroid disease in patients with AA ranges from 8% to 28%. In recent years, research between correlation of AA and thyroid disease has increased and researches have been directing more attention towards this topic.[10] For example, Seyrafi et al. found thyroid function abnormalities in 8.9% of patients and positive autoimmune antibodies associated with AA in 51.4% of patients.[11]

Treatment options for AA include topical, locally injected or systemic steroids, topical immunotherapy, topical minoxidil, topical irritants such as anthralin and systemic immune-suppressants such as cyclosporine or methotrexate.[12,13] Psychosocial support and therapy is also an important part of disease management.[14,15,16]

There have been no studies showing significant association between severity of AA and presence of thyroid dysfunction. Proving this association may help understand the pathophysiological mechanisms thereby providing screening and help reduce the systemic side effects of the disease. Therefore, the current study was aimed to find the association between Alopecia Areata and thyroid related disorders.

MATERIALS AND METHODS

This was a Cross-sectional study conducted in a tertiary care centre, over a period of two years after approval from the Institutional Ethics Committee. The study population included 100 patients aged between 7 to 70 years with clinically diagnosed Alopecia Areata enrolled randomly from the dermatology outpatient department. All consenting patients aged between 7 to 70 years, of both the sexes, with clinically diagnosed Alopecia Areata attending skin OPD, patients belonging to paediatric age group with consent from both the parents and children was obtained were included in the study. Patients with other autoimmune disorders and those on systemic steroids were excluded from the study.

A detailed history including age of onset, duration site, pattern, type and extent of alopecia areata was noted. The severity of alopecia areata was graded according to Kavak et al.,[1] into:

Mild: The presence of three or less patches of alopecia with a widest diameter of 3 cm or less, or the disease is limited to the eyelashes and eyebrows.

Moderate: Existence of more than three patches of alopecia, or a patch greater than 3 cm at the widest diameter without alopecia totalis or alopecia universalis.

Severe: Alopecia totalis or alopecia universalis.

Blood was collected for estimation of T3, T4, TSH and Anti-Thyroid Peroxidase and Anti thyroglobulin antibodies. T3, T4, TSH, Anti-Thyroid peroxidase and Antithyroglobulin antibody levels were assessed by chemiluminescence immunoassay and association between alopecia areata and thyroid dysfunction was evaluated.

Laboratory Evaluation

For each patient, the following laboratory parameters were examined:

FT4 (free thyroxine; normal range: 9.3–17 pg/ml),

FT3 (free triiodothyronine; normal range: 1.8–4.6 pg/ml),

TSH (thyroid-stimulating hormone; normal range: 0.2–5 ÌU/ml),

Antibodies against thyroperoxidase (anti-TPO Ab).

Anti Thyroglobulin antibodies (anti TG Ab)

Both, hormones and antibodies were measured by immunoassay in electro chemiluminescence. Hormone levels exceeding the established range were considered pathological. Anti-TPO Ab titre exceeding 35 units/L were considered elevated and Anti TG Ab above 20 units/L was considered to be positive.

Statistical method

Data was analyzed using SPSS version 24. Categorical data was analyzed using percentages while continuous data was analyzed using standard deviation and mean. A chi-square test was conducted to determine the association between patient characteristics and outcomes.

OBSERVATION AND RESULTS

The age-wise distribution of alopecia areata is shown in table 1. The average age of Alopecia areata patients was 29.8±11.1, with the majority of participants being between the ages of 21 to 30 (31%), and between the ages of 31 to 40 (31%).

Table 1: Age distribution among study population.

Age Distribution	%
1-10	5
11-20	19
21-30	31
31-40	31
41-50	9
51-60	5
Mean±SD	**29.8±11.1**

As demonstrated in figure 1, males outnumbered females in the gender distribution (69% to 31%). The male-to-female ratio was 2:1.

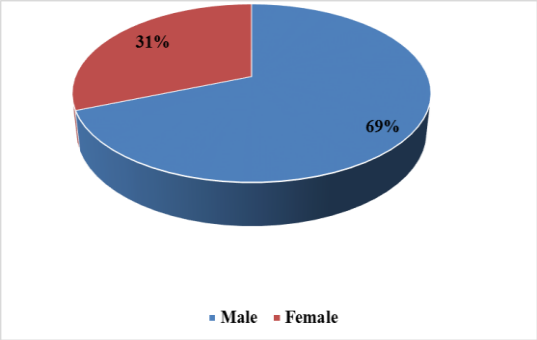

Figure 1: Gender distribution among study population.

The mean weight of the study population was 71.9±14.8 Kg. Thirty six percent of the individuals weighed between70-80 kg.

Age of onset of the disease in our study ranged widely between 7 to 60 years. The mean age of onset was 29.0±10.1 years.The disease duration ranged from 1 month to 3 years with the majority (79%) showing less than 1 year duration of onset. Seventy nine patients (79%) experienced the duration of onset of AA below one year.

History of atopy (Allergic rhinitis / recurrent dermatitis / hay fever/ asthma) was present in 60% of the study population and positive family history of AA was noted in 83% of the participants. Fifty four percent of the participants gave positive family history of other autoimmune disorders such as Diabetes mellitus, Rheumatoid arthritis and vitiligo. A majority of participants, 78% showed history of DM.

Scalp was the commonest area involved in 76 participants and next commonest site involved was the beard region seen in 22 participants [table 2]. One participant had only eyebrow lesion. One participant had lesions over scalp and beard

Table 2: Site of involvement of AA.

TYPE AA	%
SCALP	75
BEARD	22
EYEBROW	1
SCALP & EYEBROW	1
SCALP & BEARD	1

The majority of participants with scalp involvement (19%) had parietal lesions, followed by parietal+occipital lesions (11%), and frontal+parietal lesions (10%). One person had a temporal lesion and another had a temporal+parietal lesion as depicted in Figure 2.

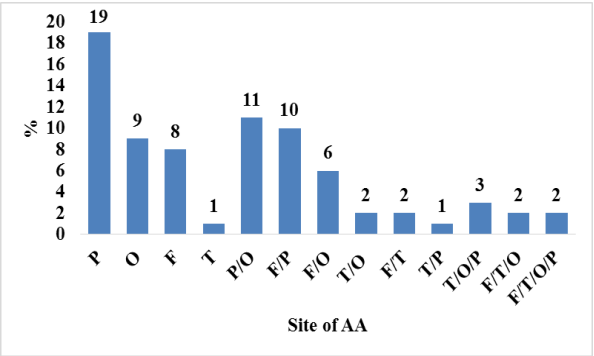

Figure 2: Scalp site of AA.

Number of lesions according to SALT scoring, ranged from from 1 to 100. The majority of the participants (57%) had single lesion, 37% had 2 to 5 lesions and remaining 6 % of participants had more than 5 lesions.

Patchy pattern of AA was the most common type noted in this study in 69 participants. Followed by diffuse type in 26 participants, ophiasis was noted in 3 participants and totalis in 2 participants as shown in figure 3. We have not encountered Reticular and perinevoid pattern in this study.

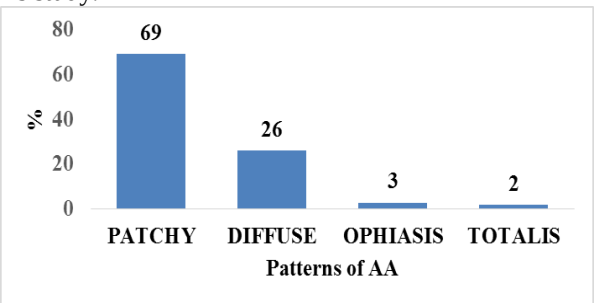

Figure 3: Patterns of AA.

Positive nail changes were noted in 13 % of the participants only. 8 patients had pitting, 2 patients had onycholysis, 1 patients had leukonychia and 1 patient had both pitting and onycholysis.

Nighty nine (99%) cases showed normal value (3.5–6.5 pmol/L) of FT3 and 98 (98%) cases showed normal value (7–17 pmol/L) of FT4. Only one case (1%) had below normal FT3 and 2 cases (2%) had below normal FT4.

The TSH value was within normal range in all the 100 participants (100%). Normal range of TPO Antibodies was considered negative and above normal range of Anti TPO Antibodies was considered positive. TPO-Ab was positive in 57% cases and TPO Ab was negative in 43% cases as shown in Figure 4.

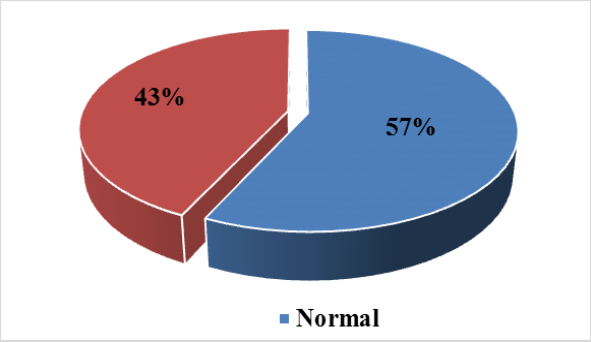

Figure 4: Anti TPO Ab.

Normal range of Anti thyroglobulin level was considered negative and above normal Anti thyroglobulin antibodies was considered positive. TG-Ab were positive in 69% cases as shown in figure 5.

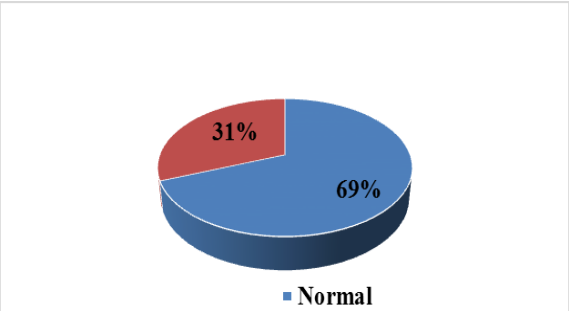

Figure 5: Anti-TG Ab.

Anti TPO Ab positivity was more frequently observed among 31-40 age group and was detected in 15 out of 31 participants in this age group. Anti TG Ab positivity was also more frequently encountered in the 31-40 age group and was detected in 11 out of 31 participants in this age group. Mostly mild severity was seen among the cases nearly 92% out of 100 cases. More cases of elevated Anti TPO Ab were observed in mild category. Most cases of elevated Anti TG were seen in mild category.

DISCUSSION

Alopecia is an ancient disease and was known to Egyptians even before Christ.[17] Despite its long history, our knowledge is actually limited. Generally, significant differences have been identified in the profile of the disease among different societies.[18]

Age

Alopecia areata can occur at any ages from infancy to old age, the first attack is most commonly seen between the age of 5 and 40 years and accounts for 70 to 80% of cases.[19] The onset of alopecia areata may be at any age, peaking between second and fourth decades. In our study, the commonest age group of occurrence was 21-30 and 31-40 years, both accounting to 31% each (Table 1). The next common age group in our study was 11-20 years accounting to 19% similar to the study of Gopal et al, 2013.[20] The maximum incidence of alopecia areata was in the age group of 20-40 years (50.4%). In Bakry et al study found that more number of patients with complaints of alopecia was seen in the 6-50 age groups[11] and Alhasan et al 72 cases with age ranging from (10-50 years).[21]

Gender

Previous studies have revealed that AA affects both sexes equally with females slightly more predominated[22]; In our study noted a male preponderance with male: female ratio (2.5:1) (Figure 1). Similar male preponderance was noted in the study done by Bakry et al (35 males and 15 females) and Alhasan et al (27 males and 15 female)[11,21] But a female predominance was observed by Park et al (592 males and 816 female).[23]

Associated family history and Atopy

In our study, family history of alopecia areata was seen in 83% cases. Meanwhile 60% of patients were associated with family history of atopy. Family history of diabetes mellitus was seen in 78% cases and other autoimmune disorders in 54% cases. Thus AA could be associated with other autoimmune disorders. But further studies are needed in this regard. There are several reports of occurrence of alopecia areata in families and in twins at the same site and also the onset of time being the same. Percentage of family history ranges from 10-27% as per Dan A. Nelson et al in their study.[24] Muller and Winkelmann and Ikeda have stated that patients of alopecia areata with atopy have earlier age of onset with severe form and longer duration of disease, but compared to these observations, we observed no relationship of associated atopic disorders with age of onset and severity of disease as 12 patients who had associated atopy had mild to moderate type of AA as compared to 3 patients who exhibited ophiasic patterns.[25] Park et al investigated the prognostic clinical features of AA, including personal or family history of AA and history of atopy which was not statistically significant.[24]

Patterns of AA

Patchy type of AA was the most commonest encountered in this study (69%) (Figure 3). In the previous studies, the frequency of patchy AA among patients with AA has been determined ranging from 23% to 86%.[26] This rate was reported to be 43.9% by Seyrafi et al.[22] and 86% by Gönül et al.[27]

Single patch was encountered in 57% of AA patients and multiple patches in the remaining 43% of participants in the present study. In the study by Gönül et al.,[27] of the AA patients, 46% had multiple patchy lesions and 42% had a single patchy lesion. In another study by Kakourou T et al,[28] the rate of single patchy type was found to be 23%, whereas the rate of multiple patchy types was found to be 63%.Thus in previous studies multiple patches were encountered more than the single patch.

Nail involvement in alopecia areata

In our study, nail involvement was seen in 13% cases. Nail pitting was the commonest finding(8 %) followed

by onycholysis (2%), leukonychia (1%) and both pitting and onycholysis(1%). King Muller and Read[25] conducted a study in 736 patients and noted pitting in 66% and leukonychia in 5.8% cases. A review found that 86% were free from nail involvement.[28]

Site involvement

In our study, alopecia areata was seen mostly in the scalp (76%) (Table 2) with the most common site affected being the parietal region (19%) (Figure 2).Our result was consistent with the study done by Muller and Winkelman's[25], who noted scalp involvement in 95% of patients, commonest area being the Parietal area. Beard involvement was noted in 22 % of patients in our study whereas Awachat AK et al[29] noted beard involvement in 12% of his cases. In our study scalp and beard were the commonest area involved over the face. Eyebrows were involved in 1% of cases. Rahnama et al[30] observed involvement of Scalp in 50 participants (96%), Eyebrows in 5 (9.6%) and beard area in 17 (33%),

FT3 and FT4

Patients with AA should be screened for thyroid functional abnormalities even in absence of manifestations of hypothyroidism. Some investigators recommended the assessment of thyroid gland size and function every six months as this will contribute to the early detection of autoimmune thyroiditis amongst patients with AA, preventing further evolution to severe hypothyroidism.[28]

Hypothyroidism is defined by low levels of free T3 & free T4, whereas subclinical hypothyroidism is defined by elevated TSH in the presence of normal free T3 and T4 levels. In our study 3 patients (3%) had hypothyroidism as defined by low T3 & T4 levels.and normal TSH levels. None of our patients had deranged TSH levels. In the study by Vanderpump et al[31], low T3 was noted in 7 (14%) patients in case group and 2 (3.7%) patients in control group and there was no difference in the rate of dysfunction of T4 in the two groups. Kakourou et al.[28] noted subclinical hypothyroidism in 5% of his 157 AA patients.

A higher frequency of hypothyroism was noted among AA patients by few authors. Thomas and Kadyan[32] reported hypothyroidism as the most frequent form of thyroid function abnormalities associated with AA (14.1%). Kasumagić-Halilović[33] observed hypothyroidism in 11.4% of AA patients and Seyrafi et al.,[22] observed hypothyroism in 8.9 % of his patients.

Our study found a low frequency of thyroid disorder (3%) among AA patients. Similar low frequency was reported by Kakourou et al[28] who noted a frequency of 5% in his study of AA patients. Similarly, Puavilai et al[34] reported that the prevalence of thyroid disease in patients with AA was relatively low (7.2%) with non-significant difference between patients and controls.

Also, in one of the largest sample study, Park and colleagues evaluated 1408 patients and observed an increased incidence of thyroid dysfunction and thyroid autoimmunity in AA patients, particularly in those having severe AA.[23]

Anti TPO Ab and anti-TG (Figure 4,5)

Studies	Elevated level (%)	
	Tg-Ab	TPO-Ab
Present study	**31**	**43**
Nanda et al.,[18]	31	-
Seyrafi et al.[22]	29.3	51
Korkij et al.,[35]	28	43
Kasumagić-Halilović[33]	23.7	23.7
Grandolfo et al.,[36]	44	44
Saif[37]	-	22

In this study Anti TPO antibodies was found to be positive in 43% and anti-thyroglobulin antibodies was found to be positive in 31% of the study participants. We also found that there was a significant positive correlation between increasing age and TPO-Ab positivity whereas Anti TG positivity was observed more frequently in younger age group

The prevalence of Thyroglobulin antibodies (Tg-Ab) in our study was more or less consistent with the studies done by Nanda et al.[18] who identified Tg-Ab in 31% of his patients and by Seyrafi et al.[22] observed serum Tg-Ab in 29.3% of their patients.Similarly, Korkij et al.[35] detected Tg-Ab in 28% of AA cases. A slightly higher percentage of Tg Ab of 39.5% was noted by Kurtev and Ilev[38] in their study.

TPO-Ab were elevated than normal in 43 patients (43%) with AA in our study. Korkij et al.[39] also noted similar result of 43% of TPO-ab positivity in their study. A 44% TPO-Ab positivity was noted by Grandolfo et al.[40] in their study and found both TG- Ab and TPO Ab more frequently in patients with AA than healthy controls. A higher percentage of TPO Ab of 51% was noted by Syerafi et al.[22] Kasumagić-Halilović[36] detected the frequency of TPO-Ab in AA to be 23.7% that was significantly higher when compared to healthy controls. However, Cunliffe et al.[41] and Puavilai et al.[34] reported that there were no significant differences between patients with AA and control subjects regarding the presence of Tg-Ab and TPO-Ab.

Vanderpump et al.,[31] concluded that the presence of TPO-Ab was strongly associated with thyroid failure during 20 years follow up of TPO-Ab positive euthyroid individuals. TPO-Ab correlated more clearly with altered thyroid functions than Tg-Ab.[32] Therefore, determination of TPO-Ab status seems useful as first triage to select subjects out of a population in whom subsequent TSH testing and follow-up is clinically relevant. These include patients with family history of autoimmune thyroid disorders, patients with other autoimmune disorders and females before and during

pregnancy.[42] Thyroid dysfunction is more common in women, and is of particular concern in women in reproductive age because abnormal maternal thyroid function during pregnancy has been associated with a wide variety of adverse maternal/fetal outcomes, including increased risk of pre-term birth, miscarriage, fetal death, impaired neuro-psychological development of the child as well as maternal post-partum thyroiditis.[43,40]

Taken together, thyroid antibodies are means to identify a certain number of subjects whose thyroid function is completely normal but are at risk of thyroid dysfunction. So it's of particular importance to follow up AA patients and positive thyroid antibodies. These subjects do not require any treatment but need to be followed up by TSH assay and morphological evaluation of the thyroid gland by ultrasonography to demonstrate an ongoing autoimmune thyroiditis even before modifications of thyroid function.[40,41]

Thomas and Kadyan[44] explained the association between AA and thyroid autoimmunity by the formation of organ specific autoantibodies that play a pathogenic role in both disorders.

Severity

Anti TPO and anti-TG antibodies were found more frequently in the mild category of AA in our study (Figure 8,9). This maybe because majority of the participants (92%) belong to the mild category of AA in our study.

To the best of our knowledge no comparative studies have been done comparing the severity of alopecia areata and the levels of auto antibodies. Additional nationwide, ethnic studies should be performed in order to further investigate the correlation.

CONCLUSION

Longer follow ups are needed to observe if AA patients develop clinical thyroid dysfunction in the future. Studies involving large sample size with control group and with long term follow up to determine the association between alopecia areata and thyroid dysfunction are required.

Limitations: Lack of control group, small sample size and lack of long term follow up could be a cause of negative findings of the study.

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