



RESEARCH ARTICLE

Increasing Epstein-Barr virus infection in Chinese children: A single institutional based retrospective study. [version 1; peer review: 1 not approved]

Kiran Devkota , Maio He, Meng Yi Liu, Yan Li, You Wei Zhang

Department of Pediatrics, Renmin Hospital, Hubei University of Medicine, Shiyan, Hubei, 44200, China

v1 **First published:** 07 Aug 2018, 7:1211 (<https://doi.org/10.12688/f1000research.15544.1>)
Latest published: 15 Feb 2019, 7:1211 (<https://doi.org/10.12688/f1000research.15544.2>)

Abstract

The Epstein-Barr virus (EBV) is a common virus in humans and the most common causative agent of Infectious Mononucleosis. EBV primary infection has recently risen in some countries and children below 2 years of age are highly susceptible. The clinical manifestations in children with EB virus infection involve multiple systems, causing severe illness, meaning attention should be paid during diagnosis and treatment.

Objective: This single institution based retrospective study was carried out with the aim of estimating the overall prevalence of EBV infection and identifying high-risk age group among children.

Methods: This study include total 253 patients under 15 years of age found to be positive for EBV DNA by PCR who were admitted to the Pediatrics Department of Renmin Hospital,(Shiyan, China) during a 4-year period from 2014 to 2017. Patients were divided into three groups; 0-<4years, 4-<6years and 6-<15years. We then calculated the percentage and prevalence of EBV DNA-positive cases.

Results: The yearly EBV prevalence rate was 4.99 per 1000 admissions in 2014, 6.97 per 1000 admissions in 2015, 10.42 per 1000 admissions in 2016, and 12.16 per 1000 admissions in 2017. Out of 253 EBV-positive cases, those under 4 years had the highest rate of EBV infection (74.7%). The rate drops to 11.06% in the 4-6 years group, and was 14.22% in the 6-15 years group. Those between 6 months and 1 year are those at the highest risk.







Conclusion: The rate of hospital admission of children due to EBV infection is increasing day by day. Children under 4 years of age are highly susceptible to infection and children of age between 6 months and 1 year are the high-risk group for EBV infection.

Keywords

Infectious mononucleosis; Prevalence; EBV DNA; Epstein-Barr virus

Open Peer Review

Referee Status:  

| | Invited Referees | |
|---|--|---|
| | 1 | 2 |
| version 2 published 15 Feb 2019 |  report |  report |
| |  | |
| version 1 published 07 Aug 2018 |  report | |
| <p>1 Anna Mania , Karol Marcinkowski University of Medical Sciences, Poland</p> <p>2 Michael J. Goldacre , University of Oxford, UK</p> <p>Any reports and responses or comments on the article can be found at the end of the article.</p> | | |

Corresponding author: You Wei Zhang (syyw125@sina.com)

Author roles: **Devkota K:** Conceptualization, Data Curation, Formal Analysis, Methodology, Project Administration, Software, Validation, Writing – Original Draft Preparation, Writing – Review & Editing; **He M:** Data Curation, Formal Analysis, Investigation, Methodology, Resources; **Liu MY:** Data Curation, Formal Analysis, Investigation, Methodology, Resources, Supervision; **Li Y:** Data Curation, Funding Acquisition, Investigation, Methodology, Project Administration, Resources; **Zhang YW:** Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Methodology, Resources, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2018 Devkota K *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution Licence](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Data associated with the article are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](#) (CC0 1.0 Public domain dedication).

How to cite this article: Devkota K, He M, Liu MY *et al.* **Increasing Epstein-Barr virus infection in Chinese children: A single institutional based retrospective study. [version 1; peer review: 1 not approved]** F1000Research 2018, 7:1211 (<https://doi.org/10.12688/f1000research.15544.1>)

First published: 07 Aug 2018, 7:1211 (<https://doi.org/10.12688/f1000research.15544.1>)

Introduction

The Epstein-Barr virus (EBV) is the most common herpesvirus in humans and the most common causative agent of infectious mononucleosis¹. It is also known as the “kissing disease”². EBV is an acute infection with a characteristic symptomatic triad of fever, sore throat and lymphadenopathy. Sprunt and Evans in 1920 coined the term infectious mononucleosis to describe an acute infectious disease accompanied by atypical large peripheral blood lymphocytes². EBV primary infection has recently risen in some countries³ and children below 2 years of age are highly susceptible^{4,5}. EBV is transmitted primarily via oral secretions and may be transmitted via penetrative sexual intercourse⁶. Transmission may occur by the exchange of saliva among children. EBV is not spread by non-intimate contact, environmental sources, or fomites⁶. During late adolescence 50–70 percent of teenagers get infected with infectious mononucleosis². Though it has a self-limiting course, it may sometimes lead to numerous rare, atypical and threatening manifestations. The clinical manifestations in children with EBV infection involve multiple systems and can cause severe illness, meaning that attention should be paid during diagnosis and treatment. The diagnosis of EBV infection is based on clinical features such as fever, pharyngitis, lymphadenopathy, hepatomegaly, and splenomegaly along with leukocytosis with a predominance of lymphocytes, >10% atypical lymphocytosis, heterophile antibodies (assessed via monospot test), PCR for EBV DNA and serological testing including antibodies for viral capsid antigens, early antigens, and Epstein-Barr nuclear antigen.

EBV DNA PCR has high specificity and sensitivity for identifying patients with infectious mononucleosis⁷.

Methods

Assessment

We retrospectively collected the EBV infection status in children <15 years old at Renmin Hospital, 3rd Affiliated Hospital of Hubei University of Medicine, Shiyan, (Hubei, China) during the 4-year period from January 1, 2014, to December 31, 2017. In total, 253 patients had with EBV infection and were positive for EBV DNA. At birth, neutrophils make up around 61% of total leukocytes and lymphocytes make up around 31%. After birth, the number of neutrophils goes down and the lymphocyte number goes up, with both reaching about 45% around the 1st week of life. This process continues and by the age of 4 years, lymphocytes reaches around 50% and neutrophils reach around 42%. On growing older, the proportion of lymphocytes starts to fall and that of neutrophils start to increases. By the age of 6 years, the proportion of neutrophils reaches up to 51% and that of lymphocytes falls to 42%⁸. Owing to this age-specific leukocytes differential, we divided patients into three age groups: <4 years, 4–<6 years and 6–<15 Years. We also made further age-specific groupings, as follows: <30 days, 1–<6 months, 6–<12 months, 1 year, 2 years, 3 years, 4 years, 5 years, 6 years, 7 years, 8 years, 9 years, 10 years, 11 years, 12 years, 13 years, and 14 years to find out the risk group for EBV infection. A diagnosis of EBV infection was achieved using real time PCR at the Pathology Department at Renmin Hospital.

Analysis

Real-time PCR ABI iiA7 was used for quantitation of EBV DNA. The primers used, targeting the EBNA-1 fragment of EBV, were as follows: 5'-GTAGAAGGCCATTTTCCAC-3' (forward) and 5'-TTTCTACGTGACTCCTAGCC-3' (reverse). PCR was conducted using the following thermocycling conditions: 93°C for 2 min, followed by 10 cycles of 93°C for 45 sec and 55°C for 60 sec, and then 30 cycles of 93°C for 30 sec and 55°C for 45 sec.

All data were analyzed using Microsoft Excel 2010. Age-specific prevalence was calculated. Prevalence was calculated as follows:

$$\text{Prevalence} = \frac{\text{number of EBV-positive children under 15 years admitted to hospital}}{\text{number of total hospital admissions for children under 15 years}}$$

Results

Out of the total of 253 patients, 151 (60%) were male and 102 (40%) were female. The male to female ratio was 3:2 (Figure 1).

The number of EBV DNA-positive cases observed increased each year. There were 36 EBV DNA positive cases in 2014 (total admissions, 7202) with a prevalence of 5.00 per 1000 admissions, 43 on 2015 (total admissions, 6163) with a prevalence of 6.98 per 1000, 77 on 2016 (total admissions, 7384) with prevalence of 10.43 per 1000 and 97 on 2017 (total admissions, 7972) with prevalence of 12.17 per 1000 admissions (Figure 2, Figure 3).

Over the 4 years studied here, the numbers of hospitalized children were highest in the 0 to < 4 years group. Of 253 EBV-positive patients, 189 (74.70%) were in group 0 to less than 4 years, 28 (11.06%) in the group of children aged 4 to <6 years, and 36 (14.23%) in those aged 6 to <15 years. Each year, in the group of children under 4 years the percentage of EBV positive cases were more and rate were in increasing trend (Figure 4, Figure 5).

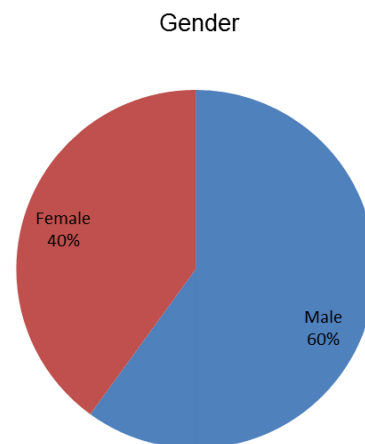


Figure 1. Sex distribution.

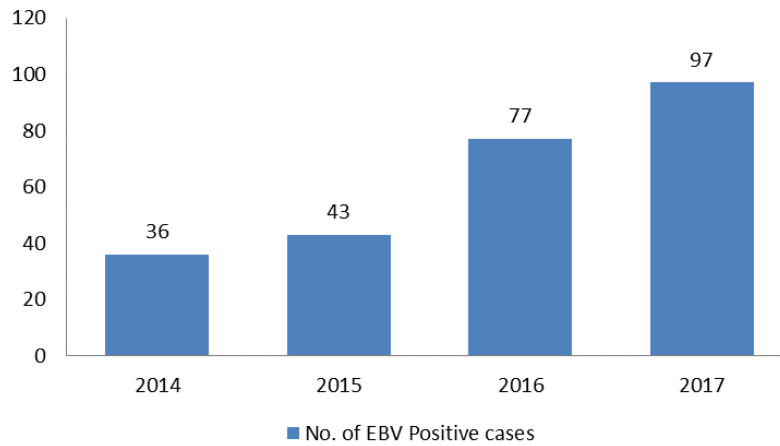


Figure 2. Yearly distribution of Epstein-Barr virus-positive patients.

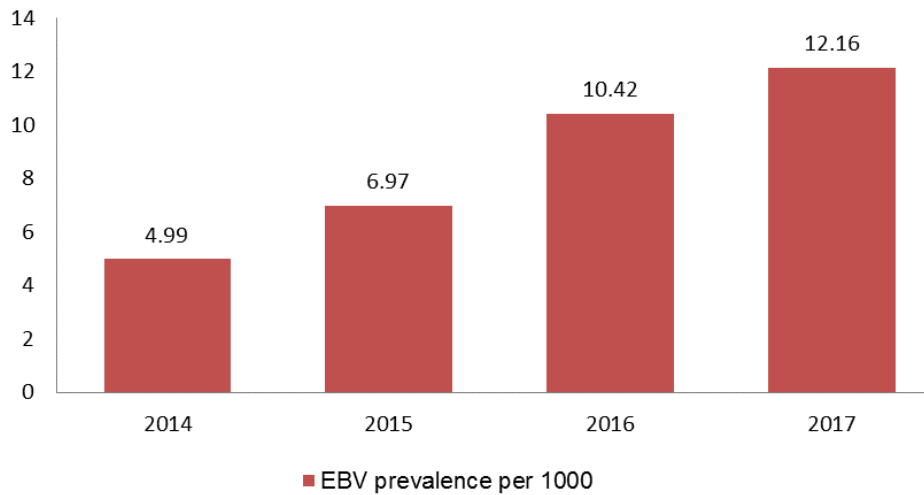


Figure 3. Prevalence of Epstein-Barr virus-positive patients per 1000 hospital admissions by year.

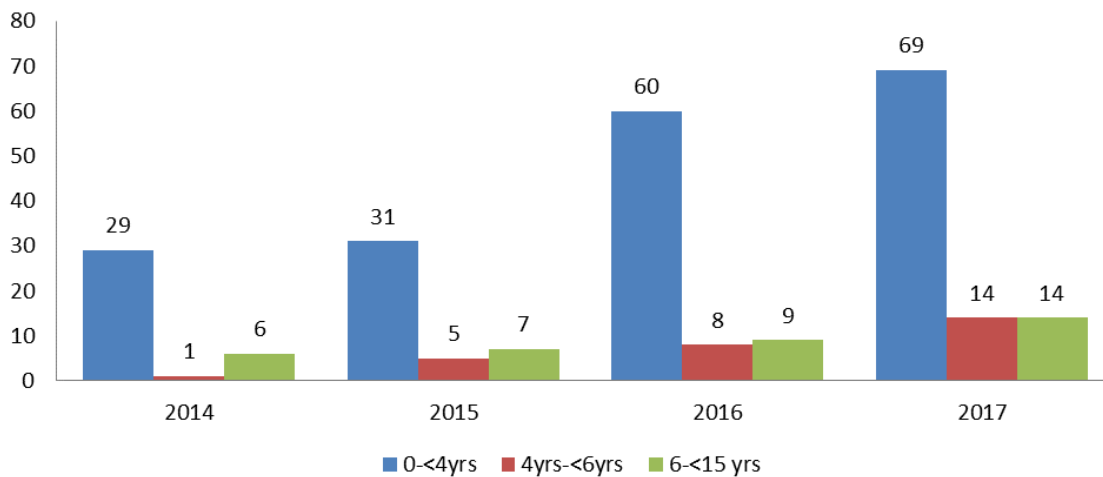


Figure 4. Age group distribution of Epstein-Barr virus-positive patients.

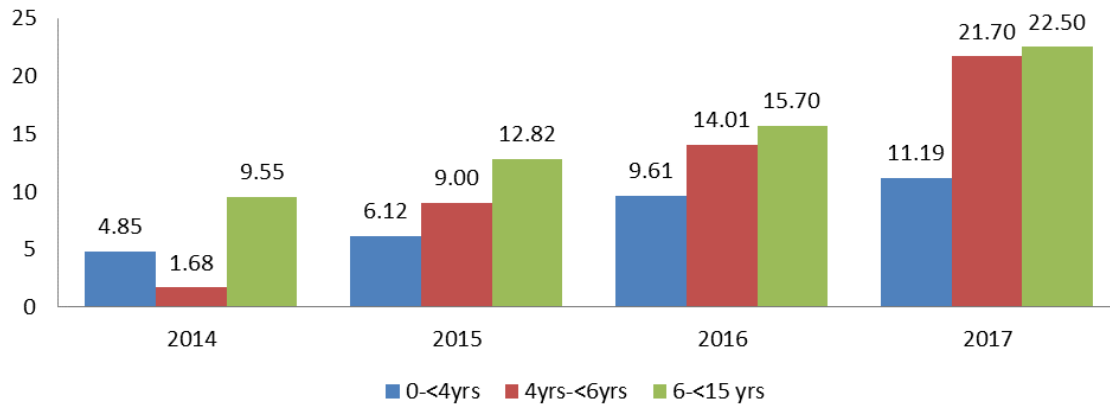


Figure 5. Prevalence of Epstein-Barr virus-positive patients cases of specific age groups per 1000 hospital admissions.

We calculated the age-specific prevalence of EBV infection to identify the high-risk group. The number of positive cases was highest in the age group 6 months- <1 year, which decreased as age increased. Prevalence is also high in this age group (Table 1 and Figure 6, Figure 7).

Dataset 1. The number of total admissions and admissions of Epstein-Barr virus (EBV)-positive children under 15 years of age for each of the years 2014–2017

<http://dx.doi.org/10.5256/f1000research.15544.d2121419>

This dataset also contains stratifications of EBV-positive individuals by age and sex.

Discussion

The incidence of EBV infection is higher in male children in Northern China¹⁰ and Turkey¹¹. In India, the male to female ratio of EBV infection in hospitalized children is 2:1^{12,13}. A Korean study found the overall male-to-female ratio of EBV infection to be 1.53:1¹⁴. Our study had a male to female ratio of 3:2. During adolescence, women acquire before men the first infection by EBV¹⁵. In the US EBV antibody titers were significantly higher for females¹⁶.

We have found that in children under 4 years, the percentage of EBV-positive cases increased each year. However, in children aged 4–<6 years this decreased, but increased in those aged 6 to <15 years. Out of the 253 EBV positive patients, those aged under 4 years made up the highest proportion (74.7%). This drops to 11.06% in those 4–<6 years, and 14.22% in those 6–<15 years. In the study done on the Northern and Southern part of China, the seroprevalence of EBV infection is more than 50% before age 3². Serological evidence of EBV infection is found in around 84% of Chinese children aged >9 years, with peak incidence observed at age 2–3 years¹⁷. However, in a study done by Gao *et al.*, the incidence of EBV-IM peaked in children at age of 4–<6 years in Northern China¹⁰. In Taiwan, the seropositive rate of EBV is high in children aged 2 years⁴. A Danish study found that EBV infection is common in young children, and children under 3 years of age constitute the largest group of hospitalizations for acute EBV infection⁵.

In a study conducted in Poland, age of infection occurred in two peaks, i) in children aged 1 to 5 years (62%), and ii) in teenagers (24.6%)¹⁸. In most developing countries nearly 70% of patients are seropositive for EBV by the age of 2 years¹⁹. However in USA, the seroprevalence increased with age, ranging from 54.1% for 6–8 year-olds to 82.9% for 18–19 year-olds¹⁶.

We found hospitalization for mononucleosis in all age groups. The number of positive cases was higher in the age group >6 months but <1 year, which decreases as age increases. The prevalence is also high on age group 6 month to 1 year. This indicates that the age group 6 months to less than 1 year is a high-risk group. The most common age group for hospitalization with acute EBV infection in Denmark was 1–2 years³. In Asia and other developing countries most of the children are infected with EBV in early life, mostly before the age of 1 year²⁰. According to Cocuz *et al.*, admissions for infectious mononucleosis were prevalent in young children, with most occurring in the 1–3 years age group (32.31% of the total IM Cases), followed by those 4–<6 years old (27.69% of the total IM Cases), then those 11–16 years old (26.15% of the total IM Cases) and finally those 7–10 years old (13.84% of the total IM Cases)²¹.

Several prior studies have reported in the last decade which shows the changes in the epidemiology of EBV infection. A Japanese study showed that the seroprevalence of EBV in 5–7 years old children was higher than 80% before the early 1990s which decreased to 59% in the years 1995²⁰. Similarly in the USA, the study showed that the seroprevalence in 6–19 year olds declined from 72% in 2003–2004 to 65% in 2009–2010²². But, the EBV primary infection is increasing in England and Wales²³. Therefore, we aimed to determine the epidemiological condition of EBV infection over the last years in the Pediatrics Department of Renmin Hospital, Shiyan, China. The EBV positivity rate in hospitalized children is increasing every year. Prevalence is also increased each year. In the years 2000 to 2016, the EBV infection rate in France has increased, whereas its seroprevalence has decreased³.

Although most EBV infections are self-limiting, sometimes they may lead to rare, atypical and threatening manifestations.

Table 1. Age-specific distribution and prevalence of Epstein-Barr virus.

| Age | 2014 | | | 2015 | | | 2016 | | | 2017 | | |
|---------------|-------|---|------|--------|----|------|-------|----|------|-------|----|------|
| | P | C | N | P | C | N | P | C | N | P | C | N |
| 0-30 days | 0 | 0 | 668 | 0 | 0 | 554 | 4.94 | 4 | 809 | 4.87 | 2 | 410 |
| ≥1-<6 months | 1.05 | 1 | 954 | 0 | 0 | 984 | 2.66 | 3 | 1124 | 1.84 | 2 | 1083 |
| ≥6-<12 months | 37.38 | 8 | 214 | 53.92 | 11 | 204 | 82.19 | 18 | 219 | 93.18 | 26 | 279 |
| 1 year | 2.18 | 4 | 1837 | 6.28 | 10 | 1592 | 10.38 | 20 | 1925 | 7.00 | 15 | 2141 |
| 2 years | 7.31 | 8 | 1094 | 7.46 | 5 | 670 | 8.05 | 8 | 869 | 15.47 | 13 | 840 |
| 3 years | 11.44 | 8 | 699 | 6.20 | 4 | 645 | 10.21 | 7 | 685 | 13.33 | 11 | 825 |
| 4 years | 1.94 | 1 | 514 | 2.42 | 1 | 413 | 8.21 | 5 | 609 | 16.97 | 10 | 589 |
| 5 years | 0 | 0 | 343 | 12.90 | 4 | 310 | 8.90 | 3 | 337 | 9.63 | 4 | 415 |
| 6 years | 11.95 | 3 | 251 | 8.16 | 2 | 245 | 17.09 | 4 | 234 | 21.73 | 5 | 230 |
| 7 years | 5.12 | 1 | 195 | 6.36 | 1 | 157 | 11.76 | 2 | 170 | 18.86 | 3 | 159 |
| 8 years | 0 | 0 | 144 | 0 | 0 | 127 | 0 | 0 | 128 | 15.87 | 2 | 126 |
| 9 years | 0 | 0 | 92 | 11.11 | 1 | 90 | 10.75 | 1 | 93 | 10.10 | 1 | 99 |
| 10 years | 14.28 | 1 | 70 | 15.87 | 1 | 63 | 27.02 | 2 | 74 | 9.52 | 1 | 105 |
| 11 years | 16.39 | 1 | 61 | 16.66 | 1 | 60 | 0 | 0 | 50 | 0 | 0 | 55 |
| 12 years | 0 | 0 | 40 | 0 | 0 | 26 | 0 | 0 | 34 | 47.61 | 2 | 42 |
| 13 years | 0 | 0 | 19 | 142.85 | 2 | 14 | 0 | 0 | 11 | 0 | 0 | 24 |
| 14 years | 0 | 0 | 7 | 0 | 0 | 9 | 0 | 0 | 13 | 0 | 0 | 12 |

P, Prevalence of Epstein-Barr virus (EBV)-positive cases per 1000; C, number of EBV-positive cases; N, total number of hospital admissions.

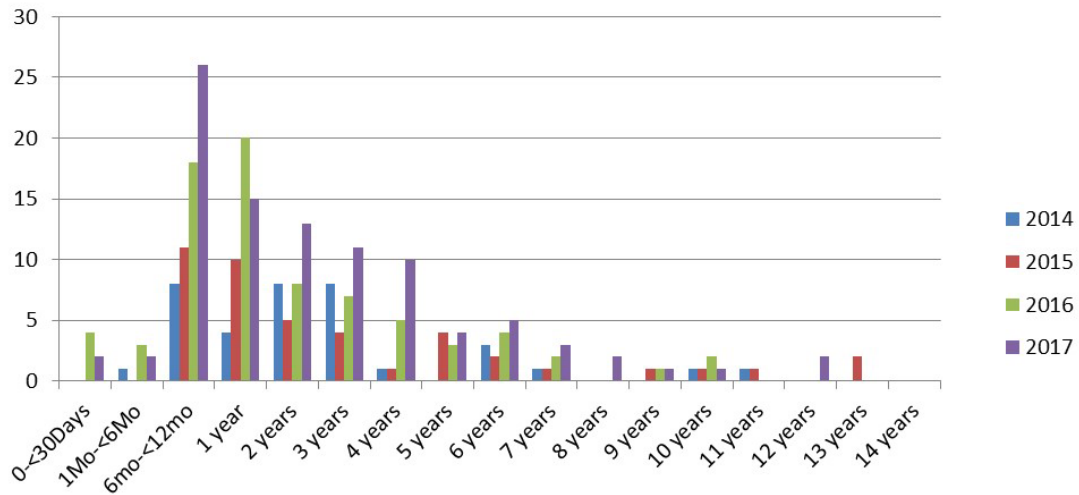


Figure 6. Age-specific distribution of Epstein-Barr virus-positive patients.

Although serious complications during the acute phase of primary EBV infection are rare¹, neurological complications, like meningoencephalitis, acute encephalitis, acute cerebellitis, transverse myelitis, and myeloradiculitis, occur more frequently in children under 2 years of age^{18,24,25}. Furthermore, in immunocompromised individuals, there was an association observed between EBV with several tumors following reactivation of the virus from latency²⁶.

Since this study was conducted in children admitted to hospital, the results might lack generalization to the entire population, but may indicate trends and bring up questions deserving further prospective study.

Increasing primary infection of EBV in children may be due to many reasons, including that the virus is active among the population around Shiyan, airborne transmission²⁷ of the virus

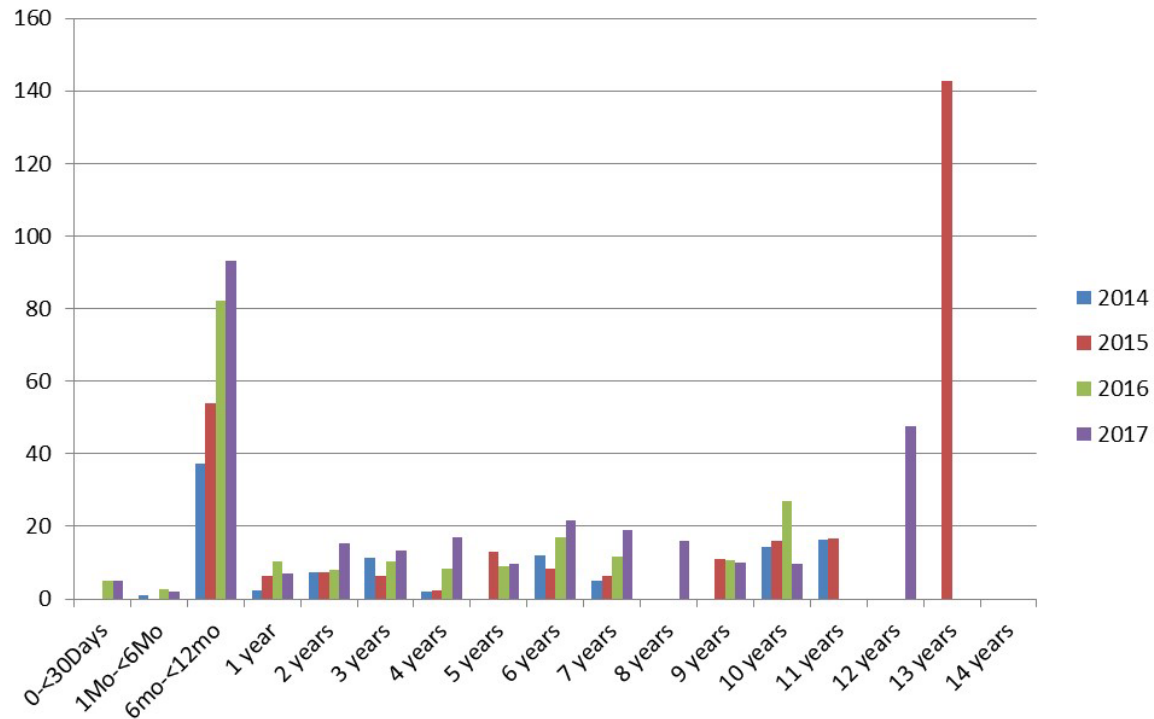


Figure 7. Age-specific distribution of Epstein-Barr virus-positive patients per 1000 hospital admissions.

is higher in this area, multiple caregivers for each infant, bottle feeding, unnecessary kissing, feeding with chewed food to babies, or through hospital acquired EBV infection e.g. from health care personals, doctors or nurses. There are several reports on the intrauterine transmission of EBV, but none has been substantiated by appropriate viral studies^{28,29}. Besides, doctors may be more familiar and experienced with the clinical presentation, symptoms, and signs of infectious mononucleosis.

The next steps should be a focus on awareness to parents and caregivers of children, and development of a vaccine against EBV to reduce the burden of EBV infection in future.

Conclusion

The rate of hospital admission of children due to EBV infection is increasing. Children under 4 years of age are highly susceptible to infection and children of age between 6 months and 1 year are the high-risk group for EBV infection. Vaccination against EBV must be considered to reduce the burden of EBV infection in future.

Data availability

Dataset 1. The number of total admissions and admissions of Epstein-Barr virus (EBV)-positive children under 15 years of age for each of the years 2014–2017. This dataset also contains stratifications of EBV-positive individuals by age and sex. DOI: <https://doi.org/10.5256/f1000research.15544.d212141>⁹.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

Acknowledgments

We wish to thank Dr Li Lian Director of Pathology Department, Renmin Hospital Dr. Liu Zheng Mei, Dr. Ke Wei, Dr. Tian Cai Xia and entire staff of doctors and nurses at the Department of Pediatrics, Renmin Hospital.

References

- Dunmire SK, Hogquist KA, Balfour HH: **Infectious Mononucleosis.** *Curr Top Microbiol Immunol.* 2015; **390**(Pt 1): 211–240. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Xiong G, Zhang B, Huang MY, *et al.*: **Epstein-Barr virus (EBV) infection in Chinese children: a retrospective study of age-specific prevalence.** *PLoS One.* 2014; **9**(6): e99857. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Fourcade G, Germe R, Guerber F, *et al.*: **Evolution of EBV seroprevalence and**

- primary infection age in a French hospital and a city laboratory network, 2000-2016. *PLoS One*. 2017; 12(4): e0175574.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Chen CY, Huang KY, Shen JH, *et al.*: **A large-scale seroprevalence of Epstein-Barr virus in Taiwan.** *PLoS One*. 2015; 10(1): e0115836.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 5. Topp SK, Rosenfeldt V, Vestergaard H, *et al.*: **Clinical characteristics and laboratory findings in Danish children hospitalized with primary Epstein-Barr virus infection.** *Infect Dis (Lond)*. 2015; 47(12): 908–14.
[PubMed Abstract](#) | [Publisher Full Text](#)
 6. Jenson HB: **Chapter 154: Epstein - Barr virus.** In *Nelson Textbook of Pediatrics*. 20th Edition. Elsevier, Philadelphia: Elsevier Inc. 2016; 1586–1590.
 7. Jiang SY, Yang JW, Shao JB, *et al.*: **Real-time polymerase chain reaction for diagnosing infectious mononucleosis in pediatric patients: A systematic review and meta-analysis.** *J Med Virol*. 2016; 88(5): 871–876.
[PubMed Abstract](#) | [Publisher Full Text](#)
 8. Radha G, Elizabeth J: **“Chapter 14: Hematology.”** In *The Harriet Lane Handbook*, 20th Edition. Elsevier, Philadelphia: Elsevier Inc. 2015; 313–314.
 9. Devkota K, He M, Liu MY, *et al.*: **Dataset 1 in: Increasing Epstein-Barr virus infection in Chinese children: A single institutional based retrospective study.** *F1000Research*. 2018.
<http://www.doi.org/10.5256/f1000research.15544.d212141>
 10. Gao LW, Xie ZD, Liu YY, *et al.*: **Epidemiologic and clinical characteristics of infectious mononucleosis associated with Epstein-Barr virus infection in children in Beijing, China.** *World J Pediatr*. 2011; 7(1): 45–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
 11. Cengiz AB, Cultu-Kantaroglu O, Seçmeer G, *et al.*: **Infectious mononucleosis in Turkish children.** *Turk J Pediatr*. 2010; 52(3): 245–54.
[PubMed Abstract](#)
 12. Ramagopalan SV, Giovannoni G, Yeates DG, *et al.*: **Sex ratio of infectious mononucleosis and possible relevance to multiple sclerosis.** *Mult Scler*. 2013; 19(3): 359–61.
[PubMed Abstract](#) | [Publisher Full Text](#)
 13. Balasubramanian S, Ganesh R, Kumar JR: **Profile of EBV associated infectious mononucleosis.** *Indian Pediatr*. 2012; 49(10): 837–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 14. Son KH, Shin MY: **Clinical features of Epstein-Barr virus-associated infectious mononucleosis in hospitalized Korean children.** *Korean J Pediatr*. 2011; 54(10): 409–13.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 15. Trastoy Pena R, Costa Alcalde JJ, Rodríguez Calviño J, *et al.*: **[Infection by the Epstein-Barr virus between the years 2006-2015 in the health area of Santiago de Compostela. Relationship with age and sex].** *Rev Esp Quimioter*. 2017; 30(6): 468–471.
[PubMed Abstract](#)
 16. Dowd JB, Palermo T, Brite J, *et al.*: **Seroprevalence of Epstein-Barr virus infection in U.S. children ages 6-19, 2003-2010.** *PLoS One*. 2013; 8(5): e64921.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 17. Huang Y, Wei C, Zheng K, *et al.*: **The impact of serological features in Chinese children with primary or past Epstein-Barr virus infections.** *Virology*. 2013; 455: 55–60.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 18. Millichap JG: **Epstein-Barr Virus Neurologic Complications.** *Pediatric Neurology Briefs*. 2015; 29(11): 88.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 19. Chabay PA, Preciado MV: **EBV primary infection in childhood and its relation to B-cell lymphoma development: a mini-review from a developing region.** *Int J Cancer*. 2013; 133(6): 1286–92.
[PubMed Abstract](#) | [Publisher Full Text](#)
 20. Takeuchi K, Tanaka-Taya K, Kazuyama Y, *et al.*: **Prevalence of Epstein-Barr virus in Japan: trends and future prediction.** *Pathol Int*. 2006; 56(3): 112–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
 21. Cocuz ME, Cocuz IG: **Infectious Mononucleosis in Children- Current Clinical and Epidemiological Aspects.** *Bulletin of the Transilvania University of Braşov*. 2016; 9(58): 55–60.
[Reference Source](#)
 22. Balfour HH Jr, Sifakis F, Sliman JA, *et al.*: **Age-specific prevalence of Epstein-Barr virus infection among individuals aged 6-19 years in the United States and factors affecting its acquisition.** *J Infect Dis*. 2013; 208(8): 1286–93.
[PubMed Abstract](#) | [Publisher Full Text](#)
 23. Morris MC, Edmunds WJ, Hesketh LM, *et al.*: **Sero-epidemiological patterns of Epstein-Barr and herpes simplex (HSV-1 and HSV-2) viruses in England and Wales.** *J Med Virol*. 2002; 67(4): 522–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 24. Çelik T, Çelik Ü, Tolunay O, *et al.*: **Epstein-Barr virus encephalitis with substantia nigra involvement.** *J Pediatr Neurosci*. 2015; 10(4): 401–403.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 25. Mazur-Melewska K, Breńska I, Jończyk-Potoczna K, *et al.*: **Neurologic Complications Caused by Epstein-Barr Virus in Pediatric Patients.** *J Child Neurol*. 2016; 31(6): 700–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 26. Ali AS, Al-Shraim M, Al-Hakami AM, *et al.*: **Epstein - Barr virus: Clinical and Epidemiological Revisits and Genetic Basis of Oncogenesis.** *Open Virol J*. 2015; 9: 7–28.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 27. Payne DA, Mehta SK, Tying SK, *et al.*: **Incidence of Epstein-Barr virus in astronaut saliva during spaceflight.** *Aviat Space Environ Med*. 1999; 70(12): 1211–3.
[PubMed Abstract](#)
 28. Horwitz CA, McClain K, Henle W, *et al.*: **Fatal illness in a 2-week-old infant: diagnosis by detection of Epstein-Barr virus genomes from a lymph node biopsy.** *J Pediatr*. 1983; 103(5): 752–755.
[PubMed Abstract](#) | [Publisher Full Text](#)
 29. Goldberg GN, Fulginiti VA, Ray CG, *et al.*: **In utero Epstein-Barr virus (infectious mononucleosis) infection.** *JAMA*. 1981; 246(14): 1579–1581.
[PubMed Abstract](#) | [Publisher Full Text](#)

Open Peer Review

Current Referee Status: 

Version 1

Referee Report 12 September 2018

<https://doi.org/10.5256/f1000research.16956.r37372>



Anna Mania 

Department of Infectious Diseases and Child Neurology, Karol Marcinkowski University of Medical Sciences, Poznań, Poland

The study presents results of retrospective analysis conducted to estimate the overall prevalence of EBV infection and identify high risk groups among children.

This study included 253 patients under 15 years of age positive for EBV DNA by PCR, were admitted to the Pediatrics Department in China during a 4-year period from 2014 to 2017. Patients were divided into three groups; 0-<4years, 4-<6years and 6-<15years. The percentage and prevalence of EBV DNA-positive cases was calculated on that basis.

The highest rate of EBV infection (74.7%) was observed in the group under 4 years of age, 11.06% and 14.22% in the 4-6 years and in the 6-15 years group, respectively.

The authors mention increasing number of EBV-infected individuals in recent years. Noticing the highest number of cases in children between 6 month to 1 year.

Certain limitations of the study were visible:

1. The authors confirm EBV infection by PCR, however I could not find the information concerning the type of the specimen – blood, saliva, urine, anything else?
2. Significant proportion of EBV infected patient may be asymptomatic; the term infection is not equivalent to the disease, therefore it is a pity that data concerning clinical symptoms are not mentioned.

Minor comments:

1. Citing articles are not equivalent to given numbers e.g –study conducted in Poland is given at the 25 positions in the list, not 18;

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: infectious diseases, pediatrics

I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 04 Feb 2019

Kiran Devkota, Hubei University of Medicine, China

Respected Professor

Thank you so much for you time and consideration. I have tried to make clear on the queries that you have noted.

Competing Interests: No competing interests were disclosed.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research