# Relation of cytomegalovirus to alopecia areata: therapeutic trial with oral ganciclovire drug

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## Abstract

Alopecia areata (AA) is lost hair from a few or all regions of the body, for the most part from the scalp. Etiology and pathogenesis of alopecia areata being not totally comprehended, is accepted to be multifactorial in ancestry. Recently, studies suggested an association between alopecia and types of viruses, therefore we concerned to investigate the association between CMV infection and alopecia areata. This study included of 100 individuals (50 alopecia patients and 50 healthy). Mean age of study groups were 20.90 ± 11.07 and 22.64±12.29 years of cases and control group respectively. Mean of age onset of patients were 20.83 ± 10.0. Out of 50 patients 52% were male, the rest were female. However, 1:1 of control group was male: female. 40% of patients had a positive family history for this disease. Alopecia areata affected on scalp in 78% of cases. All patients had a high concentration of CMV IgM. With treatment of oral ganciclovire drug, a decrease of anti-CMV IgM levels and an increase of CMV IgG levels were observed.

**Key words**: Alopecia areata; CMV; IgM; IgG; ELISA

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## Introduction

Alopecia areata (AA) is lost hair from a few or all regions of the body, for the most part from the scalp. This is a distinctive reason of non-scarring alopecia which occurs in intersecting, diffuse or inconsistent cases [1]. Such ailment can spread to the entire epidermis (Alopecia universalis) or to the complete scalp (Alopecia totalis). However, AA has a proclaimed incidence rate of 0.1-0.2% having a 1.7% lifetime danger for women & men who are affected likewise [2]. Etiology and pathogenesis of alopecia areata being not totally comprehended, is accepted to be multifactorial in ancestry [3]. However, psychological, environmental, genetic and immunological factors are the utmost strong explanations, however, their

specific role is impeccably unrecognized [3, 4]. These evidences are in favor of a thought that alopecia also have detrimental psychological impacts while causing a deep emotional endurance which leads to work related, social and personal complications [5,]. A mutual linkage is present among the identity and hair especially for ladies [6]. The recent proofs contribute the genetic role and autoimmune origin which are further restrained by an unfamiliar environmental effect [7]. Several genetic factors contribute in the alopecia areata development. Moreover, about 10-25% positive family history cases were apparent [8, 9, 10]. Immunological causes are believed to be the most significance in this regard, as their prominence has been reported from time to other time [11,12].

Cytomegalovirus (CMV) is termed as β-herpesvirus of humans with a high seroprevalence for adults. CMV illness dominatingly happens as an entrepreneurial disease in patients with extreme immunosuppression and seldom happens in immunocompetent patients [13]. Being a member of human herpesviridae viruses, the CMV comprise of a double standard DNA which can occupy the several host organs and tissues more specifically the tissues of epithelium [14]. Lately, a research proposed a relationship amongst the viruses' types for instance virus of hepatitis C and hepatitis B and alopecia [15]. Though, the impacts of CMV infection on alopecia areata patient's incidence is vague. There is no such investigation observed that presented the recovery of condition of alopecia patients with anti-CMV treatment. Because of this reason, we were anxious about investigating an association amongst the CMV infection & alopecia areata and to present the outcome of oral ganciclovire drug in AA.

## Patients and methods

The current research was categorized as case control study. A fifty alopecia areata with positive serological test for CMV were recruited, who attended out-patient dermatology clinics, in AL-Yarmok teaching hospital/Baghdad province and AL Hussein-Teaching hospital Dhi-Qar province in Iraq, during the period of January' to May' 2018. The patients included of (26 males, 24 females), age ranging from 3 to 50 years. A clinical inspection was carried out to observe the type and site of lesions. The 50 healthy persons were contained in control group which were harmonized by socioeconomic status to patient group, sex and age who had no history related to alopecia areata or viral infection. The clinical finding of patients was refined by expert dermatologist. Each of the patient and healthy filled the questionnaire which comprised of family history, socioeconomic data, personal information, history, and present state of disease. Those patients without any formal instructions were rounded out by interrogating with the aid of an assistant. The criteria of elimination were

based on [patients having former diseases which can impact the outcomes of immunity, pregnant allergy to ganciclovire drug, other causes of alopecia, positive fungal infection.

**Blood collection**

The venous blood of 5mL volume was collected in sans metal sterile tubes from antecubital vein of healthy and alopecia areata volunteers. Those sample which showed the hemolysis signs were discarded. Blood was placed at room temperature to clot for about 25 minutes. After that blood was centrifuged at 3000 r/m for 15 minutes for serum isolation. For anti-cytomegalovirus (IgG & IgM) analysis the isolated serum was stored at −80°C after aliquoting in 1.5 micro centrifuge tubes. A sterile environment was preferred for blood collection and serum separation [16].

**Detection of HCMV IgG and IgM antibodies**

ELISA test was used for the detection of antibodies to CMV in human sera. In brief, 100 µl of diluted patients' serum (1:100 with serum diluents), the HCMV antigen pre-coated microtiter plates' wells were utilized to pipette out the two well positive controls and one well negative control. All the plates were incubated at 25 °C for fifteen minutes and then were rinsed with 300 µl diluted washing solution five times for the removal of residual serum. Similarly, a conjugate of human IgG and 100 µl of enzyme labelled antibodies were added for incubation just like above mentioned procedure. After that these were well washed with 300 µl washing solution for 5 times to discard the boundless material further, substrate solution of 100µl such as tetramethylbenzidine was pipetted out and 15 minutes incubation was carried out for inducing the color development. The completion of reaction took place by accumulation of stop solution. The resultant dye measurements were taken through a spectrophotometer at 450nm wavelength contrary to substrate blank. (Awareness Technology, Palm City, USA). The outcomes were deduced conferring the instruction of manufacturer. The individual absorbance values like <1.1 and <1.0 deliberated each samples' positive and negative values respectively for IgG ELISA. Moreover, the results of test were categorized as equivocal which represents the absorbance among the 1.0 and 1.10 values. Samples were reflected as negative & positive in individual values of absorbance amongst the 0.90 & 1.10 for IgM ELISA. In the individual absorbance values of 0.90-1.10, the samples are presented as equivocal.

All those patients with positive test for CMV were given full course of ganciclovire drug (5mg/kg for 10 days) and follow him for 3 months with monthly clinical, photographic and laboratory assessment.

### Statistical analysis

The SPSS (Version 17) was utilized to analyze the data. For whole variables, a descriptive statistic was used. The categorical scale data process exhibited as mean, frequency, standard deviation, and percentage and a chi-square test was used for its analysis.

## Results

The clinical features of patients are showed in table 1. This study included of 100 individuals (50 alopecia patients and 50 healthy), aged 3 to 50 years with mean age of 20.90 ± 11.07 years and 22.64±12.29 years of cases and control group respectively. The patients and control group were divided in age groups ranging 1-9 years, 10-19 years, 20-29 years, 30-39 years and above 40 years. Mean of age onset of patients were 20.83 ± 10.0. 26 of patients were male, the rest were female. However, 25:25 of control group was male: female. Moreover, about thirty patients showed no alopecia areata family history whereas, an indication of a positive family history was found in twenty patients. The majority of patients were affected with alopecia before aged 40 years with mean age of onset 20.83±10.0.

**Table 1**

The clinical features of patients and control group.

| Parameter | Patients | | Control | | *P*-value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Age (years) | | | | | |
| Mean ± SD | 20.90 ± 11.07 | | 22.64±12.29 | | 1.00 |
| Mean Age of onset | 20.83 ± 10.0 | | | | |
| Gender | | | | | |
| Male | 26 | 52% | 25 | 50% | 0.50 |
| Female | 24 | 48% | 25 | 50% | |
| Total | 50 | 100% | 50 | 100% | |
| Family history | | | | | |
| Positive | 20 | 40% | — | — | |
| Negative | 30 | 60% | — | — | |
| Total | 50 | | | | |

P-value ≤ 0.05: Significance

In present study, Scalp was observed in 39 (78%) patients alone, however scalp with beard involved 6 (12%) cases. In otherwise alopecia areata affected on scalp and eyebrow of 5 (10%) of cases. This is shown in figure 1.

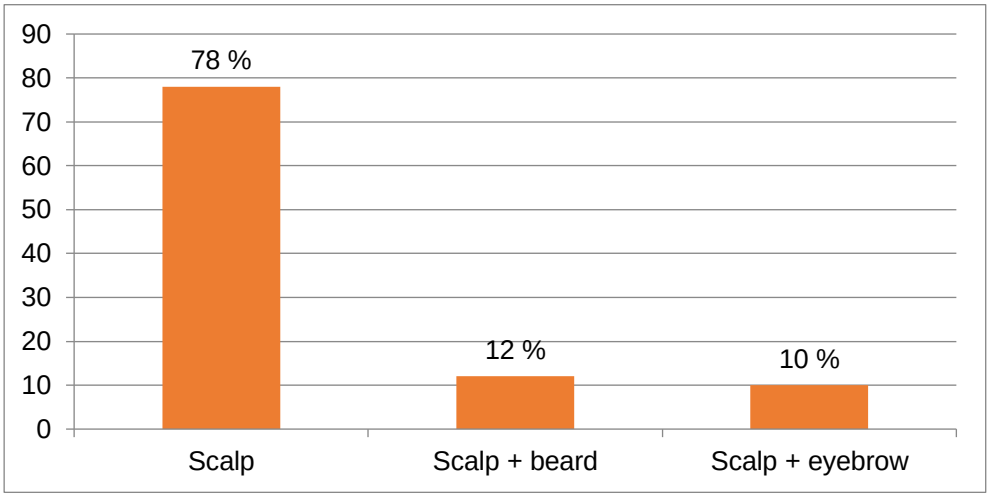


**Figure 1**
**Site of lesion**

CMV IgM antibodies were higher in all patients at visited the outpatient clinic of dermatology. We found in 20 (40%) of patients had a concentration between 1-5 g/L of CMV IgM while 6 (12%) had a concentration more than 10 g/L of CMV IgM. However, 24 (48%) of patients had a concentration between 6-10 g/L of CMV IgG, (Table 2).and clinical response was followed (figure 2).

**Table 2.**
CMV IgM, IgG detection in alopecia areata Prior and Post treatment.

| Immunoglobulin (g/L) | Prior treatment of ganciclovire | | | Post treatment of ganciclovire | | *P*-value |
|---|---|---|---|---|---|---|
| | Range | n | % | n | % | |
| CMV IgM in patient sera | < 1 | 0 | 0% | 40 | 80% | 0.00 |
| | 1 – 5 | 20 | 40% | 6 | 12% | |
| | 6 – 10 | 24 | 48% | 4 | 8% | |
| | > 10 | 6 | 12% | 0 | 0% | |
| | Total | 50 | 100% | 50 | 100% | |
| CMV IgG in patient sera | < 1 | 47 | 94% | 0 | 0% | 0.00 |
| | 1 – 5 | 3 | 6% | 30 | 60% | |
| | 6 – 10 | no | – | 17 | 34% | |
| | > 10 | no | – | 3 | 6% | |
| | Total | 50 | 100% | 50 | 100% | |

P-value ≤ 0.05: Significance

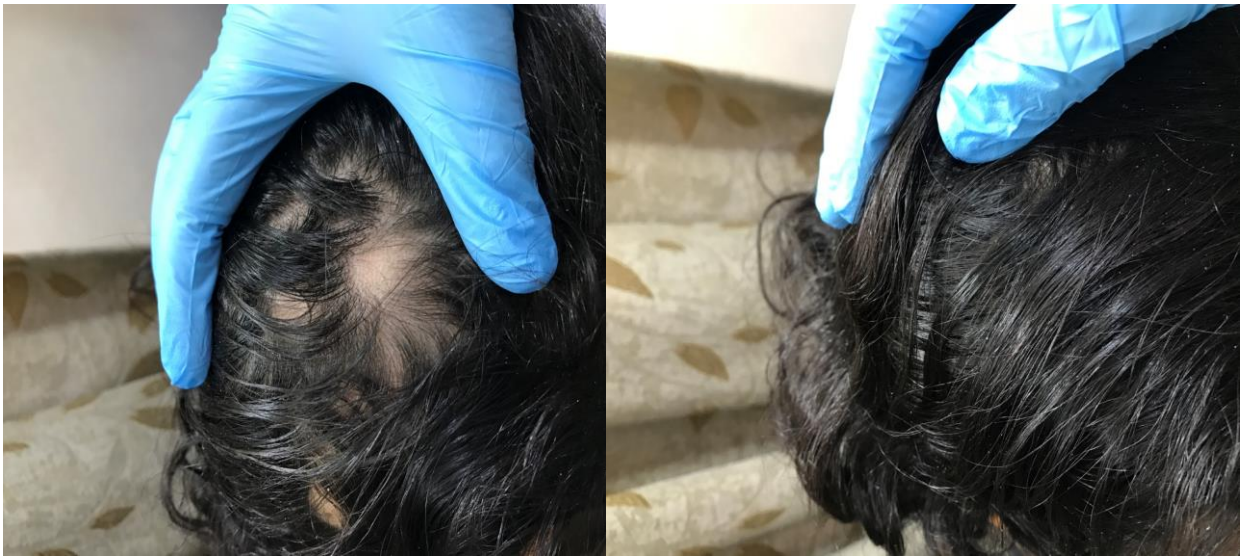

**Figure 2**

patient with AA (A) before using oral ganciclovire while (B) after the treatment

## Discussion

In this study, the majority of patients were affected with alopecia before aged 40 years with mean age of onset 20.83±10.0. With similar finding Ejaz et al [4] showed the most of patients were in age groups 20-40 years with mean age of onset 21.4 years. the frequency of male patients with alopecia areata group was same as compared to females. This finding is similar with Kutrev et al [17] who also suggested that both sexes in alopecia areata were equal. However, Ahmed et al. [18] showed a female preponderance in alopecia areata. Also, Seyrafi et al [19] found a female preponderance to male in their study. The current research indicated a positive family history for alopecia areata among 40% of patients. This finding was higher compare with other studies [8,9,10] they reported that 10 -25% of approximate cases presented a positive family history. Regarding the site of lesion, we found the most common site affected by alopecia areata was scalp, either alone in 78% of cases or affected with another sit such as beard or eyebrow. This finding resembles with Bharathi et al [20] who observed that the scalp was involved in 88% of cases.

The correlation between CMV and alopecia areata was first described by Skinner et al [21] who found no association between CMV and development of alopecia areata. We studied the prevalence of CMV antibodies among alopecia areata. In this study, we showed that the levels of anti-CMV (IgM) in patient sera were increased that indicates the involvement of the CMV as a cause of alopecia areata. With treatment by oral ganciclovire drug, a decrease of anti-CMV IgM levels and disappearance of CMV antigens were observed in the early stage

of alopecia areata, maybe due to host defenses against viral infection. Contrariwise, we observed an increase of IgG levels, this indicates to a cure from previous viral infection.

## Conclusion

Based on this finding, we think a substantial relatedness is present amongst the CMV infection and Alopecia areata and CMV may resulting in A.A and so anti CMV drug play a role and advice screening test for CMV in patients who suffering from AA.

## Ethical Approval

The study was approved by the Ethical Committee.

## Conflicts of Interest

The authors declare that they have no competing interests.

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