Alopecia Areata and Thyroid Dysfunction Association- A Study from Eastern Nepal

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ABSTRACT

Background

Alopecia areata (AA) is one of the non-scarring alopecia. Its etiology has not been well established till date. The most convincing hypothesis is autoimmune process for its causation. Amongst all, most frequent association was found with thyroid disorder.

Objective

To study the association of thyroid dysfunction in patients with alopecia areata.

Method

All patients of alopecia areata attending dermatology outpatient department and currently not receiving any treatment for alopecia areata were enrolled in the study. Relevant history and examination findings were recorded in the preset pro-forma. All of them were subjected for thyroid function test by chemiluminescence microparticle immunoassay method. Then thyroid function test of cases was compared with that of equal number of age and sex matched healthy controls.

Result

A total of 75 patients were enrolled in both case and control groups. Mean age of case and control groups were 29.40±9.90 and 28.96±9.89 years respectively (P=0.786). Median Severity of Alopecia Tool score was 2.47 (IQR=0.96-5.79). Prevalence of thyroid disorder was significantly higher in alopecia areata group (17.3%) as compared to the control group (1.3%) (P=0.001). Likewise, in individuals with abnormal thyroid function, alopecia areata disease severity grade and median severity of alopecia tool (SALT) score was higher as compared to those with normal thyroid function.

Conclusion

We found a significant association between alopecia areata and thyroid dysfunction. Hence thyroid function evaluation must be considered in individuals with alopecia areata. However, further studies with larger sample size are recommended before its generalization.

KEY WORDS

Alopecia areata, Severity of alopecia tool score, Thyroid function test

INTRODUCTION

Alopecia areata (AA) is a common cause of non-scarring alopecia. Its frequency ranges from 0.7-3.8% of patients attending the dermatology clinics.[1,2] The cause of AA has not been well explained. Out of many proposed pathogenic processes, autoimmune mechanism holds stronger and convincing evidence.[3] Autoimmune diseases were found in 56% of AA patients in the report by Goh et al. In which, thyroid disease was the second most common association (19%) after atopy.[4]

Frequency of thyroid dysfunction in AA patients varies from 7 to 24% in different studies.[5,6] Prevalence of thyroid disease was only 7% in a study by Puavilai et al. with no significance difference between AA and control group.[5] It was 8.9% in a study from Pakistan and 18.3% in a study from India.[7] Likewise, subclinical hypothyroidism was detected in 16% of AA patients in a report from Egypt.[8] Till now, highest prevalence (24%) has been reported from an Australian study.[6] Till date, only few studies have evaluated the association between AA severity and thyroid dysfunction; and they have reported that individuals with severe AA had higher frequency of thyroid disorder.[4,7,9] However, we couldn't find any published studies from Nepal on this matter. Hence, we assessed thyroid function in AA patients and compared it with an equal number of controls in a tertiary referral hospital of eastern Nepal. Likewise, we also studied the relation between thyroid dysfunction and AA severity.

METHODS

This was a case-control study done over a year period, from August 2015 to July 2016 in the dermatology outpatient clinic of BPKIHS, Dharan, Nepal. Ethical clearance was obtained from institutional research committee (IRC No./584/015). All new patients of AA giving voluntary consent were enrolled in the study. However, those patients not willing to participate in the study, diagnosed case of thyroid disorder, age <14 years, pregnant females, any patients on treatment for AA (either topical or systemic) within last one month were excluded from the study.

After written consent, data were collected in the pre-set pro-forma. All patients were diagnosed clinically by the consultant dermatologist of the department and skin biopsy was considered in doubtful cases. A complete medical history, including the patient's age, sex and associated diseases, including history of thyroid disorders were noted. Similarly detail history regarding the onset, course and duration of the disease, past and family history of AA were also elicited.

Physical examinations were performed in all patients with special attention to the extent and pattern of the AA at the first visit. The severity of AA was graded into: mild, moderate, severe and snake shaped plaques extending to the scalp border or loss of hair in the shape of a wave at the circumference of head defined as ophiasis, as proposed by Kavak et al.[10]

Global AA severity score or severity of alopecia tool (SALT) was calculated in all patients as per standard protocol.[11]

Laboratory evaluations including thyroid function tests (TFT), which included, serum levels of free triiodothyronine (FT3), free thyroxine (FT4), and thyroid stimulating hormone (TSH), were done in every patient by, chemiluminescence microparticle immunoassay method using Maglumi 1000. Normal range for each entity was taken as: FT3=0.69-2.02 ng/ml, FT4=4.4-11.6 µg/dl and TSH=0.4-6.2 microIU/L. Interpretation of TFT report was done as: 1) TSH >6.2-10 microIU/L, with normal T3 and T4: Subclinical hypothyroidism, 2) Decreased T3, T4 with raised TSH: Hypothyroidism, 3) Decreased TSH (<0.4 micro IU/L) with normal T3 and T4: Subclinical hyperthyroidism 3) Raised T3, T4 and decreased TSH: Hyperthyroidism. Other investigations were considered only for management purpose if indicated. For the control group, age and sex matched healthy individuals were taken and all of them were also subjected for TFT analysis in the same way as cases.

All patients were treated according to standard treatment protocol for AA. Patients with abnormal TFT report were referred to department of Internal Medicine for further management.

Statistical Analysis was done using SPSS version 11.5. For descriptive statistics percentage, proportion, mean, median, standard deviation, inter quartile range were calculated, whereas for inferential statistics, chi-square test, independent t-test and kruskal-wallis test were calculated at 95% CI and p=0.05.

RESULTS

Clinico-epidemiological profiles: A total of 75 patients were enrolled in both case and control groups. Mean age of case and control group were 29.40±9.90 and 28.96±9.89 years respectively (P=0.786). Male and female in the AA group were 40 (53.3%) and 35 (46.7%) with male: female ratio being 1.14:1. Similarly, male and female in the control group were 39 (49.4%) and 36 (50.7%) with male and female ratio of 1.08 (P=0.870). In AA group, female (22.9%) had more TFT abnormality as compared to male (12.5%). Similarly, higher percentage of TFT abnormality (37.5%) was found in age group of 42-56 years; however they were statistically not significant (P=0.237 and 0.578 respectively) (table 1).

Many of the AA patients had personal history of atopy (22/75, 29.33%). Maximum of them had allergic rhinitis in 72.72% (16/22), followed by bronchial asthma in 40.90% (9/22) individuals. Only six patients (6/75, 8%) had positive family history of AA. Few of the AA patients (16%, 12/75) also pointed out some triggering factors for hair loss, and most of them being hair care products like hair oil, gel and shampoo.

Table 1. Thyroid function test findings of AA patients in different age and gender

Characteristics		Thyroid Function Test		P-value
		Normal	Abnormal	
Gender (n=75)	Male	**35 (87.5%)**	**5 (12.5%)**	**0.237** (Chi-square test)
	Female	**27 (77.1%)**	**8 (22.9%)**	
Age group (years) (n=75)	14-28	**28 (82.4%)**	**6 (17.6%)**	**0.578** (Chi-square test)
	28-42	**26 (86.7%)**	**4 (13.3%)**	
	42-56	**8 (62.5%)**	**3 (37.5%)**	

Median disease duration was two months (IQR=1-5) and median number of AA lesions were two (IQR=1-4). Median Severity of Alopecia Tool (SALT) score was 2.47 (IQR=0.96-5.79). Most of them (41%) had moderate AA severity grade (fig. 1), followed by mild in 32% and snake shaped pattern (ophiasis) in 27%. However, severe AA was not found in our patients. Histopathological findings of the cases have been shown in fig. 2.

Figure 1. Moderate AA [Scalp involvement (left), Beard involvement (right)]

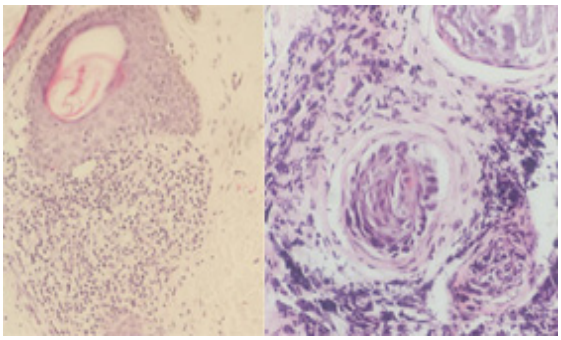

Figure 2. 10X, vertical section (left) and 40X, Horizontal section (right): Dense perifollicular lymphocytic infiltrate

Thyroid Function Test: TFT was abnormal in 17.3% (13/75) patients in the case group. Out of them, 12 had sub-clinical hypothyroidism and only one had hyperthyroidism. Prevalence of abnormal thyroid function was significantly higher in AA group (17.3%) compared to the control group (1.3%) (P=0.001) (table 2).

Relation between TFT and AA Severity: The median SALT score was more in patients with abnormal TFT compared to the normal TFT; however they were statistically not significant (p=0.195) (table 3). Similarly, prevalence of abnormal TFT was increased once the AA disease severity grade was increased but they were statistically not significant (p=0.217) (table 4).

Table 2. Prevalence of abnormal thyroid function

Thyroid Function Test	Case group (n=75)	Control group (n=75)	P-value
Normal	**62 (82.7%)**	**74 (98.7%)**	0.001 (Chi-square test)
Abnormal	**13 (17.3%)**	**1 (1.3%)**	

Table 3. Relation between TFT and SALT score

Thyroid Function Test	SALT Score (Median, IQR)	P-value
Normal	**2.16 (IQR:0.9-5.20)**	0.195 (Kruskal-wallis test)
Abnormal	**3.5 (IQR:1.08-9.01)**	

Table 4. Relation between TFT and grade of AA

Grade of AA	Thyroid Function Test		P-value
	Normal (n=62)	Abnormal (n=13)	0.217 (t-test)
Mild	**21 (87.5%)**	**3 (12.5%)**	
Moderate	**27 (87.1%)**	**4(12.9%)**	
Snake shaped plaque (Ophiasis)	**14 (70.0%)**	**6(30.0%)**	

DISCUSSION

Although many different pathogenic causes have been proposed, the determination of the exact underlying etiology of AA is extremely problematic.[12,13] Hedstrand et al. and Roselino et al. in their different studies, explained immunological, psychological, environmental and genetic factors for its causation, the most relevant cause is yet to be identified.[12,13] There are lots of evidences concerning the contribution of autoimmune processes in the pathogenesis of AA and they are more convincing too.[14] Abnormal accumulation of C3, IgG and IgM occurs in the hair follicles along with decreased and disturbed T lymphocyte function of the affected regions in AA suggesting strong immunologic mechanism for its causation. Which shows both humoral and T-cell mediated immune alteration. Amongst all autoimmune diseases, autoimmune thyroid dysfunction is the one in which both mechanisms play an important role unlike other autoimmune diseases, where primary pathogenesis revolves around T-cell mediated immunity.[15,16] Also, this hypothesis has been supported by many past studies.[4,17] Hence to see the AA and thyroid dysfunction association we did this study in tertiary referral hospital of eastern Nepal.

We studied 75 AA patients over a year period. Mean age of patients was 29.40±9.90 years with median disease duration 2 months (IQR=1-5). Median Severity of Alopecia Tool (SALT) score was 2.47 (IQR=0.96-5.79). In our study, many AA patients had personal history of atopy (22/75, 29.33%). Maximum of them had allergic rhinitis in 72.72% (16/22), followed by bronchial asthma in 40.90% (9/22)

individuals. Similarly, in Goh et al. study (USA), atopy was most frequent association (46%) amongst AA patients.[4]

Most of our patients had mild and moderate (32 and 41%) AA severity grade, which is comparable to other studies.[7,9] In the study by Ahmed et al. severe AA was present in 17% patients and ophiasis was present only in 1.8% of the patients.[7] However, in our study ophiasis was present in a larger number of patients (27%) whereas, severe AA was not present in any of them.

Prevalence of abnormal thyroid function was significantly higher in AA group (17.3%) compared to the control group (1.3%) (P=0.001). Similar to our study, a study from India also observed that the thyroid disorder was the systemic disease with highest frequency (18.3%) in AA patients.[9] Likewise, a recent Australian study also reported that almost one fourth (24%) of AA patients had thyroid abnormalities.[6] Thyroid dysfunction was also found in AA patients in a study done in Pakistan but its prevalence was half (8.9%) as compared to our study.[7]

Almost all of our AA patients with thyroid dysfunction had hypothyroidism. Among 13 (17.3%) AA patients 12 (16%) had hypothyroidsm, to be specific, all of them had subclinical hypothyroidism; and only one patient (1.3%) had hyperthyroidism. Our finding of thyroid dysfunction status is comparable to the previous study by Lyakhovitsky et al. in which, the hypothyroidism was more frequent among AA patients. In that study, out of 78 AA patients, 15 (19%) had thyroid dysfunction; and of those 15 patients, 14 (18%) had hypothyroidism and one (1%) had hyperthyroidism.[6] Similarly, in a study by Ahmed et al. out of 10 AA patients with thyroid dysfunction, most of them (9; 90%) had hypothyroidism and only one (10%) had hyperthyroidism.[16] Similar was the finding in an Egyptian study with 16% prevalence of subclinical hypothyroidism in AA patients.[8] In contrast to our study, prevalence of thyroid dysfunction was almost half (8.9%) as compared to our study in the report by Ahmed et al from Pakistan and Seyrafi et al. from Iran.[7,18]

When we co-related AA severity and TFT, ophiasis type of AA has maximum TFT abnormality (6/13, 46%) followed by moderate (4/13, 31%) and mild (3/13, 23%) grades of AA. In a previous study, out of 10 patients with thyroid dysfunction, most of them (40%) had more severe and other clinical pattern of AA. Similarly equal distribution of mild and moderate AA grade was found in remaining 60% of the AA patients.[7] Likewise, in a study by Thomas et al. higher percentage of AA patients (69.23%), with thyroid disorders had moderate to severe type of AA; which was chronic and recurrent also.[9] Similarly in a study from USA, alopecia totalis and universalis were significantly more in patients with thyroid disease. Out of 207 alopecia totalis and universalis patients, 52 (25.12%) had thyroid disease. However among 295 patchy AA patients, 46 had thyroid disease (15.59%). Similarly 16% patients with persistent patchy AA had associated thyroid abnormalities.[4]

In our study, the prevalence of abnormal TFT was increased once the AA severity grade got increased (table 4). Similarly, SALT score was more in individuals with abnormal TFT as compared to those with normal TFT (table 3). But both of them were statistically not significant. The reason could be because of less number of patients in individual subgroup of AA. So, we need further studies with larger sample size to see the exact association of AA severity and abnormal TFT.

There are few limitations in our study, they are: small sample size, unavailability of dermoscopic evaluation, and inability to assess antithyroid antibody level in our subjects because of feasibility factor and financial constrain. Similarly, different organ-system specific symptoms of thyroid dysfunction have not been evaluated in this study. Also, since our study is mono-centered study, that can also affect generalization of the obtained results.

CONCLUSION

There is significant association of alopecia areata with thyroid dysfunction, as evidenced by increased prevalence of thyroid dysfunction in individuals with alopecia areata compared to the healthy controls. Though thyroid dysfunction was more in individuals with severe form of alopecia areata, it was statistically not significant. Since there are no published studies on related topic from Nepal till date, we need further studies with larger sample size and even multi-centered studies, if possible to see the association of thyroid dysfunction with alopecia areata disease severity.

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