ORIGINAL RESEARCH

Evaluation of Serum Cardiac Troponin I Levels in Patients of Alopecia Areata and Healthy Individuals

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ABSTRACT

Background& Objectives: Alopecia areata is a fairly common cause of non-scarring alopecia in the general population. Although the association of cardiovascular risks are studied more commonly in androgenetic alopecia, it is highly unexplored in alopecia areata which is quiet commonly associated with other autoimmune conditions. Recently there are few studies which show association of alopecia areata with cardiovascular comorbidities. **Objectives:** To evaluate the heart disease biomarker cardiac troponin I levels in patients of alopecia areata and healthy adults and to find the association of cardiac troponin I levels with severity of alopecia areata.**Methods:**After assessing the severity of alopecia areata using SALT [Severity of Alopecia Tool] score and ruling out co-existing cardiac disease, serum cardiac troponin I levels were assessed in alopecia areata patients and healthy normal individuals by using ELISA kit and levels were compared.**Result:**There was no significant difference in troponin I levels between both the groups ($P < 0.05$).There was also no correlation between the severity of alopecia areata and troponin levels ($P < 0.05$) and $r = 0.156$.**Conclusion:**Our study could not find any correlation with troponin levels and alopecia areata unlike very few foreign studies.We don't have any Indian studies yet. Probably with more studies we might be able to understand the cardiovascular morbidity associated with alopecia areata.

Key words: Alopecia areata, Cardiac Troponin I levels, SALT score.

INTRODUCTION

Alopecia areata is a common chronic inflammatory disease that causes non-scarring 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. Early ideas about the aetiology were numerous and included infectious, metabolic, vascular, neuropathic and trophoneurotic theories. The current view, that alopecia areata is an autoimmune disease, was first suggested by Rothman in a discussion of a paper presented by Van Scott.[1]

The incidence rate is around 0.1–0.2% with a projected lifetime risk of 1.7%. The onset of alopecia areata may occur at any age.[2] However, in most affected individuals the first episode occurs before the age of 40, with the peak age of onset between the second and fourth decades. The frequency of alopecia areata is same in both sexes.

Alopecia areata is associated with several autoimmune diseases including thyroiditis, lupus erythematosus, vitiligo and psoriasis.[3] While alopecia areata is not directly a life threatening disease, recent studies in humans and mice suggest a potential correlation with higher risk of heart disease and stroke. Increased levels of Cardiac Troponin I in blood plasma in patients with alopecia areata was found in a study by Wang et al.[4] Elevated levels of this factor can indicate increased heart tissue damage. The data suggests that development of alopecia areata may involve more systemic and debilitating effects beyond the skin. A more comprehensive evaluation of alopecia areata patients' heart health is warranted.

The development of androgenetic alopecia is associated with the risk of developing cardiovascular diseases, but the association of alopecia areata with cardiovascular diseases in humans is largely unexplored. With this background, we felt it is necessary to explore the hidden risk factors for cardiovascular diseases with respect to alopecia areata.

MATERIALS AND METHODS

This is a case control study done in patients attending OPD at a tertiary care hospital. The study was done over a period of one and half years from May 2018 to November 2019.

Selection of the cases: After obtaining the clearance from the ethical committee, we proceeded with the study. We have enrolled 45 cases based on the fullfilment of inclusion criteria [clinically and dermoscopically confirmed cases of Alopecia areata(old and new)with severity based on SALT score and patients of either sex aged more than 18 years those who are willing to participate in the study and gives informed consent] . We have excluded those with known cardiac illness and those who are not willing to give consent.

Controls: A control group of 45 healthy normal individuals which were age and sex matched, were taken for comparison in this study.

Clinical Assessment: Participants were age (±1.0 year) and gender-matched with clinically healthy subjects. A complete history was elicited from all patients, with details of age, gender, family history of alopecia areata, disease duration and presence of associated diseases recorded as per the proforma A complete dermatological examination was performed and Severity of Alopecia Tool [SALT] score was calculated. Along with systemic examination, baseline investigations like ECG were done to rule out coexisting cardiovascular comorbidities.

Assay protocol: 5ml venous blood sample was drawn from both cases and controls and serum was separated by centrifuging the sample at 3000 rpm for 10 minutes. Serum thus separated was stored in cryovials at -80℃ cryopreservation. The baseline cardiac troponin I levels was measured using an Elabscience serum cardiac troponin I ELISA kit. ELISA for cardiac troponin I was performed as per standard protocols and manufacturers guidelines. The values were recorded at a wavelength of 450 nm and a standard curve was plotted on a linear graph. The values were then calculated from the standard curve. Results were expressed in nanograms per millilitre as mean ± standard deviation. Data was analysed using appropriate statistical methods.

Methodology for stastistical analysis:

Mean and standard deviation was used to calculate the numerical data. To test the difference across the groups, independent t test or Mann Whitney U test was used based on the normality of the distribution. Pearson correlation was used to analyse the correlation of SALT score with serum cardiac troponin I levels.

RESULT

The mean age of patients was 30.20 + 7.521 years and ranged from 19 to 50 years. The mean age of controls was 29.91 + 7.588 years and ranged from 21 to 50 years. In our study among 45 cases , 23 (51.1%) were female and 22 (48.9%) were male and both sexes were equally affected by the disease. Out of 45 controls 23 (51.1%) were female and 22 (48.9%) were male. In our study, 31 (68,8%) of cases had up to 5 patches, 11 (24.4%) cases had 6 to 10 patches and 3 (6.66%) cases had more than 10 patches. The mean duration of the disease in our study was 3.96 + 2.977 months. 64.4% of the cases were having the duration of the disease less than 6 months and 35.5% had the disease for more than 6 months.

In our study, all the 45 cases (100%) had scalp involvement, 32 (71.1%) cases had both scalp and beard involvement, and 30 (66.66%) cases had both scalp, beard and moustache involvement.

26 (57.78%) cases had SALT score < 25, 15 (33.33%) cases had SALT score between 26 to 50 and 4 (8.88%) cases had SALT score between 51 to 75 and no cases had SALT score between 76 to 100.The average SALT score was 22.60+ 15.75.

13 (28.9%) cases were receiving ILS, 2 cases (4.4%) were using only minoxidil, 2 cases (4.4%) were using both minoxidil and ILS, 9 cases (20%) were on oral steroids and 19 cases (42.2%) were not started on any treatment.

The mean serum cardiac troponin I levels were 1.45567 + 1.720465 ng/ml in alopecia areata patients compared to 1.34067 + 1.770424 ng/ml of the controls, with a mean difference of 0.115 ng/ml and the difference was statistically not significant (p value = 0.383, < 0.05) [Table 1]. There was no correlation between the SALT score and Cardiac Troponin Levels (r = 0.156).

Table 1:

		Minimum	Maximum	Mean	S.D	Mean Diff	P Value
Cardiac troponin Levels	CASES	0.000	10.000	1.45567	1.720465	0.115	0.383
	CONTROLS	0.000	10.000	1.34067	1.770424		

DISCUSSION

Alopecia areata is a common chronic inflammatory disease that causes non-scarring hair loss. Early ideas about the aetiology were numerous and included infectious, metabolic, vascular, neuropathic and trophoneurotic theories. The current view, that

alopecia areata is an autoimmune disease, was first suggested by Rothman in a discussion of a paper presented by Van Scott. Alopecia areata is associated with several autoimmune diseases including thyroiditis, lupus erythematosus, vitiligo and psoriasis. Alopecia Areata is a form of inflammatory autoimmune disease targeting hair follicles. While alopecia areata is not directly a life threatening disease, recent studies in humans and mice which are mentioned below suggest a potential correlation with higher risk of heart disease and stroke. Increased levels of Cardiac Troponin I are noted in the blood of patients with alopecia areata. Elevated levels of this factor can indicate increased heart tissue damage. The data suggests that development of alopecia areata may involve more systemic and debilitating effects beyond the skin. A more comprehensive evaluation of alopecia areata patients' heart health is warranted.

According to the study conducted by Wang *et al* [4] on 89 alopecia areata patients, 72 AGA (Androgenetic Alopecia) patients and 34 subjects with no hair loss before matching for age and sex, AA (Alopecia Areata) subjects ranged from those with less than 25%, patchy hair loss to subjects with alopecia totalis (AT) and/or alopecia universalis (AU). The mean plasma cardiac troponin I level was highest in alopecia areata subjects, moderately higher in androgenetic alopecia subjects, and lowest in subjects without hair loss ($p<0.05$). Alopecia areata subjects not receiving treatments had highest levels of cardiac troponin.

The study conducted by Kang *et al* [5] investigated the risk for subsequent risk of a stroke in alopecia areata patients in a large-scale retrospective cohort study. They identified 3231 patients with alopecia areata included in the study group from 2004 to 2011 in the "Longitudinal Health Insurance Database 2000" in Taiwan. They found that incidence rates of stroke during the 3-year follow-up periods were 5.44 and 2.75 per 1000 person-years for patients with and those without alopecia areata, respectively. They concluded that patients with alopecia areata were associated with a higher risk of stroke in the 3-year follow-up period.

In a study conducted by Hirsso *et al* [6] was to examine the relationships between metabolic syndrome-related risk factors, cardiovascular diseases (CVD) and alopecia among Finnish population. This study showed a high prevalence of alopecia in the general male Finnish population varying from 17% to 73% among men aged 25–74 years, and its association with CVD particularly in age groups older than 55 years. In addition, insulin resistance, as a metabolic syndrome-related risk factor, was associated with alopecia in middle-aged men. An association between alopecia and CVD was strengthened in this study.

The study conducted by Wang *et al* [7]on C3H/HeJ mouse model for alopecia areata and heart tissue response to adrenocorticotropic hormone exposure, exhibited both atrial and ventricular hypertrophy, and increased collagen deposition compared to normal haired littermates. ELISA indicated cardiac troponin-I was elevated in the serum and significantly increased in alopecia areata heart tissue. ACTH treatment induced significant increase in cTnI release into the culture medium in a dose-dependent manner for both alopecia areata and control mice. In conclusion, murine alopecia areata is associated with structural, biochemical, and gene expression changes consistent with cardiac hypertrophy in response to ACTH exposure.

According to Lim *et al* [8] alopecia areata in particular, may have comorbid neuropsychiatric and metabolic conditions. Patients with alopecia areata may be at an increased risk of heart disease, as has been established for rheumatoid arthritis and psoriasis. They found a significant increase of LDL in patients with alopecia areata compared with controls, but only for females. By interrogating several large data sets for comorbid conditions in alopecia areata, they have revealed preliminary evidence that suggests the complex causal structure underlying alopecia areata could also influence metabolic parameters.

The reasons for discordant results between our study and the study by Wang *et al* [4] could be:

- In our study, we excluded patients more than 60 years but in their study even the patients above 60 years were included.
- Small sample size compared to their study.
- Cardiac troponin I could be altered in many other systemic disease which went undetected during patient selection.
- Alopecia Totalis and Alopecia Universalis cases didn't give consent for the study and they were left out from the study.
- There are many parameters other than Cardiac Troponin I which can be evaluated for cardiovascular risks, which are better indicators compared to Cardiac Troponin I levels which are generally elevated as a marker of acute event.

Most of the patients in our study were on some or the other treatment as opposing to the study by Wang *et al* ,which could have acted as a confounding factor to obtain significant difference between cases and controls.

CONCLUSION

As we all know that development of androgenetic alopecia is associated with risk of developing cardiovascular diseases, but the association of alopecia areata with cardiovascular diseases in humans is largely unexplored. Eventhough our study did not find any association to cardiovascular risk; we need many more studies which can shine some light into this aspect.

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