

The Positivity Rate of Epstein-Barr Virus Anti-Viral Capsid Antigen IgG among Children with Infectious Mononucleosis in Diyala-Iraq

Mohammad Kassem Saleh¹, A. S. H. Hasan^{2*}, Nadhum G. Noaman²

¹Diyala Directory of Health, Diyala, Iraq

²College of Medicine-Diyala University, Diyala, Iraq

Email: *razak1957@yahoo.com

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Abstract

Background: Epstein-Barr virus (EBV) is a double-stranded linear DNA human herpesvirus that is transmitted primarily through saliva during childhood. Although the majority of primary EBV infections are clinically asymptomatic, clinical cases are presented as infectious mononucleosis (IMN) syndrome. **Objectives:** This study was conducted to explore the rate of EBV anti-VCA IgG among children who were clinically suspected as having IMN in Diyala province. **Subjects and Methods:** This is a cross sectional study that was carried out during 2018 in Diyala province-Iraq. A total of 370 blood samples were collected from 190 children under 15 years of age who were clinically suspected as having IMN, and 180 apparently healthy children as controls. The anti EBV VCA IgG antibodies were detected in serum using the VCA IgG ELISA kit (from Dia.Pro Diagnostic Bioprobesrl-Italy). Statistical analysis was carried out using the SPSS-version 25. A statistical significance was considered whenever the P value was ≤ 0.05 . **Results:** The results showed that the IgG positivity rate among suspected IMN patients was insignificantly higher in the age group 10 - 14 years old children (80.8%, $P = 0.364$). In control subjects the highest positivity rate was in the age group of 1 - 4 years with a statistically significant difference (79.5%, $P = 0.002$). In suspected IMN patients, the age group of 10 - 14 years had the highest mean concentration \pm SD of anti-VCA IgG 44.018 ± 38.644 arbitrary units per milliliter (arbU/ml), while in controls, the highest value 38.018 ± 34.908 (arbU/ml) was in the age group of 1 - 4 years, with insignificant difference in either group ($P = 0.257$ and 0.072 , respectively). The results also showed that in both suspected IMN patients and control subjects, females showed higher IgG positivity rate (70.6%, and 75.5%) compared to males (64.8%, and 65.1%) with insignificant difference in both groups ($P = 0.392$ and 0.126) respectively. Similarly, the

IgG mean concentration \pm SD was insignificantly higher in females in both suspected IMN patients and control subjects ($P = 0.447$ and 0.256) respectively. 21 (87.5%) of IgM positive suspected IMN patients were also IgG positive with a statistically significant association ($P = 0.028$). **Conclusion:** The positivity rate of anti-EBV VCA IgG among apparently healthy subjects in Diyala province was 70.6%, which increases by age with slight association with clinical suspicion of infectious mononucleosis.

Keywords

Epstein-Barr Virus, Infectious Mononucleosis, Anti-VCA IgG

1. Introduction

Epstein-Barr virus (EBV) is a DNA lymphotropic herpesvirus and the causative agent of infectious mononucleosis. EBV is highly prevalent since it affects more than 90% of individuals worldwide and has been linked to several malignancies [1]. Over 90% of the population is seropositive for EBV worldwide. Most children are infected by the age of 2 years in developing countries, while in developed countries EBV infection occurs more often in late childhood and adolescence [2]. The majority of primary EBV infections in infants and young children are clinically silent. In older patients, it is accompanied by symptoms of infectious mononucleosis (IMN) in about 50% of cases [3]. IMN is a clinical syndrome characterized by pharyngitis, cervical lymphadenopathy, fever, and lymphocytosis, and is most often caused by EBV [4]. In addition to IMN, EBV also causes other clinical syndromes and is associated with various lymphoid and non-lymphoid malignancies [5].

One of the commonly used diagnostic techniques is enzyme linked immunosorbent assay (ELISA). The presence of anti-VCA IgM antibodies indicates current infection while anti-VCA IgG antibody is a marker of past infection and indicates immunity [5]. In China, among children 22 days to 14 years of age with suspected EBV infection, the positivity rate for EBV infection was 14.3% [6]. Similar studies had yielded comparable results [7] [8] [9].

Chabay and Preciado (2013) reported that the anti-VCA IgG prevalence among children less than 15 years of age in Argentina was 72% [10]. Similar results were also found in most previous studies [8] [11] [12]. Epstein-Barr virus infection is very common in the United States since more than 90% of adults are antibody positive by the age of 35 years. In contrast, the EBV antibodies prevalence among children is lower, ranging from 20% to 80% depending on age and geographic location [13]. EBV seroprevalence in pregnant women in Finland has remained the same in the last 20 years [14]. In Scotland, among university-aged population, 75% were seropositive and almost half of the remaining seronegative students experienced seroconversion during their time at university [15]. In China, children under 4 years of age are highly susceptible to infection and

children between 6 months and 1 year of age are the high-risk group for EBV infection. Therefore, vaccination against EBV was recommended to reduce the burden of EBV infection in future [16].

2. Subjects, Materials and Methods

This is a cross sectional study that was carried out during 2018 in Diyala province-Iraq, for the serological detection of anti-viral capsid antigen IgG antibodies against Epstein-Barr virus in clinically suspected cases of IMN as well as apparently healthy children less than 15 years of age.

A total of 370 blood samples were collected as follows; 190 samples from children under 15 years of age who were clinically suspected as having IMN, and 180 samples from normal apparently healthy children (under 15 years of age). A questionnaire form was pre-constructed for this objective including socio-demographic information. The anti EBV VCA IgG antibodies were detected in serum using the VCA IgG ELISA kit (from Dia. Pro Diagnostic Bioprobesrl-Italy). Human privacy was respected by taking parents' consent. Statistical analysis of data was carried out using the SPSS-25 (Statistical Packages for Social Sciences-version 25). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range. The significance of difference in means were tested using Students-t-test. The significance of difference of percentages were tested using Pearson Chi-square test (χ^2 -test). Statistical significance was considered whenever the P value was equal to or less than 0.05.

3. Results

Table 1 shows that both suspected IMN patients and apparently healthy subjects had approximately similar positivity rates for anti-VCA IgG (67.9% and 70.6%) respectively. As a result, there is no statistically significant association between the two groups ($P = 0.580$).

Table 2 demonstrates that IgG positivity rate among suspected IMN patients increases with age (from 60% among those less than 1 year of age, to 80.8% in those 10 - 14 years old), however the difference was statistically insignificant ($P = 0.364$). On the other hand, control subjects showed the highest positivity rate in the age group of 1 - 4 years (79.5%) and the lowest in those less than 1 year of age (39.1%) concluding that there is a statistically significant association between IgG status and age in control subjects ($P = 0.002$).

Table 1. Association of anti-VCA IgG status with clinical suspicion of IMN.

Anti-VCA IgG status	Suspected IMN patients		Apparently healthy	
	No.	%	No.	%
Positive	129	67.9	127	70.6
Negative	61	32.1	53	29.4
P value	0.580			

Table 3 shows that in suspected IMN patients, the age group of 10 - 14 years had the highest mean concentration \pm SD of anti-VCA IgG (44.018 ± 38.644), while in control subjects, the highest value (38.018 ± 34.908) was in the age group of 1 - 4 years. The difference was statistically insignificant in either group ($P = 0.257$ and 0.072) respectively.

In both suspected IMN patients and control subjects, females showed higher IgG positivity rate (70.6%, and 75.5%) respectively compared to males (64.8%, and 65.1%) respectively. Nonetheless, the difference was statistically insignificant in both groups ($P = 0.392$ and 0.126) respectively, as shown in **Table 4**.

Table 5 shows that the IgG mean concentration \pm SD is higher in females in both suspected IMN patients and control subjects (34.094 ± 34.323 and 34.824 ± 34.205) respectively. However, no statistically significant association was found in either group ($P = 0.447$ and 0.256) respectively.

Table 2. Association of anti-VCA IgG status with age.

Age (years)	Anti-VCA IgG status							
	Suspected IMN patients				Control			
	Positive		Negative		Positive		Negative	
	No.	%	No.	%	No.	%	No.	%
<1	12	60.0	8	40.0	9	39.1	14	60.9
1 - 4	56	64.4	31	35.6	62	79.5	16	20.5
5 - 9	40	70.2	17	29.8	40	74.1	14	25.9
10 - 14	21	80.8	5	19.2	16	64.0	9	36.0
P value	0.364				0.002			

Table 3. Association of anti-VCA IgG concentration with age.

Age (years)	Anti-VCA IgG concentration (arbU/ml)			
	Suspected IMN patients		Control	
	Mean \pm SD arbU/ml	Range	Mean \pm SD arbU/ml	Range
<1	26.210 \pm 35.292	0.278 - 100	16.831 \pm 32.027	0.139 - 100
1 - 4	29.985 \pm 32.930	0 - 100	38.018 \pm 34.908	0.104 - 100
5 - 9	32.717 \pm 33.853	0 - 100	30.049 \pm 32.909	0.174 - 100
10 - 14	44.018 \pm 38.644	0.208 - 100	31.509 \pm 36.766	0 - 100
P value	0.257		0.072	

Table 4. Association of anti-VCA IgG status with gender.

Gender	Anti-VCA IgG status							
	Suspected IMN patients				Control			
	Positive		Negative		Positive		Negative	
	No.	%	No.	%	No.	%	No.	%
Male	57	64.8	31	35.2	56	65.1	30	34.9
Female	72	70.6	30	29.4	71	75.5	23	24.5
P value	0.392				0.126			

Table 5. Association of anti-VCA IgG concentration with gender.

Gender	Anti-VCA IgG concentration (arbU/ml)			
	Suspected IMN patients		Control	
	Mean \pm SD rbU/ml	Range	Mean \pm SD arbU/ml	Range
Male	30.281 \pm 34.499	0 - 100	28.946 \pm 35.014	0 - 100
Female	34.094 \pm 34.323	0 - 100	34.824 \pm 34.205	0.139 - 100
P value	0.447		0.256	

4. Discussion

It was revealed that the positivity rate of IgG among apparently healthy subjects in this study was 70.6%, which was not significantly different when compared to the rate among suspected IMN patients ($P = 0.580$), indicating that there is no association between IgG positivity rate and clinical suspicion of IMN.

These current findings were compatible with the results of most previous studies, concerning the rate among children less than 15 years of age [8] [11] [12]. Moreover, Chabay and Preciado (2013) reported that the anti-VCA IgG prevalence among children less than 15 years of age in Argentina was 72% [10]. On the other hand, Dowd *et al.* (2013) and Balfour *et al.* (2013) reported lower IgG positivity rates among children aged 6 - 14 years in the United States (59.6%, and 54.6%) respectively. These rates would have probably been even less if the age group of less than 6 years was included in these studies. However, when the age group of 15 - 19 years was taken into account in these studies, the rates increased to 66.7% and 64.4% respectively [17] [18]. The inconsistency between the current study and the aforementioned studies is a reflection of the difference in the peak age of acquiring EBV primary infection in Iraq and the USA.

Results of the present study showed a statistically significant association between age and IgG positivity rate among apparently healthy subjects ($P = 0.002$) with the highest rate being in the age group of 1 - 4 years (79.5%) and the lowest in those less than 1 year of age (39.1%). However, no such significant association was found among suspected IMN patients, but the positivity rate increased with age. When taking the entire study population into account, the positivity rates were indicating an increase in the rate with age.

Similar findings were reported by Huang *et al.* (2013) in the study conducted in China, in which the patients were classified into five age groups. The IgG seropositivity rate increased among children aged 8 - 36 months and then plateaued among children aged 36 - 108 months. For children aged ≥ 9 years, the positivity rate was 84.2% [12].

In another study conducted in Taiwan, Chen *et al.* (2015) stated that children under 1 year of age had similar IgG seropositivity rate as that of children between the ages of 1 and 2 years, however the age-specific seropositivity rate quickly rose in the early life. Among the 2 years old children 52.8% of them had positive anti-VCA IgG response. The rate further increased to 88.7% in the age group of 5 - 7 years. For people aged 14 - 16 years, the rate reached 93%. These

findings had lead to the conclusion that the positivity rate significantly increased with age [11]. Moreover, a similar trend of increasing rate with age was also found in most previous studies [10] [17] [18].

The overall IgG positivity rate in the current study population was 73% among females and 65% among males, with no statistically significant effect of gender on the positivity rate. These findings were reconcilable with many previous studies [11] [18]. Additionally, Dowd *et al.* (2013) observed that the IgG positivity rate was 68.9% among females and 64.2% among males in the USA [17]. However, Pourahamad *et al.* (2014) reported that the IgG positivity rate was 87.2% among males and 82.9% among females in Iran (the mean age of the study group was 23 years, which is much higher than that of the current study, and hence the overall higher rates of IgG positivity) [19]. In another study in Argentina, the IgG positivity rate among males and females was 72% and 71% respectively [10]. These minor inconsistencies in results might be due to differences in the overall male to female ratio in the study group of these studies compared to the present one.

5. Conclusion

In conclusion, the positivity rate of anti-VCA IgG among apparently healthy subjects in Diyala province was 70.6%. There is no association between IgG positivity rate and clinical suspicion of IMN, the IgG positivity rate increases with age, and the overall IgG positivity rate was 73% among females and 65% among males.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Smatti, M.K., Al-Sadeq, D.W., Ali, N.H., Pintus, G., Abou-Saleh, H. and Nasrallah, G.K. (2018) Epstein-Barr Virus Epidemiology, Serology, and Genetic Variability of LMP-1 Oncogene among Healthy Population: An Update. *Frontiers in Oncology*, **8**, 2. <https://doi.org/10.3389/fonc.2018.00211>
- [2] Ryan, K.J., Ray, C.G., Ahmad, N., Drew, W.L., Lagunoff, M., Pottinger, P., Reller, L.B. and Sterling, C.R. (2014) *Sherris Medical Microbiology*. 6th Edition, McGraw-Hill Education, New York.
- [3] Kliegman, R.M., Stanton, B.F., St Geme, J.W., Schor, N.F. and Behrman, R.E. (2016) *Nelson Textbook of Pediatrics*. 20th Edition, Elsevier, Inc., New York.
- [4] Ralston, S.H., Penman, I.D., Strachan, M.W. and Hobson, R.P. (2018) *Davidson's Principles and Practice of Medicine*. 23rd Edition, Elsevier, Inc., New York.
- [5] Carroll, K.C., Morse, S.A., Mietzner, T. and Miller, S. (2016) *Jawetz, Melnick, & Adelberg's Medical Microbiology*. 27th Edition, McGraw-Hill Education, New York.
- [6] Chen, Q., Hu, Z. and Zhang, Q.H. (2013) Analysis of Epstein Barr Virus Infection in 761 Hospitalized Children. *Chinese Journal of Contemporary Pediatrics*, **15**,

- 183-186. <https://doi.org/10.1016/j.yped.2012.03.014>
- [7] Sohn, M.J., Cho, J.M., Moon, J.S., Ko, J.S. and Yang, H.R. (2018) EBV VCA IgM and Cytomegalovirus IgM Dual Positivity Is a False Positive Finding Related to Age and Hepatic Involvement of Primary Epstein-Barr Virus Infection in Children. *Medicine*, **97**, e12380. <https://doi.org/10.1097/MD.00000000000012380>
- [8] Fourcade, G., Germi, R., Guerber, F., Lupo, J., Baccard, M., Seigneurin, A., Semanova, T., Morand, P. and Epaulard, O. (2017) Evolution of EBV Seroprevalence and Primary Infection Age in a French Hospital and a City Laboratory Network, 2000-2016. *PLoS ONE*, **12**, e0175574. <https://doi.org/10.1371/journal.pone.0175574>
- [9] Balfour, H.H., Odumade, O.A., Schmeling, D.O., Mullan, B.D., Ed, J.A., Knight, J.A., *et al.* (2013) Behavioral, Virologic, and Immunologic Factors Associated with Acquisition and Severity of Primary Epstein-Barr Virus Infection in University Students. *The Journal of Infectious Diseases*, **207**, 80-88. <https://doi.org/10.1093/infdis/jis646>
- [10] Chabay, P.A. and Preciado, M.V. (2013) EBV Primary Infection in Childhood and Its Relation to B-Cell Lymphoma Development: A Mini-Review from a Developing Region. *International Journal of Cancer*, **133**, 1286-1292. <https://doi.org/10.1002/ijc.27858>
- [11] Chen, C.Y., Huang, K.Y.A., Shen, J.H., Tsao, K.C. and Huang, Y.C. (2015) A Large-Scale Seroprevalence of Epstein-Barr Virus in Taiwan. *PLoS ONE*, **10**, e0115836. <https://doi.org/10.1371/journal.pone.0115836>
- [12] Huang, Y., Wei, C., Zheng, K. and Zhao, D. (2013) The Impact of Serological Features in Chinese Children with Primary of Past Epstein-Barr Virus Infections. *Virology Journal*, **10**, 55-62. <https://doi.org/10.1186/1743-422X-10-55>
- [13] Dunmire, S.K., Verghese, P.S. and Balfour Jr., H.H. (2018) Primary Epstein-Barr Virus Infection. *Journal of Clinical Virology*, **102**, 84-92. <https://doi.org/10.1016/j.jcv.2018.03.001>
- [14] Puhakka, L., Sarvikivi, E., Lappalainen, M., Surcel, H.M. and Saxen, H. (2016) Decrease in Seroprevalence for Herpesviruses among Pregnant Women in Finland: Cross-Sectional Study of Three Time Points 1992, 2002 and 2012. *Infectious Diseases*, **48**, 406-410. <https://doi.org/10.3109/23744235.2015.1123290>
- [15] Linton, M.S., Kroeker, K., Fedorak, D., Dieleman, L. and Fedorak, R.N. (2013) Prevalence of Epstein-Barr Virus in a Population of Patients with Inflammatory Bowel Disease: A Prospective Cohort Study. *Alimentary Pharmacology & Therapeutics*, **38**, 1248-1254. <https://doi.org/10.1111/apt.12503>
- [16] van Zyl, D.G., Mautner, J. and Delecluse, H.J. (2019) Progress in EBV Vaccines. *Frontiers in Oncology*, **9**, 104. <https://doi.org/10.3389/fonc.2019.00104>
- [17] Dowd, J.B., Palermo, T., Brite, J., *et al.* (2013) Seroprevalence of Epstein-Barr Virus Infection in U.S. Children Ages 6-19, 2003-2010. *PLoS ONE*, **8**, e64921. <https://doi.org/10.1371/journal.pone.0064921>
- [18] Balfour, H.H., Sifakis, F., Sliman, J.A., Knight, J.A., Schmeling, D.O. and Thomas, W. (2013) Age-Specific Prevalence of Epstein-Barr Virus Infection among Individuals Ages 6 - 19 Years in the United States and Factors Affecting Its Acquisition. *The Journal of Infectious Diseases*, **208**, 1286-1293. <https://doi.org/10.1093/infdis/jit321>
- [19] Pourahamad, M., Hooshmand, F., Nezhad, S.O. and Sepidkar, A. (2014) EBV Seroprevalence in Married and Unmarried Women and Men in Iran. *Reports of Biochemistry and Molecular Biology*, **2**, 94-97.