

Secular and seasonal trends of infectious mononucleosis among young adults in Israel: 1978–2009

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Abstract Recent evidence that infectious mononucleosis (IM) may be sexually transmitted prompted the present analysis. Infectious mononucleosis is a notifiable disease in the Israel Defense Forces (IDF). For the present study, the archives of the IDF were reviewed for all cases of IM from January 1, 1978 to December 31, 2009, and the rates were

calculated. Annual rates decreased from 2.99 cases per 1,000 in 1979 to a low of 0.38 cases per 1,000 young adults in 1987. Between 2002 and 2009, the average annual rate was 0.88 cases per 1,000, just half the average rate of 1.69 observed between 1989 and 2001. Average monthly rates varied from a low of 0.90 cases per 10,000 in February to a high of 1.50 cases per 10,000 in August. The difference in the average rates between winter (1.02 cases per 10,000 soldiers) and summer (1.29 cases per 10,000 soldiers) was significant ($p < 0.01$). Analysis of the long-term epidemiology of IM shows that the infection rate has varied over time, and that the disease is more prevalent in the warmer months. This seasonality trend was also observed in several STD, raising the possibility of considering this mode of transmission in IM.

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Introduction

Infectious mononucleosis (IM) is an important public health problem with rare but significant long-term consequences. The disease has a worldwide distribution, though it occurs most frequently in industrialized countries, particularly in adolescents and young adults of higher socioeconomic status [1]. The estimated annual incidence of IM in the United States is 45 cases per 100,000 in the general population [2, 3] and 345 to 671 cases per 100,000 in the 15–19-year age group [3, 4]. IM is caused by infection with Epstein-Barr virus (EBV), a tumorigenic herpes virus also associated with several lymphoproliferative diseases, such as Burkitt lymphoma and Hodgkin disease, as well as with nasopharyngeal carcinoma. Clinically, IM is characterized by a classic triad of fever, pharyngitis, and lymphadenopathy [5].

Recent biological and epidemiological studies have provided evidence that EBV is a sexually transmitted disease. Sixbey et al. [6] showed that EBV replicates in cervical epithelial cells in sexually active women. Using culture and cytohybridization studies, they detected the virus in cervical secretions and EBV DNA in epithelial cells from cervical samples. Balancing these findings, Israele et al. [7], in a polymerase chain reaction (PCR) analysis, detected EBV DNA in urethral discharges from men attending a clinic for sexually transmitted diseases. Half the examinees were concurrently excreting the virus from their oropharynx. Another study performed on HIV-infected patients demonstrated EBV in anal cell samples [8].

Secular trends of IM have been mostly irregular, and dynamic changes are very frequent. It is clear that with a better understanding of the annual and seasonal trends of IM, efforts to control the spread of the disease can be more timely, accurate and effective. Detailed information on the population impact of IM is generally not available since it is not a notifiable disease in many countries, and the non-specific symptoms can be attributed to a variety of other causes. This study was performed in the Israel Defence Force (IDF), where IM has been a notifiable disease since 1978. Physicians are required to routinely report all suspected or confirmed cases in military personnel to the Epidemiology Section of the Army Health Branch. This mandatory notification has yielded a large, unique, population database for the disease.

Patients and methods

The archives of the Epidemiology Section, Army Health Branch were carefully reviewed for all documented cases of IM from January 1, 1978 (start of mandatory notification) to December 31, 2009 (latest available data). Our analysis covered all compulsory and career IDF personnel. Since military service is mandatory in Israel for males and females, the population represents a sample of the young adult population in Israel, excluding ultra-orthodox Jews and Israeli Arabs as well as people with severe chronic illnesses who are largely exempted from service, and are thus under-represented in the population. Reserve personnel were excluded from the study.

The diagnosis of IM infection in the IDF is based on the clinical presentation, relevant epidemiologic data, and when available confirmation by positive serology. For the present study, cases of IM were identified by the diagnosis reported by the military physician on the notification form.

Statistical analysis

The annual rates of IM cases were calculated by dividing the number of cases each year by the mean annual military population in the same year. The average monthly rates of IM cases were calculated by dividing the number of cases each month by the mean annual population and calculating the average. Geographically, the state of Israel is located between 29° and 33° north of the equator, which is characterized as a subtropical region. The rainy season extends from October to early May, and rainfall peaks in December through February. For the purpose of this study summer was defined as April to September and winter as October to March. Average rates of IM for summer (April to September) and winter (October to March) were calculated in the same manner. The two-tailed binomial test was used to compare incidence rates between summer and winter. All statistical tests were performed with WINPEPI Computer Programs for Epidemiologists (WINPEPI, version 11.1; copyright JH Abramson & PM Gahlinger, 1993–97).

Results

The distributions of age, sex, and service type in the study population for the overall study period were as follows: male conscripts (aged 18–21 years), 53%; female conscripts (aged 18–20 years), 25%; male career personnel (aged 22–45 years, mainly 22–30 years), 19%; and female career personnel (aged 21–45 years), 3%.

Annual epidemiology

The secular trends in annual incidence rates (Fig. 1) could be roughly divided into three periods. Between 1978 and 1988, there was a gradual decrease in incidence, from a peak of 2.99 cases per 1,000 in 1979 to an all-time low of 0.38 cases per 1,000 in 1987. Between 1989 and 2001, rates remained relatively stable, with an average of 1.69 cases per 1,000 per year. During the final period, between 2002 and 2009, the average annual incidence rate dropped to 0.88 cases per 1,000.

Seasonal epidemiology

The average monthly seasonal incidence of IM in the military population is presented in Fig. 2. The average monthly rates varied from a low of 0.90 cases per 10,000 in February to a high of 1.50 cases per 10,000 in August. The rates in summer (1.29 cases per 10,000 soldiers) were

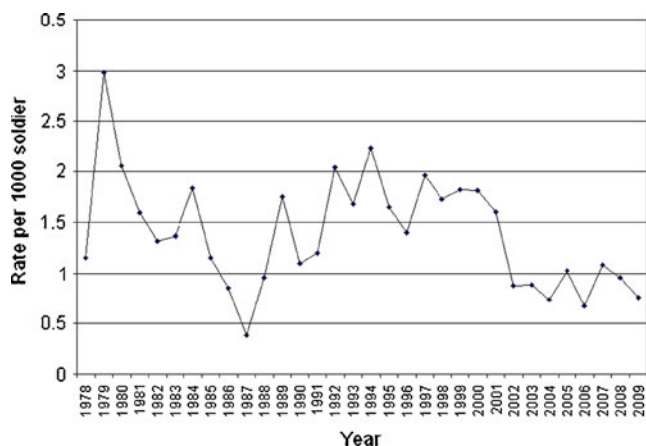


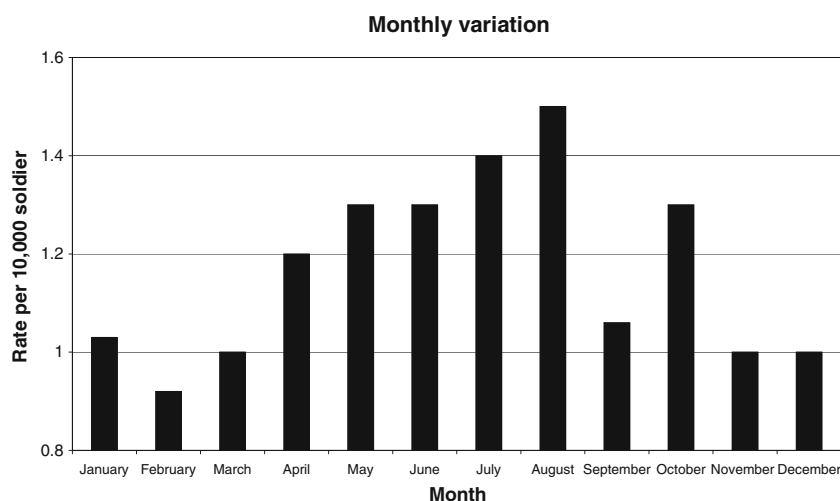
Fig. 1 Infectious mononucleosis in the Israel Defence Force, annual incidence rates per 1,000 young adults, 1978–2009

significantly ($p < 0.01$) higher than the rates in winter (1.02 cases per 10,000 soldiers).

Discussion

The results of this long-term epidemiology study suggest that the rates of IM in the IDF have varied significantly over the last 30 years, with occasional peaks. The most clear time trend was a decrease from an all time peak in 1979 to an all-time low in 1987. Researchers believe that widespread fear of HIV infection led to safer sexual practices, and to an overall decline in all STDs during that time period [9]. Similar decline during this time period was previously observed by our group for gonorrheal infection, another STD, in the Israeli military and civilian populations [10]. We were not able to see if this correlation is valid as well for other STDs such as syphilis and HIV due to extremely low incidence of these diseases in the IDF.

Fig. 2 Infectious mononucleosis in the Israel Defence Force, average monthly incidence rates per 10,000 young adults, 1978–2009



Interestingly, there was a clear seasonal pattern, with a predominance of the infection in the warmer months of the year. In an earlier epidemiological study by our group, we found that gonorrheal infection occurs predominantly in the warmer months [10], and we hypothesized that this seasonal variance was associated with the seasonal variance of sexual activity, which was found to be higher in spring and summer. A similar relationship may apply to EBV infection. The main known mode of transmission of EBV is saliva. Among children, the infection is probably transmitted through saliva present on the hands of caregivers; among young adults, kissing is considered the main route [11]. The virus can also be transmitted by blood transfusion, but this mode is rare. Furthermore, earlier reports from US colleges and universities did not describe a definite seasonal pattern for IM [12], in a more recent previous study of the clinical, laboratory, and seasonality patterns of IM in the same target population as the present one, though for a period of only 4 years (total, 590 patients), our group clearly demonstrated a strong tendency for the warmer months of the year [5]. Together with the present larger-scale study, these findings [5, 10, 11] support recent biological and epidemiological studies suggesting that EBV may be considered a sexually transmitted disease, at least among young adults [6–8].

Given the summer predominance of IM, its probably contagious nature, and its tendency to appear in clusters and thereby interfere with military activities, the IDF has taken several interventional steps to control the disease incidence. These included intensified health education and prevention programs and the distribution of clinical guidelines to army physicians just before the summer season.

There are some possible limitations of this study. We suspect that not all physician-reported cases of IM were

indeed laboratory-confirmed. However, it is unlikely that the rate of laboratory confirmation changed over time, so this would not affect the validity of the trend or season analysis. Another possible bias is missed/non-reported cases of IM in soldiers who sought medical attention in the private civilian sector during leave. However, as sick days were mandatorily reported to the military medical system during the study period, a very low rate of missing cases is assumed. In addition, the database does not contain data on the mode of transmission, making it impossible for us to study this aspect of the disease epidemiology.

Our findings suggest that particular attention should be addressed to the increased rates of IM during the warmer months of the year. A seroepidemiological study complementing this report is currently underway in the IDF to shed light on trends in susceptibility of young adults in Israel over time and on exposure to EBV during military service.

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Conflict of interest None

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