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Research Article

**SERO-POSITIVITY OF CYTOMEGALOVIRUS AMONG  
PATIENTS SUFFERING FROM MULTIPLE SCLEROSIS**<sup>1</sup>Dr. Zarmeen Sultan, <sup>1</sup>Dr. Nabeel Sultan, <sup>2</sup>Dr. Hafiz Muhammad Ihsan Majeed<sup>1</sup>Jinnah Hospital Lahore<sup>2</sup>DHQ Nankana Sahib**Article Received:** April 2020**Accepted:** May 2020**Published:** June 2020**Abstract:**

**Objective:** MS (Multiple Sclerosis) is a complicated disease of CNS. Various factors of environment as various viruses are thought to be the most important cause of MS. The purpose of this research work was to assess the sero-positivity of CMV (Cytomegalovirus) in the patients suffering from MS in comparison with their healthy controls.

**Methodology:** This study is a case-control research work carried out in Sheikh Zayed Hospital, Lahore. With the utilization of the method of ELISA, we detected Ig-M & Ig-G antibodies to CMV in the patients of MS as well as their gender and age matched controls. IgM titer of CMV greater than twenty five and IgG titer of CMV greater than 0.60 were considered as sero-positive in accordance with the test kit of laboratory.

**Results:** There were total eighty two patients of MS including sixty four females and eighteen males in this research work. There were thirty eight age and sex matched controls including twenty nine females and nine males in this research work ( $P > 0.050$ ). Median CMV Ig-M [IQR] titer in the group of MS was 3.25 from 2.97 to 5.10 versus 3.50 from 2.50 to 5.70 in the group of controls ( $P = 0.660$ ); likewise, median CMV Ig-G [IQR] titer in the patients of MS group was 15.15 from 8.10 to 22.50 versus 7.75 from 5.30 to 22.0 in the group of controls ( $P = 0.0110$ ). In accordance with the clinical course, median of IgG was 14.94 from 7.30 to 24.0 in RRMS & 20 from 9.80 to 22.0 in SPMS and IgM median was 4 from 2.90 to 6.50 and 3 from 2.70 to 4.0 correspondingly.

**Conclusion:** CMV sero-positivity was much high in the group of MS as compared to the group of controls, so it may perform a vital part in the pathogenesis of the MS, but there is need of further research works to consolidate the findings of this research work.

**KEY WORDS:** CMV, MS, sero-positivity, accordance, methodology, comparison, controls, median.

**Corresponding author:****Dr. Zarmeen Sultan,**

Jinnah Hospital Lahore

QR code



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**INTRODUCTION:**

MS is an inflammatory demyelinating abnormality of CNS in which there is not known etiology and various factors of genetics and environment are not able to describe its pathogenesis [1-3]. Herpes viruses are suggested to be have the involvement in the etiology of MS. Abnormal immunological results confirmed the role of the infection as an important risk factor that was present in the spinal fluid [4], but so far no agent was present to have association with this complication. Different research studies have associated the infectious mononucleosis with the MS [5-8], moreover, an excessive amount of the other viruses are analyzed to identify the sinister viruses as HHV-6 [9, 10], HHV-7 & HHV-8 [11]. Herpes family is the common cause of infection of CMV which has relation with the many other autoimmune complications like SLE [12]. There are few researches works available regarding the CMV sero-positivity in AQP-4 positive central nervous system autoimmunity [13].

The CMV incidence is a variable in various geographic regions, racial populations and various levels of socio-economic status like 50.40%, in USA [14]. CMV can be the reason of a primary infection regardless of age normally without any authentic symptoms but establishes hidden infection, so it could have involvement in the chronic autoimmune complications as MS. There are few research works which were not able to show any association between CMV and MS [15, 16] but isolation of CMV carried out from a sample of chimpanzee with acute demyelinating complication [17] and the findings of one other research work showed the high amount of antibody of CMV in MS patients with Vitamin-D sufficiency as compared to their healthy controls [18]. So, there is uncertain role of the CMV in the development of MS. This research work carried out to assess the sero-positivity of CMV in our population with MS as compared to their healthy controls for the investigation of the relationship between MS and CMV.

**METHODOLOGY:**

This research work carried out in Sheikh Zayed Hospital, Lahore. Total amount of the patients with MS in the region were 1391 with 35.50 persons per 100,000 population in accordance with the findings of one research work conducted in 2007 [19]. We selected the patients from a recorded data on the computer. The confirmation of the MS diagnosis

carried out on the basis of the MC Donald standard. All the patients have RRMS or SPMS course but none of the patients was present in relapsing phase. Exclusion of the 8 patients carried out because of the recent acute relapse. We selected total 38 age and sex matched healthy persons as controls. We took the written consent of the patients after describing them the purpose of this research work. The collection of the baseline data carried out on well-organized questionnaire. From the participants of both groups, we collected five cc sample of blood and we freeze the specimens in negative twenty centigrade after the centrifugation.

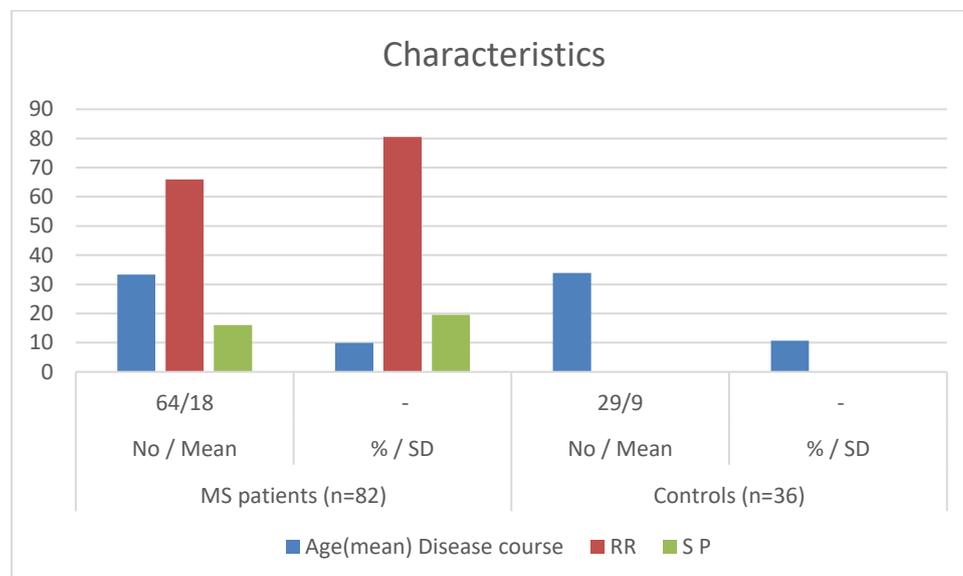
The determination of Ig-M and Ig-G carried out with the help of ELISA kit. CMV Ig-M titer of greater than twenty five and CMV Ig-G titer greater than 0.60 were considered as seropositive in accordance with the laboratory findings. The ethical committee of the institute gave the permission to conduct this research work. T test was in use for the analysis of the demographic data and Mann Whitney test method was in use for the comparison of level of antibodies of CMV in patients and healthy controls.

**RESULTS:**

A sum of total eighty two patients of MS in which sixty four were females and eighteen were males and thirty eight healthy controls in which twenty nine were males and nine were females, were the participants of this research work (P value > 0.050). The average age of the patients was  $33.30 \pm 9.96$  ranging from 18 to 53 years and average age was  $33.90 \pm 10.70$  ranging from 18 to 57 in healthy controls. There were 80.50% (n: 66) patients present with RRMS (Relapsing-Remitting MS) and 19.50% (n: 16) patients were present with SPMS (Secondary progressive MS) course. The most frequent presenting signs were sensory, optic neuritis & motor symptoms successively. In the patients group, average interval between 1<sup>st</sup> and 2<sup>nd</sup> attack was  $1.740 \pm 1.960$  years, average duration of disease was  $6.140 \pm 4.66$  years, average amount of attacks was  $1.40 \pm 0.83$  and average EDSS was  $2.380 \pm 1.80$ . Median IQR titer of CMV Ig-M in the group of MS patients was 3.250 U/ml ranging from 2.97 to 5.10 versus 3.50 U/ml ranging from 2.50 to 5.70 in the group of healthy controls (P value = 0.660), likewise, Median IQR titer of CMV Ig-G in patients of MS group was 15.150 U/ml ranging from 8.10 to 22.50 versus 7.750 U/ml ranging from 5.30 to 22 in the healthy controls (P value = 0.0110).

**Table-I: Characteristics of groups.**

Groups	MS patients (n=82)		Controls (n=36)		p-value
	No / Mean	% / SD	No / Mean	% / SD	
Female /Male	64/18	-	29/9	-	
Age(mean) Disease course	33.3	9.96	33.9	10.7	0.6700
RR	66	80.5			
S P	16	19.5			
	Value	Range	Value	Range	P-value
CMV IgG, U/ml	15.15		7.75		0.0110
Median[IQR]		[8.10-22.50]		[5.30-22.0]	0.5700
	RR 14.94U/ml	[7.30-24.0]			
	SP 20.2U/ml	[9.80-22.0]			
CMV IgM, U/ml	3.25		3.5		0.6600
Median[IQR]		[2.970-5.10]	[2.50-5.70]		0.2500
	RR 4.0U/ml	[2.90-6.50]			
	SP 3.0U/ml	[2.70-4.0]			



Considering medical course, CMV Ig-G was 14.940 U/ml ranging from 7.30 to 24 in RRMS and 20.20 U/ml ranging from 9.80 to 22 in SPMS and CMV Ig-M was 4 U/ml ranging from 2.90 to 6.50 and 3 U/ml ranging from 2.70 to 4 correspondingly. We found no significant difference between the patients of both groups in accordance to CMV Ig-G (P value = 0.570) and CMV Ig-M (P value = 0.250). We also found no difference of the antibodies of CMV between the patients of MS and healthy controls according to the disease course (Table-1).

### DISCUSSION:

The findings of this research work showed that median CMV Ig-G in the patients suffering from MS was higher than the healthy controls but it was not much significant. Many research works carried out for the detection of the viruses role in the MS development and some works among them showed that the infection of herpes virus is more common in CSF and serum of the patients of MS in comparison with the other neurological complications [20]. One other research work

showed that it has no direct relation with the MS as an etiology [21] and one other research work stated that it can perform an indirect part as an activator of the process of underlying diseases [22]. CMV is very frequent infection of viruses which belongs to the herpes family of viruses, with diverse incidence rates in various regions of world: roughly under 85.0% in African Americans by age of twenty one, 96.80% after seven year of age in Turkey [23], to mean of 57.0% in continent of Australia [24], 48.070% in country China [25] and 97.690% in

pregnant females of Iran [26]. Currently, laboratory-based symptoms of active and latent infection of CMV have been detected in relationship with course and onset of various autoimmune abnormalities like systemic lupus erythematosus [27] and SSC (Systemic Sclerosis) [28].

Markedly, in one research work, increased levels of Ig-G anti-CMV were present with association with production of the lupus-associated autoantibodies DNA & RNA [29]. Reactivated memory T-cells may be reason of autoimmune neurologic abnormality after many years of onset of complication [30]. We found only one case report of neuro-myelitis optica following the infection of CMV [31].

### CONCLUSION:

Sero-positivity of the CMV in our population is very high in patients suffering from MS as compared to their healthy controls so, this may propose a possible relationship between the MS development and CMV. There is need of further research works to with large number of sample size to consolidate the findings of this research work.

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