

Original Article

The Sero-Epidemiology of Infectious Mononucleosis in Neyshabur during 2010-2014

Salehi M¹, Shokuhi-Mostafavi S Kh^{2*}, Mirzaee M³, Mobini M⁴, Gholami M⁵, Asghar Heydari M⁵

1. Medical Diagnostic Laboratory of Neyshabour, Center of Medical, Pathological and Genetic Diagnostic Services, Iranian Academic Center for Education, Culture and Research (ACECR), Mashhad Branch, Mashhad, Iran
2. Department of Microbiology, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran
3. Department of Laboratory Sciences, Borujerd Branch, Islamic Azad University, Borujerd, Iran
4. Young Researchers and Elite Clup, Islamic Azad University, Tonekabon Branch, Tonekabon, Iran
5. Isfahan University, Isfahan, Iran

Abstract

Background and Aims: EBV is a human herpesvirus that infects more than 90% of the world's population. Although, benign and asymptomatic in most cases, the infection can cause many nonmalignant and malignant disorders of lymphoid and epithelial origins. The objective of this study was detected in IM prevalence in Neyshabur, Northeast Iran from 2010-2014.

Materials and Methods: This cross-sectional descriptive epidemiological survey was performed in Neyshabur between 2010 and 2014 to reveal the prevalence of infectious mononucleosis. A total of 114 patients were studied. Briefly, patients with a positive test for specific IgG and IgM were determined as positive cases.

Results: the overall prevalence of IM was 14%. The mean age±SD for infectious mono test is 18.96± 15.79. the age groups of 0-10 and 21-30 years old, were the most positive cases in this period. In addition, 31-40 and upper 50 years were not positive cases. Male patients were significantly more positive and likewise, it was observed that the spring and summer seasons had significantly higher positive cases of IM. Among the five years of this study, it was a decreasing status from 2010 (23.1%) to 2014 (9.1%), although a slight fluctuation was occurring.

Conclusions: the prevalence of IM was low in Neyshabur city. Moreover, children and male patients had relatively higher prevalence of the disease. Furthermore, it was observed a higher rate of IM in the spring and summer seasons.

Keywords: Epstein-Barr virus, infectious mononucleosis, Neyshabur city, Iran

Introduction

Epstein-Barr virus (EBV) is in the genus herpesvirus infecting more than 90% of the world's population (1). Although

the disease is benign and asymptomatic for the most cases, EBV has the can cause many nonmalignant and malignant disorders of lymphoid and epithelial origins (2). EBV infection is mostly asymptomatic in children; however, first exposure during adolescence develops itself as an infectious mononucleosis (IM) in 30 to 70% of cases (3, 4). Some individuals are more vulnerable than others to develop clinical symptoms from delayed infection, while there is no reason (5, 6). The CD8+ T cells play a key protective role for the

*Corresponding author: Seyyed Khalil Shokuhi Mostafavi, PhD; Department of Microbiology, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran.
Email: Shokuhi64@yahoo.com

control of latent EBV infection however they are recognized to be the main mediators of the disease during IM (7, 8). Furthermore, observations suggest that other immune mediators are possibly important for the control and prevention of acute symptomatic EBV infection (9). Results from a recent phase II clinical trial revealed that the induction of neutralizing antibodies is effective in the prevention of symptomatic acute IM after primary infection (10). In spite of these effective results, very little emphasis has been noted upon the investigation of humoral immunity during primary infection, however defects in antibody level could contribute to the disease burden during acute IM (11). The virus can persistently shed in saliva for duration of six months (12). A study in southern Iran showed that the prevalence of EBV among Acute Lymphoblastic Leukemia (ALL) patients was high (13). Another survey indicated a relationship between EBV and breast cancer among women in Iran (14).

Methods

Viruses. This cross-sectional descriptive epidemiological survey was performed in Neyshabur between 2010 and 2014 to reveal the prevalence of infectious mononucleosis in Neyshabur during 2010-2014.

A total of 114 patients were studied.

Sample collection

Briefly, blood samples from patients were collected and the sera samples were prepared. Any patient with positive test for specific IgG and IgM were determined as positive cases.

Ethical approve. Approval for this study was obtained from the Research and Technology deputy of ACECR, Mashhad Branch.

Data analysis. Data were analyzed with SPSS version 20 (IBM SPSS Statistics for Windows, Version 20), and the chi-square test. P values <0.05 were considered statistically significant.

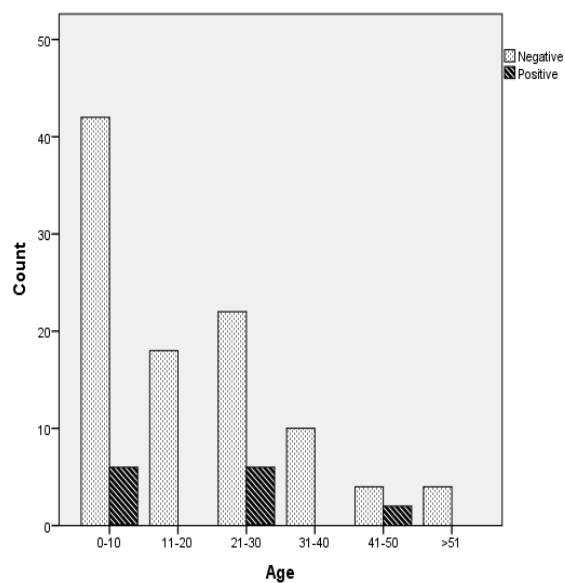


Fig.1. The age distribution of patients in this study.

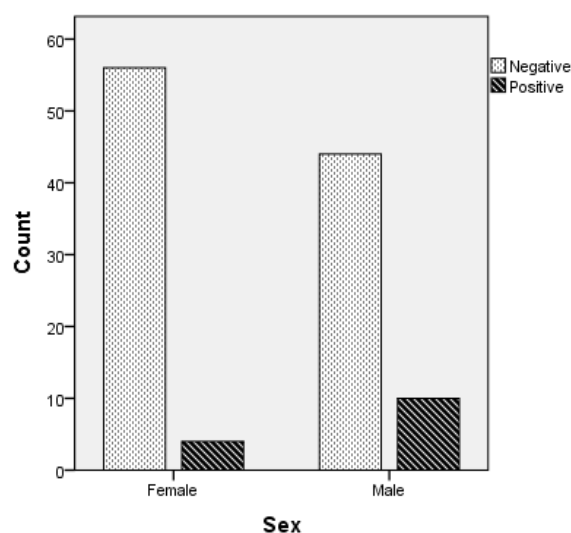


Fig. 2. The genders of this study and comparison between 2 groups.

Results

The mean age \pm SD for infectious mono test is 18.96 \pm 15.79. As shown in table 1, the overall prevalence of IM among 5 years was 14%. The age groups of 0-10 and 21-30 years old were the most positive cases in this period. In addition, 31-40 and upper 50 years were not positive cases. Male patients were significantly more positive and likewise, it was observed that the spring and summer seasons had significantly higher positive cases of mononucleosis (Table1 and Figures 1-3).

Table 1: The age, sex and seasonal distribution of positive cases of mononucleosis.

Demographic features	No.	Positive cases (%)	Odds ratio	95% CI	p value	
Age	0-10	48	6 (12.5)	Baseline		
	11-20	18	0 (0)	0.875	0.786-0.974	0.116
	21-30	28	6 (21.4)	1.909	0.550-6.621	0.303
	31-40	10	0 (0)	---	---	---
	41-50	6	2 (33.3)	3.5	0.523-23.418	0.176
	>51	4	0 (0)	---	---	---
Sex	Male	54	10 (18.5)	3.182	0.935-10.831	0.054
	Female	60	4 (6.7)			
season	Spring & summer	52	10 (19.2)	0.290	0.085-0.987	0.038
	Fall & winter	62	4 (6.45)			
Total		114	14 (12.3)			

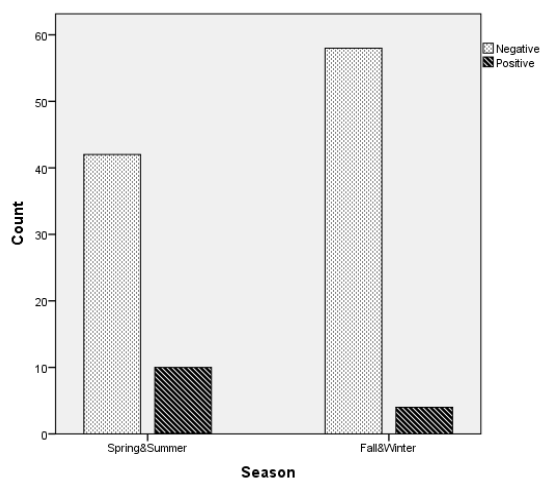


Fig. 3. The highest and lowest time seasons in which the positive cases of mononucleosis were observed.

Among the five years of this study, it was a decreasing status from 2010 (23.1%) to 2014 (9.1%), although a slight fluctuation was occurred (table2 and figure3).

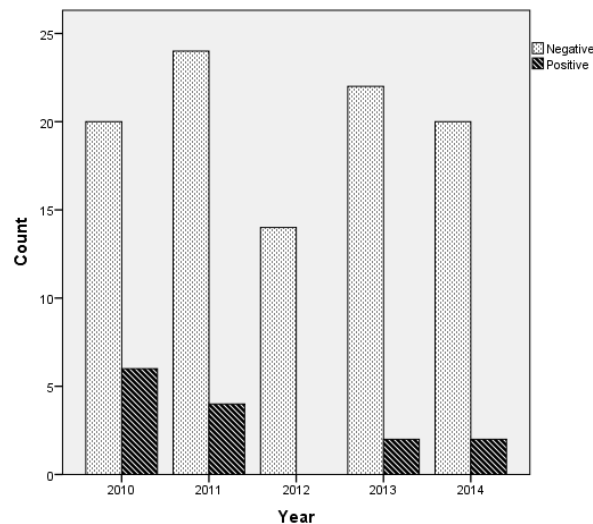


Fig. 4. The prevalence of mononucleosis in the each year of 2010-2014.

Table 2: The number and positive cases of mononucleosis in each year of this period (2010-2014).

year	NO.	Positive cases (%)
2010	26	6 (23.1)
2011	28	4 (14.3)
2012	14	0 (0)
2013	24	2 (8.3)
2014	22	2 (9.1)
Total	114	14 (12.3)

Discussion

In this study, the mean age \pm SD for infectious mono test was 18.96 \pm 15.79, and the age groups of 0-10 and 21-30 years old were the most positive cases in this period. The presence of the disease in children has been reported in several previous studies with different disorders and indications; such as enhanced cytotoxicity of specific T-cells (15), rash following amoxicillin treatment (16) and presence of soluble HLA-G in serum of children (17). In addition, patients with 31-40 and upper 50 years were all negative for the test. Several previous surveys have suggested the lymphocyte count as a valid diagnostic screen test in adults infected with mononucleosis with different results (18, 19). In this study, Male patients were significantly more positive and likewise, it was observed that the spring and summer seasons had significantly higher positive cases of mononucleosis. Similarly, Ramagopalan revealed that Males were more frequently infected with IM for all age groups apart from age ranges of 10–14 (FMR 1.50 and 95% confidence interval (CI) (20). Regarding differences between genders for infection susceptibility of Epstein-Bar virus, there have been several hypotheses, such as different social behaviors and thus interpersonal contact and exposure (21). Visser determined no evidence of relation between season and EBV infection in children (22). Seasonal fluctuations, sun radiation and vitamin D affect the immune system against EBV and several studies have similarly shown this effect (23, 24). On the other hand, we observed that among the five years of this study, it was a

decreasing status from 2010 (23.1%) to 2014 (9.1%), although a slight fluctuation was occurred.

References

1. Kong Q-L, Hu L-J, Cao J-Y, Huang Y-J, Xu L-H, Liang Y, et al. Epstein-Barr virus-encoded LMP2A induces an epithelial-mesenchymal transition and increases the number of side population stem-like cancer cells in nasopharyngeal carcinoma. *PLoS Pathog.* 2010;6(6):e1000940.
2. Jenson HB. Epstein-Barr virus. *Pediatrics in Review-Elk Grove.* 2011;32(9):375.
3. Balfour HH, Sifakis F, Sliman JA, Knight JA, Schmeling DO, Thomas W. Age-specific prevalence of Epstein-Barr virus infection among individuals aged 6–19 years in the United States and factors affecting its acquisition. *Journal of Infectious Diseases.* 2013;208(8):1286-93.
4. Lorenzetti MA, Gantuz M, Altcheh J, De Matteo E, Chabay PA, Preciado MV. Distinctive Epstein-Barr virus variants associated with benign and malignant pediatric pathologies: LMP1 sequence characterization and linkage with other viral gene polymorphisms. *Journal of clinical microbiology.* 2012;50(3):609-18.
5. Ozbek SM, Ozbek A, Yavuz MS. Detection of human cytomegalovirus and Epstein-Barr Virus in symptomatic and asymptomatic apical periodontitis lesions by real-time PCR. *Medicina oral, patologia oral y cirugia bucal.* 2013;18(5):e811.
6. Draborg AH, Duus K, Houen G. Epstein-Barr virus in systemic autoimmune diseases. *Clinical and Developmental Immunology.* 2013;2013.
7. Angelini DF, Serafini B, Piras E, Severa M, Coccia EM, Rosicarelli B, et al. Increased CD8+ T cell response to Epstein-Barr virus lytic antigens in

the active phase of multiple sclerosis. *PLoS Pathog.* 2013;9(4):e1003220.

8. Grywalska E, Markowicz J, Grabarczyk P, Pasiarski M, Rolinski J. Epstein-Barr virus-associated lymphoproliferative disorders. *Postepy Hig Med Dosw (Online)*. 2013;67:481-90.

9. Rickinson AB, Long HM, Palendira U, Münz C, Hislop AD. Cellular immune controls over Epstein-Barr virus infection: new lessons from the clinic and the laboratory. *Trends in immunology*. 2014;35(4):159-69.

10. Simon KC, O'Reilly EJ, Munger KL, Finerty S, Morgan AJ, Ascherio A. Epstein-Barr virus neutralizing antibody levels and risk of multiple sclerosis. *Multiple Sclerosis Journal*. 2012;18(8):1185-7.

11. Nagarajan T, Marissen WE, Rupprecht CE. Monoclonal antibodies for the prevention of rabies: theory and clinical practice. *Antibody Technology Journal*. 2014;4.

12. Balfour HH, Verghese P. Primary Epstein-Barr Virus Infection: Impact of Age at Acquisition, Coinfection, and Viral Load. *Journal of Infectious Diseases*. 2013;jit096.

13. Mahjour SB, Ghaffarpassand F, Fattahi MJ, Ghaderi A, Ghiam AF, Karimi M. Seroprevalence of human herpes simplex, hepatitis B and Epstein-Barr viruses in children with acute lymphoblastic leukemia in southern Iran. *Pathology & Oncology Research*. 2010;16(4):579-82.

14. Kadivar M, Monabati A, Joulaee A, Hosseini N. Epstein-Barr virus and breast cancer: lack of evidence for an association in Iranian women. *Pathology & Oncology Research*. 2011;17(3):489-92.

15. Chiang A, NING J, Chan K, editors. Emergence of highly functional antigen-specific T cells towards Epstein-Barr virus corresponds to viral control and enhanced cytotoxicity in children with infectious mononucleosis and primary asymptomatic infection. 16th International Symposium on EBV and Associated Diseases; 2014.

16. Chovel-Sella A, Tov AB, Lahav E, Mor O, Rudich H, Paret G, et al. Incidence of rash after amoxicillin treatment in children with infectious mononucleosis. *Pediatrics*. 2013;131(5):e1424-e7.

17. WANG H-y, TIAN K-g, FU M, ZHENG X-q. Detection of plasma soluble HLA-G and lymphocyte subsets in peripheral blood of children with infectious mononucleosis [J]. *Chinese Journal of Nosocomiology*. 2012;5:011.

18. Biggs TC, Hayes SM, Bird JH, Harries PG, Salib RJ. Use of the lymphocyte count as a diagnostic screen in adults with suspected Epstein-Barr virus infectious mononucleosis. *The Laryngoscope*. 2013;123(10):2401-4.

19. Biggs T, Hayes S, Harries P, Salib R, Bird J. In response to Use of the lymphocyte count as a diagnostic screen in adults with suspected Epstein-Barr virus infectious mononucleosis. *The Laryngoscope*. 2014;124(11):E448-E.

20. Ramagopalan SV, Giovannoni G, Yeates DG, Seagroatt V, Goldacre MJ. Sex ratio of infectious mononucleosis and possible relevance to multiple sclerosis. *Multiple Sclerosis Journal*. 2012;1352458512450627.

21. Hwang A, Hamilton A, Cockburn M, Ambinder R, Zadnick J, Brown E, et al. Evidence of genetic susceptibility to infectious mononucleosis: a twin study. *Epidemiology and Infection*. 2012;140(11):2089-95.

22. Visser E, Milne D, Collacott I, McLernon D, Counsell C, Vickers M. The epidemiology of infectious mononucleosis in Northern Scotland: a decreasing incidence and winter peak. *BMC Infectious Diseases*. 2014;14(1):151.

23. Lossius A, Riise T, Pugliatti M, Bjørnevik K, Casetta I, Drulovic J, et al. Season of infectious mononucleosis and risk of multiple sclerosis at different latitudes; the EnvIMS Study. *Multiple Sclerosis Journal*. 2013;1352458513505693.

24. Crump C, Sundquist J, Sieh W, Winkleby MA, Sundquist K. Season of birth and risk of Hodgkin and non-Hodgkin lymphoma. *International Journal of Cancer*. 2014;135(11):2735-9.