VIRAL INFECTIONS, PREVALENCE AND COSTS: A 5-year, hospital based, retrospective observational study in Shiraz, Iran

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ABSTRACT
Objective: Many patients suffering from viral infections attend to health care centers. Data gathered from viral infections is limited to specific cases such as AIDS, viral hepatitis and Influenza. There is a significant lack of reliable documentation about other viral infections. In this study the prevalence and related costs of viral infections in hospitals of Shiraz University of Medical Sciences were reviewed.

Methodology: In this cross-sectional study the data were extracted from files of 1319 patients with viral infection admitted in two university hospitals during a five year period (1999-2004). The frequencies of different viral infections along with their demographic data were analyzed.

Results: The mean age of the patients was 29.24 with the range of 90 years. Hospitalization days were 8636 in 40 different wards in two hospitals. US$ 30.84 was the daily mean cost for each admitted patient. Viral meningitis was most frequent (14.2%) and 8.4% of patients died during hospitalization.

Conclusion: This study confirms the necessity of expanding management programs for viral infections especially hepatitis B in youths in Iran. Unspecified viral infections cost much more than specified viral diseases. Viral infection costs can be reduced by finding more sensitive and specific diagnostic methods.

KEYWORDS: Viral infections, prevalence, Shiraz, Iran.

INTRODUCTION
Infectious diseases remain a leading cause of death. Of the estimated 54 million deaths worldwide in 1998, about one fourth to one-third was due to infectious diseases, most of them in developing countries and among children globally.1,2 Viral infections are among the most important causes of human disease and, annually, many patients refer to health care centers suffering from viral infections. It seems that due to limitation of health care facilities, viral infections are a great threat for developing countries; as an example the HIV/ AIDS epidemic in sub-Saharan Africa has already orphaned a generation of children, and it is projected that by 2010, 18 million African children under the age of 18 are likely to be orphans from this single cause.3

The economic costs of viral infections are significant and their related deaths and disabilities are likely to have the greatest impact on the capabilities of communities especially developing countries.4,5 It was estimated that the cost of rubella elimination in developing countries during 1997-2017 would be US$ 4.5

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Prevalence, Treatment cost of viral infection

million, compared with more than US$ 60 million for treatment of CRS cases in the absence of an elimination initiative. In Iran infections diseases consume some 6 percent of GDP. As far as we know data on viral infections in Iran are limited to specific cases such as AIDS, rubella and viral hepatitis. Because of the enormous variations in viruses and their epidemiology and pathogenesis, there is no single, magic-bullet approach to its control. The control of these infections requires knowledge not only about the model of transmission but also seasonal incidence and prevalence. Although there have been reports on different aspects of each of viral disease, literature search did not reveal any publication from Iran, comparing epidemiological and economical aspects of different viral infections in the same setting for defining priorities. As Shiraz is the biggest city in the southern part of Iran and the university hospitals in Shiraz serve as referral centers for about one quarter of patients in Iran, we planned this study to gain estimates of prevalence and costs of viral infections in the city. The results of this study would allow us to inform clinicians and health policy makers in Iran and those countries with similar demographic conditions (especially neighboring countries) for initiating and executing programs on treatment & prevention.

PATIENTS AND METHODS

A retrospective analysis of all diagnosed cases of viral infections was carried out at Nemazee and Faghihi university hospitals in Shiraz, Iran over a period of 5 years (1999-2004). The Nemazee and Faghihi hospitals are main viral Infection referral centers in Fars province (population 3,767,983) (Iran Tourism and Touring Organization) and also provides secondary and some primary level care to the population of the south of Iran. These hospitals have 1097 beds and 58 Wards. For this study, the data were extracted from records, which were maintained since January 1999 to December of 2004. Classification of viral infections was done according to the World Health Organization international classification of diseases.

The charts of those patients found to have viral infections were further analyzed regarding characteristics such as incidence of death, age, gender, primary and final diagnosis and admission days. Diagnostic criteria for viral infections were based on serological, cytological and clinical examination. A separate analysis of discharge data from two hospitals was carried out with adjustment for miscoding and estimates of direct hospital costs including admission, treatment, nursing, drugs, instruments and Paraclinical tests.

As the study did not require any intervention on the patients and had no extra sampling, informed consent and formal approval from the institution review committee were not considered. The statistical package for social science (11.5) software package (spss inc., Chicago, Il), was used for statistical analysis. A p value of <0.05 was considered to be statistically significant.

RESULTS

From 1999 to 2004, 135624 patients were admitted to these two hospitals and among them 1319 patients were hospitalized with diagnosis of viral infection. About 62.9% of cases hospitalized with viral infections were males. The mean age of patients with viral infection was 29.24 years (range, 1-91 years). Viral meningitis was most frequent (14.2%) among other viral infections. Diagnosis for youngest patients was unspecified viral meningitis (2 cases), mumps encephalitis (2 cases) and diagnosis for the oldest patient was reported herpes zoster. Total hospitalizations were 8636 days and mean length of stay in hospital was 6.54 days (range, 1-66), minimum hospitalization (1 day) was related to AIDS and maximum (66 days) for post measles otitis media. The patients were admitted in 40 different wards in two hospitals. Internal pediatric ward of Nemazee hospital had the most admissions (20.4%). In 36.4% of the patients, diagnosis of viral infections were along with other diseases and 4.7% of them were primary false diagnosis which after more work up changed to a viral infection. The peak of seasonal incidence was in spring (29.5%). Almost 76% of cases were related to
10 first infections (Table-I). 8.4% of patients expired during hospitalization. AIDS had highest mortality rate (26.12%). The mean daily cost per patient was 246720 Rials (30.84 USD) and unspecified viral infection without complication excluding viremia had the highest daily costs for patients (Table-II). Skin viral diseases were the most frequent in adulthood but most of the viral infections in children were related to CNS disorders.

DISCUSSION

Health authorities need to make evidence based decisions for improving public health. Eradication or control requires the ability to detect these diseases and use the information for preventing further spread. Microbiologists and epidemiologists should be more involved in such disease control activities.

Though many viral infections are subclinical and self limiting, this study confirmed that hospitalization due to viral infections is not uncommon. A hospital based study can estimate all costs in hospitalized patients and though its burden on the community. There is no similar comprehensive study for all viral infections in our region in order to compare our data with them, but there are some reports on a single disease in our region.

Viral (aseptic) meningitis is serious but rarely fatal in persons with normal immune systems. In a hospital based study in Saudi Arabia on children under the age of 5 years old 32% of all meningitis cases were labeled as viral meningitis.11 Enteroviruses, are the most common cause of viral meningitis. Considering the fact that the viral meningitis are more prevalent in childhood in other studies, our data showed that it is not that rare in adults in our region, except for Mumps meningoencephalitis with mean age of about 11 years in our study (Table-I). As viral meningitis is most often spread through direct contact with respiratory secretions, general education for good personal hygiene can help reduce the infection rate.

Herpes zoster was the second most prevalent disease in our study and if herpes zoster eyelid dermatitis cases as the least one in our study would be added to the sum of the patients suffering herpes zoster, the number of patients equalize to the meningitis cases. Immunodeficiency increases the risk of
developing zoster and amplifies the associated morbidity.\textsuperscript{13} The other main risk factor is increasing age.\textsuperscript{14} Therefore, it is important that immunodeficient patients are appropriately managed to prevent this complication and avoid prescribing immuno-suppressive drugs in unnecessary conditions especially in elderly. Varicella cases which is caused by similar virus was seen in lower age ranges with the mean age of 18.54 years and it accounted for 6.1\% of all viral infections in our study. Though the herpes zoster had a higher burden of disease than varicella, but considering the above mean age of varicella infection in this study, overall high VZV sero-susceptibility in our community and no routine vaccination in Iran,\textsuperscript{15} zoster must be an important component of disease surveillance in order to determine the full impact of vaccination on the epidemiology of varicella zoster virus.

Hepatitis, especially hepatitis B comprised a remarkable proportion of the hospitalized patients in our study. Other studies also have shown HCV and HBV patients were more likely to be hospitalized and stay in hospital for a long time and as a consequence it increased the cost per admission and per patient.\textsuperscript{16-18} Hepatitis B and all of its complications including hepatitis D (HDV) are globally preventable by hepatitis B vaccination. In Iran, universal vaccination has been commenced from 1991, so it seems that the number of HBV infected cases would be decreased gradually. Finally, AIDS had the highest mortality rate. The public health burden of HIV, given the fairly widespread use of effective medications, may be on the decline.\textsuperscript{19} Despite the general concern over the financial burden that the AIDS epidemic imposes on its victims, on society in general, and in particular on health-care services where patients with the disease have been concentrated, data on the medical costs of such treatment are surprisingly scarce.

This study showed that viral infections are a significant cost burden to the health care system, the mean daily costs per patient related to 10 most prevalent viral diseases in this study was equal to the one third of total expenditure on health per capita in Iran.\textsuperscript{7} Prevention of viral infections progression could result in substantial economic benefits to the whole society. Hospitalization costs make up a large proportion of total disease costs which should be decreased as much as possible.

As shown in Table-II, it can be concluded that the costs for viral diseases in the community can be reduced by finding more sensitive and specific diagnostic methods. Many disease outbreaks with major consequences for public health require sophisticated facilities available only in a well equipped reference laboratory.

The demographic features of hospitalized patients in this study were similar to those reported by others, including the male predominance for viral infections\textsuperscript{20-22} and range of age.\textsuperscript{23-24} Although the mean age of the patients with HBV infection shows that vaccination program which commenced in 1993 had a partial success, but high prevalence of this disease among other viral infections is alarming hence

<table>
<thead>
<tr>
<th>Total Costs Per Patient</th>
<th>Mean Daily Costs</th>
<th>Disease</th>
<th>Mean Daily Costs</th>
<th>Disease</th>
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<tbody>
<tr>
<td>5046 USD</td>
<td>27 USD</td>
<td>Viral meningitis</td>
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<tr>
<td>6350 USD</td>
<td>36 USD</td>
<td>Herpes zoster without mention of complication</td>
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<tr>
<td>5384 USD</td>
<td>33 USD</td>
<td>Viral hepatitis “B” without hepatic coma</td>
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<td>1599 USD</td>
<td>17 USD</td>
<td>Other Viral hepatitis without hepatic coma</td>
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<tr>
<td>3162 USD</td>
<td>38 USD</td>
<td>AIDS (without specific infections)</td>
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<tr>
<td>3433 USD</td>
<td>44 USD</td>
<td>Viral hepatitis (without complications)</td>
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<td>1986 USD</td>
<td>30 USD</td>
<td>Varicella without mention of complication</td>
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<td>2206 USD</td>
<td>36 USD</td>
<td>Mumps meningo encephalitis</td>
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<tr>
<td>2776 USD</td>
<td>59 USD</td>
<td>Unspecified viral infection without complication, exclude viremia</td>
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<tr>
<td>843 USD</td>
<td>19 USD</td>
<td>Herpes zoster dermatitis of eyelid</td>
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more attention should be paid to vaccination. So effective preventive measures are needed, designed to target both vulnerable groups and groups that could be drawn into the next phase HBV spread, such as drug abusers, migrant workers, refugees and displaced persons, transport workers and young people in general. However, at present, even basic activities such as condom promotion are largely absent and extensive educational program is needed in this case. It should be noted that we were only able to assess the limited viral infections which caused hospitalization and inevitably outpatient viral infections were missed. Due to lack of reliable documents we could not consider the other relevant medical costs or the costs associated with the productivity losses. For these reason, further investigation and studies for precise calculation of costs of viral infections is necessary for more accurate economic evaluation.

REFERENCES