

## VIRAL INFECTION INDUCES ALOPECIA AREATA IN NASIRIYAH, IRAQ

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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  $20.90 \pm 11.07$  and  $22.64 \pm 12.29$  years of cases and control group respectively. Mean of age onset of patients were  $20.83 \pm 10.0$ . Out of 50 patients 52% were male, the rest were female. However 1:1 of control group were 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.

**Keywords:** Alopecia areata, viral infection, Iraq.

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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<sup>[1]</sup>. 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 effected likewise<sup>[2]</sup>. Etiology and pathogenesis of alopecia areata being not totally comprehended, is accepted to be multifactorial in ancestry<sup>[3]</sup>. However, psychological, environmental, genetic and immunological factors are the utmost strong explanations, however, their specific role is impeccably unrecognized<sup>[3, 4]</sup>. 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<sup>[5]</sup>. A mutual linkage is present among the identity and hair especially for ladies<sup>[6]</sup>. The recent proofs contribute the genetic role and autoimmune origin which are further restrained by an unfamiliar environmental effects<sup>[7]</sup>. Several genetic factors contribute in the alopecia areata development. Moreover, about 10-25% positive family history cases were apparent<sup>[8-10]</sup>. Immunological causes are believed to be the most significance in this regard, as their prominence has been reported from time to other time<sup>[11,12]</sup>. Cytomegalovirus (CMV) is termed as  $\beta$ -herpesvirus of humans with a high seroprevalence for adults. CMV illness dominantly happens as an entrepreneurial disease in patients with extreme immunosuppression and seldom happens in immune competent patients<sup>[13]</sup>. 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<sup>[14]</sup>. Lately, a research proposed a relationship amongst the viruses' types for instance virus of hepatitis C and hepatitis B and alopecia<sup>[15]</sup>. Though, the impacts of CMV infection on alopecia areata patient's incidence is vague. There are 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 and alopecia areata and to present the outcome of oral ganciclovir drug in AA.

## MATERIALS 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, AL Hussein-Teaching hospital Dhi-Qar, Iraq, during the period of January'to May' 2017. The patients included of (26males, 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 that 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 was 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 and IgM) analysis the isolated serum was stored at  $-80^{\circ}\text{C}$  after aliquoting in 1.5 micro centrifuge tubes. A sterile environment was preferred for blood collection and serum separation<sup>[16]</sup>.

### 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 300µl diluted washing solution five times for the removal of residual serum. Similarly, a conjugate of human IgG and 100µl of enzyme labelled antibodies were added for incubation just like above mentioned procedure. After that these were well washed with 300µl washing solution for 5 times to discard the boundless material further, substrate solution of 100µl such as tetramethylbenzidine was pipette 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 and 1.10 of IgM ELISA. In the individual absorbance values of 0.90-1.10, the samples are presented as equivocal. All those patient with positive test for CMV were given full course of ganciclovir 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 statistics 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  $20.90 \pm 11.07$  years and  $22.64 \pm 12.29$  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  $20.83 \pm 10.026$  of patients were male, the rest were female. However 25:25 of control group were 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  $20.83 \pm 10.0$ .

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.

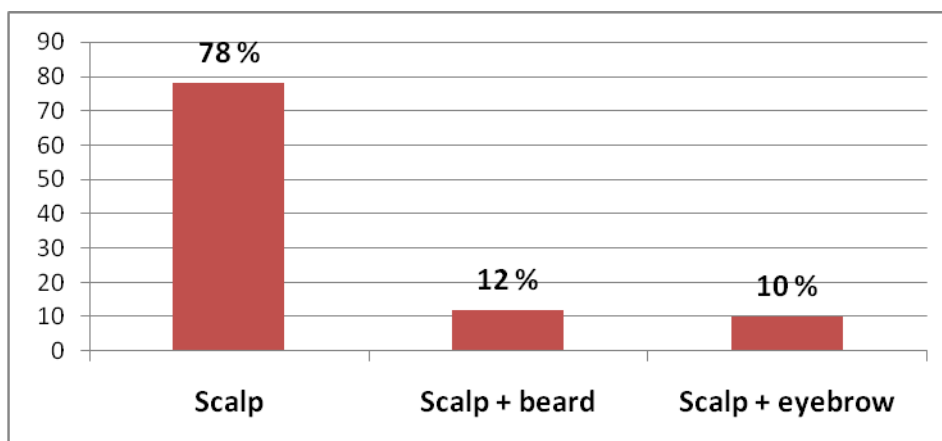


Figure 1: Site of lesion

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 ganciclovir			Post treatment of ganciclovir		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 ganciclovir 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  $20.83 \pm 10.0$ . With similar finding Ejaz *et al.*<sup>[4]</sup> 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.*<sup>[17]</sup> who also suggested that both sexes in alopecia areata were equal. However, Ahmed *et al.*<sup>[18]</sup> showed a female preponderance in alopecia areata. Also Seyrafi *et al.*<sup>[19]</sup> 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<sup>[8-10]</sup>, 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 other sit such as beard or eyebrow. This finding resemble with Bharathi *et al.*<sup>[20]</sup> 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.*<sup>[21]</sup> who found no association between CMV and development of alopecia areata. We studied the prevalence of CMV antibodies among alopecia areata. This study 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 ganciclovir 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 the this findings, 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 roleand advice screening test for CMV in patients who suffering from AA.

## ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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