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Association of Alopecia Areata with other Autoimmune Diseases: A Cross- Sectional Study in Western Nepal

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ABSTRACT

Introduction: Alopecia areata (AA) is a common chronic inflammatory disease that causes nonscarring hair loss. The severity ranges from small patches of hair loss which usually recover spontaneously, to complete alopecia where the prognosis for hair regrowth is poor.[1] AA has affected approximately 2% of the general population [2,3]. The estimated lifetime risk in the general population is 2%. [4] The prevalence rate of AA is around 0.1 to 0.2%.[5]

Methods: A single centered, hospital based, prospective cross-sectional analytical study was conducted in the Department of Dermatology of Manipal Teaching Hospital. The study was conducted from July 2023 to December 2023 after the permission of Institutional Research Committee (Reference ID: MCOMS/IRC/575/GA) and obtaining written and informed consent from the patients. We recruited 39 patients with diagnosis of alopecia areata who presented to the Department of Dermatology during the study period. Sampling was done by non-probability convenience method. Data were applied with appropriate statistical tests, results with p value <0.05 were considered significant.

Results: There was a total of 39 patients of which 56.4% (22) were females and 43.6% (17) were males. The patient's ages ranged from 8 years to 65 years with mean age being 32.49 ± 13.51years. Patients were classified according to the severity of the disease. Among 39 patients, 30 (76.8%) had mild disease, seven (17.9%) had moderate and two (5.1%) of them had severe disease. In our study we could not find statistically significant association between alopecia areata and other autoimmune diseases such as diabetes mellitus, thyroid abnormality, vitiligo and atopy.

Conclusions: In this study there was no significant association between alopecia areata and other autoimmune disorders like diabetes mellitus, thyroid dysfunction, anaemia, atopy and vitiligo. The lack of significant association in our study doesn't exclude the importance of screening of these diseases in a patient with alopecia areata.

Keywords: *Alopecia Areata; autoimmune diseases; diabetes mellitus; hyperthyroidism; hypothyroidism.*

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INTRODUCTION

Alopecia areata (AA) is a common chronic inflammatory disease that causes nonscarring hair loss. The severity ranges from small patches of hair loss which usually recover spontaneously, to complete alopecia where the prognosis for hair regrowth is poor.[1] AA has affected approximately 2% of the general population [2,3]. The estimated lifetime risk in the general population is 2%. [4] The prevalence rate of AA is around 0.1 to 0.2%.[5]

There have been reports of the association of AA with the other autoimmune diseases including hypethyroidism diabetes mellitus, vitiligo, Addison's disease, pernicious anaemia. [6-9] The association between AA and atopic dermatitis has been reported. [10,11] Atopy increases the risk of developing alopecia areata.[12] On the basis of patterns it can be classified as reticular, ophiasis, sisaipho, linear and perinevoid types. [6,13]

The primary objective of the study was to find out the associations of other autoimmune diseases in patients of alopecia areata.

METHODS

A single centered, hospital based, prospective cross-sectional analytical study was conducted in the Department of Dermatology of Manipal Teaching Hospital. The study was conducted from July 2023 to December 2023 after the permission of Institutional Research Committee (Reference ID: MCOMS/IRC/575/GA) and obtaining written and informed consent from the patients.

We recruited 39 patients with diagnosis of alopecia areata who presented to the Department of Dermatology during the study period. Sampling was done by non-probability convenience method. Patients of all ages and both sex with clinically diagnosed alopecia areata were included in the study whereas pregnant female, patient of alopecia under chemotherapy and those having telogen effluvium simultaneously were excluded.

Alopecia areata was classified as mild, moderate and severe. Mild disease included hairless patches less than 3 cm in diameter and less than 3 patches or limited to eyebrows and eyelashes. Moderate disease included more than 3 patches of alopecia or at least a patch more than 3 cm in diameter. Severe disease involved either alopecia totalis or alopecia universalis.[13]

In case of difficulty in diagnosis dermatoscope was used to rule out other differential diagnosis such as, telogen effluvium, trichotillomania, androgenetic alopecia. In order to find out other autoimmune associations we measured Hemoglobin (Hb), Erythrocyte sedimentation rate (ESR) serum Thyroid stimulating hormone (TSH), Beta-N-1-deoxyfructosyl haemoglobin (HbA1C), Random blood sugar (RBS) and Antinuclear antibody (ANA). Hemoglobin within the range of 12 to 15 gm/dl, ESR less than 20mm/hr, TSH within the range of 0.5 to 5mIU/L, HbA1C less than 5.7% and RBS less than140 mg/dl were considered normal. ANA value less than or equal to 1:40 dilution (or < 1.0 IU) was considered negative.

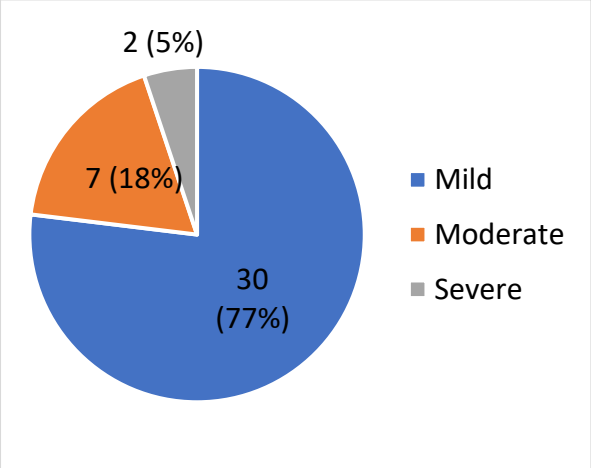
After completion of the data entry and all the consent form, we performed statistical analysis using SPSS version 25. For quantitative data we used t-test and for qualitative data chi-square was used. For quantitative data mean ± SD was written and for qualitative data percentage and numbers were written. P value of <0.05 was considered significant at the confidence interval of 95%.

RESULTS

There were a total of 39 patients of which 56.4% (22) were females and 43.6% (17) were males. The patient's ages ranged from 8 years to 65 years with mean age being 32.49 ± 13.51years. Patients were classified according to the severity of the disease. Among 39 patients, 30 (76.8%) had mild disease, seven (17.9%) had moderate and two (5.1%) of them had severe disease (Figure1). Similarly, six patients had ophiasis pattern of

alopecia, among which five patients had mild form of alopecia areata. Leukotrichia was detected in twelve patients, mostly associated with moderate form of the disease. 17(43.6%) out of 39 patients had mild to moderate psychosocial impact due to alopecia areata.

Figure 1: Distribution of the patients according to the severity of alopecia areata(n=39)



In our study, 3 patients (7.7%) showed low Hb level while other 3(7.7%) showed high Hb level which was not statistically significant. Similarly, 12 patients (31%) out of 39 had high ESR. High HbA1C was observed in 13 patients (33%), 4 (10%) of them had high RBS and high ANA was seen in 14(36%) patients. These findings were also not statistically significant. TSH was deranged only in 6 patients (15%) which statistically didn't indicate any association with AA. The relationship between different markers along with their respective p- values are listed in Table 1.

Table 1: Correlation of biochemical markers with severity of alopecia areata (n=39)

Markers	Number of patients n (%)		p-value
	Mild	Moderate/Severe	
Hb **Normal** **Deranged**	 25 (75.8%) 5 (83.3%)	 8 (24.2%) 1 (16.7%)	1.00
TSH **Normal** **Deranged**	 26 (78.8%) 4 (66.7%)	 7 (21.2%) 2 (33.3%)	0.60
HbA1C **Normal** **High**	 21 (80.8%) 9 (69.2%)	 5 (19.2%) 4 (30.8%)	0.44
RBS **Normal** **High**	 28 (80.0%) 2 (50.0%)	 7 (20.0%) 2 (50.0%)	0.23
ANA **Normal** **High**	 19 (76.0%) 11 (78.6%)	 6 (24.0%) 3 (21.4%)	 1.00

DISCUSSION

Alopecia areata (AA) is a common, chronic and inflammatory non-cicatricial cause of patchy or diffuse hair loss. It's etiopathogenesis is not well understood. In our study we could not find statistically significant association between alopecia areata and other autoimmune diseases such as diabetes mellitus, thyroid abnormality and atopy which could be due to small sample size of our study and because of the non-probability sampling or it could be just by chance. According to a study done in Nepal, thyroid disorder in AA is more common in female than male which was also observed in our study[14] In a recent study there was no significant association of thyroid dysfunction with severity of AA as shown in our study.[15] Similarly there was a significant correlation between alopecia areata and thyroid dysfunction in one study.[13] Since thyroid disorders are relatively common in our part of the world and if a person has one autoimmune disease he or she is more likely than others to develop some other autoimmune condition. Alopecia areata is an autoimmune condition that causes hair loss that occurs in people with autoimmune thyroid disease more often than expected by chance. Likewise, one study found almost one fourth patients of alopecia areata had thyroid disorders.[16] AA affects upto 2% of general population [2,3] with highest prevalence among patient aged 30 to 49 years [17] which is also consistent with our study. Many research papers show female predominance in the occurrence of AA and they are also more likely to have concomitant psychosocial effect more than male.[18] Different studies also suggest burden of AA more in Asian patients which signify relation of genetic and environmental factors in pathogenesis of AA. [17,18]

Collapse of hair follicle immunity is a major precondition for the development of AA which can be induced by inflammation leading to autoimmune responses against autoantigens expressed in the bulge area throughout the hair cycle.[19] A case report showed autoimmune process against hair follicles being a major pathogenic factor for the hair loss in the form of destruction of hair bulbs, lymphocytic infiltration into hair follicles and expression of HLA-DR antigen on epithelial cells of the follicles.[20] Understanding the etiology of AA will help to upgrade treatment and improve the prognosis of the disease.

In one study most common comorbid Autoimmune disease (AUD) in AA was found to be thyroid disease followed by vitiligo and systemic lupus erythematosus SLE.[21] Studies demonstrating both humoral and cell mediated autoimmune response in AA suggests its association with other autoimmune disease (AUD) with similar pathogenesis and also points to the coexistence of AUD and AA in a patient. AA has 16% greater risk for concurrently having or eventually developing other AUD. [22] Thus, this association warrants therapeutic regimens that will act on a particular AUD that will directly help in the treatment of AA. But there are not enough researches done regarding this association in our part of the world.[18] So, our study aimed to provide more data on the association of other AUD with AA. Diabetes mellitus (DM) was found to be the most frequent AUD in AA followed by atopic dermatitis, anemia and lastly thyroid disorders.[23] Hence these frequent associations focus on evaluation of AUD in individuals with alopecia areata and accordingly in our study we performed various laboratory investigations for the diagnosis of autoimmune disease in patient with AA. The lack of significant association in our study doesn't exclude the importance of screening of these diseases in a patient with AA because early diagnosis of AUD is critical from the perspective of cardiovascular and neuropsychiatric morbidities. This lack of association in our study could be due to less number of cases and also could be due to absence

of controls or it could be just by chance .In a study done 3 years back, the patients with AA had higher risk of developing insulin resistance suggesting common inflammatory pathogenesis or shared genetic background between DM and AA.[24] There are not enough evidences regarding significance of treatment of DM in AA but various case reports show simultaneous development of DM with AA. So, laboratory investigation for DM in clinically diagnosed AA patient will lead to its early diagnosis as seen in a case report done earlier where 28 years old male with beard AA having 5 months history of facial hair loss had incipient DM and nascent thyroid disease.[22]Similarly a case report commented on development of alopecia almost at the same time as the symptoms of diabetes was appearing and mentions that each disease probably progressed simultaneously at least in the final stage with AA complicated in the form of alopecia totalis and alopecia universalis and DM complicated in the form of diabetic coma. Though hair loss couldn't be regressed inspite of improvement in that patient with insulin therapy.[20] There are not enough studies regarding significant association of anemia and AA but few data show presence of pernicious or iron deficiency anemia with AA. In our study only 3 out of 39 patients had anaemia which is not significant. As Iron is an important micronutrient in DNA synthesis that exhibit significant role in tissues with high cellular turnover like the hair follicle matrix, its deficiency shows sign of chronic diffuse hair loss.[25] So, studies are done to see impact of iron supplementation in patients with AA but significant results are not achieved. This can also be due to lack of appropriate large-scale placebo controlled clinical trials. However, significant decrease in ferritin level seen in mainly premenopausal women with non-scarring hair loss suggest that iron supplementation can be taken as an adjuvant therapy after analysis of serum ferritin in patients with AA.[26,27]Twenty five percentage of patients with disorders of autoimmune pathogenesis have tendency to develop another autoimmune disease.[28] Other autoimmune disease associated with AA are DM, Thyroid disorders, Atopy ,Anemia, Systemic lupus erythematosus (SLE), Psoriasis, Vitiligo and Ulcerative colitis. A study evidenced association of SLE with AA and focuses to consider for screening of SLE on patients with relevant symptoms.[29] These associations will also help to improvise treatment for better prognosis as seen in this case report where administration of Tofacitinib (Janus kinase inhibitor) improved clinical symptoms of Ulcerative colitis within 7 days and AA was recovered in 14 days with hair growth [30]. Thus, various factors need to be considered during assessment of patient with AA. One of the past studies stated onset of AA before 6 years, disease lasting more than 1-year, extensive hair loss involving more than 50% of the scalp, nail involvement, atopy or autoimmune disease and a positive family history to be the possible indicators of poor prognosis in AA.[19]

The limitations of our study include that it was performed in a single tertiary centre with limited sample size so it can't reflect the general population.

CONCLUSIONS

In this study there was no significant association between alopecia areata and other autoimmune disorders like diabetes mellitus, thyroid dysfunction, anaemia, atopy and vitiligo because the lack of significant association in our study doesn't exclude the importance of screening of these diseases in a patient with alopecia areata.

CONFLICT OF INTEREST

None

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None

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