

ASSESSMENT OF PARAMETERS OF SEVERITY OF INFLUENZA EPIDEMICS IN REPUBLIC OF MACEDONIA

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A retrospective analysis of the reported flu cases in Republic of Macedonia (RM) in the period 1980-2001, and its impact on the nonspecific overall mortality in the RM, and on the hospitalizations at Clinic of Infectious Diseases in Skopje (CIDS), was performed. A number of flu cases reported was particularly high in the years 1989, 1992, 1995, 1997, 1999 and 2000, with peak in January and February, being as high as from 34.133 to 94.657. The highest morbidity, with 4820.8/100.000, was noted in 1992. In the years 1997, 1999 and 2000, the oldest age group (60 (33.809 patients in total) was present in 12.7%, 10.5% and 12.0%, respectively, compared with only 6.4% out of cases reported in the period analysed. A positive correlation between the number of registered cases with influenza and overall deaths in RM, was found. In the most affected month, the highest percent of deaths were noted in 1989 (January, 11.3%), 1992 (January, 10.4%), 1997 (January, 10.7%), 1999 (March, 10.7%) and 2000 (February, 10.3%), compared with seasonal average monthly mortality of only 9.5%. A positive correlation between the number of registered flu cases in RM and hospitalizations at CIDS, was found as well. A number of winter hospitalizations was substantially higher in the years signed, being as high as even 26.9%. During the first three months in the years when the highest number of reported flu cases in RM was registered, number of hospitalized patients compared with non-epidemic years was highest as well, as was the percent of inpatients with respiratory tract infections, particularly with pneumonia/influenza, being as high as 78.2% in 1992. Influenza-related hospitalizations might provide a more sensitive index than mortality for assessing the severity of individual influenza epidemics.

In regions having a temperate climate, influenza epidemics occur predominately during the winter months, and are usually associated with increased morbidity and mortality. It is worth noted that influenza affects 10% to 15% of the world's population annually. Economic losses also are considerable. As illustration, in the United Kingdom, about 150 million working days lost to influenza cost the economy about £6.75 billion each year. During the past 25 years, excess rates of hospitalization in the United States during influenza season have reached as high as 270 per 100.000, with an average of 20.000 associated deaths and economic losses in the range of \$3 billion to \$5 billion annually. Influenza causes significant morbidity and mortality especially in various high-risk groups, including persons with chronic cardiopulmonary disease, diabetes mellitus, and advanced age and those residing in long-term care facilities, as well as in persons with human immunodeficiency virus infection or acquired immunodeficiency syndrome.

Since first published argument study about influenza associated mortality in London, some 150 years ago, written by William Farr, to nowadays, numerous, different statistical methods have been used to determine the magnitude and severity of influenza epidemics. Special attention has been paid to statistical models which

determine the excess mortality (number of deaths above expected deaths in absence of influenza) during time period in which influenza viruses circulate. On the other hand, fatal outcome is very rare in cases with uncomplicated influenza infection. It represents only one fraction of overall health burden in some population caused by influenza. It is well known that epidemics caused by influenza virus type A (H3N2) usually result in increased number of hospitalizations and death cases, unlike epidemics caused by influenza virus A (H1N1) and B, which only cause increased hospitalizations, and do not increase the mortality. From these reasons, some researches think that determination of excess mortality caused by pneumonia and influenza, does not properly reflect severity of one influenza epidemic.

In 1918-1919, an influenza pandemic killed 21 million people worldwide and more than 500.000 in the United States. Currently, the Centers for Disease Control and Prevention (CDC) estimates that 20.000 people die in the United States each year from influenza, and 110.000 are hospitalized. Ninety percent of the deaths from influenza reported each year in the United States occur in the elderly. However, an estimated 2000 to as high as 8000 influenza-related deaths occur in persons younger than 65 years, an age cohort for whom influenza vaccine

is not currently recommended. Regarding morbidity, hospitalization rates for persons aged 15 to 64 years are 20 to 400 per 100.000 population vs 200 to more than 1000 per 100.000 population for those older than 65 years. Thus, the impact of influenza on young adults in terms of morbidity and quality of life is also substantial, even if less than that on the elderly.

While the effects of influenza on the elderly and persons of any age with chronic underlying conditions are well known, mounting evidence suggests that the medical, social, and economic consequences of influenza for other populations may be substantially underestimated. Also looming in the future is the next pandemic of influenza, which, depending on the virulence and penetrance of infection, could result in as many as 200.000 excess deaths and economic losses in excess of \$160 billion in the United States. Preventing disease by expanding influenza vaccination may be a logical next step.

Primary goal of this study was to estimate the relation of increased number of influenza cases to general mortality in Republic of Macedonia, as well as the excess hospitalizations with pneumonia and influenza at the Clinic for infectious diseases in Skopje.

MATERIAL AND METHODS

An epidemiological-descriptive and statistical informative method of work have been used. We analyzed and evaluated data of reported cases of infectious diseases that we got from State office for health protection in Skopje (Zavod za zdravstvena zastita-Skopje), as well as statistical mortality data from State statistics bureau (Drzaven zavod za statistika), as well as official records from the Clinic for infectious diseases in Skopje for analysis of number of hospitalized patients with clinically confirmed diagnosis. We made retrospective analysis of reported influenza cases in Republic of Macedonia in the period 1980-2001. We also analyzed influenza influence on the overall mortality and number of hospitalizations.

RESULTS AND DISCUSSION

In the analyzed period, there have been 530.491 registered cases of influenza, or an average of 24.113 cases per year. The number of reported

influenza cases was especially high in 1989, 1992, 1995, 1997 and year 2000, with monthly peaks in January and February when 34.133 and 94.657 cases were reported, respectively. Highest number of diseased was reported during 1992 season (94.657) with morbidity of 4820,8/100.000. During the same years and months when we have highest number of reported influenza cases there has been increased general mortality in R. Macedonia.

On the following few figures (Fig. 1, 2 and 3) positive correlation between influenza morbidity distribution and general annual mortality for the years 1989, 1992 and 1997 is shown, with coefficient of correlation (r) ranking from 0.700 to 0.827.

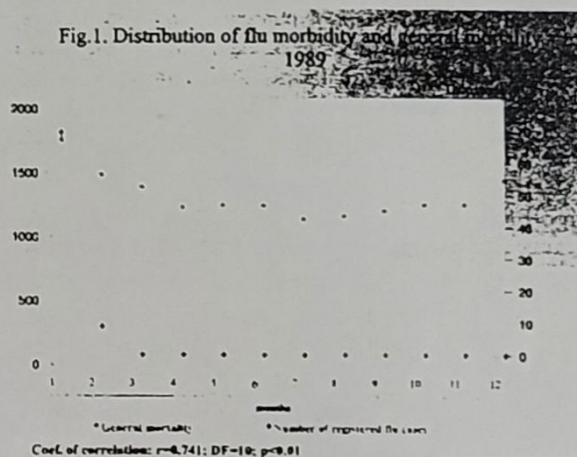


Figure 1. Distribution of flu morbidity and general mortality (absolute numbers) - 1989

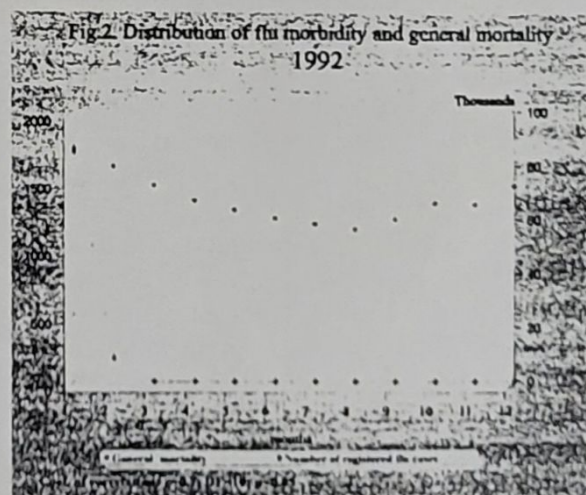


Figure 2. Distribution of flu morbidity and general mortality (absolute numbers) - 1992

Influenza maintains its seasonal character of acute respiratory disease and has highest percentage of diseased during winter months, with

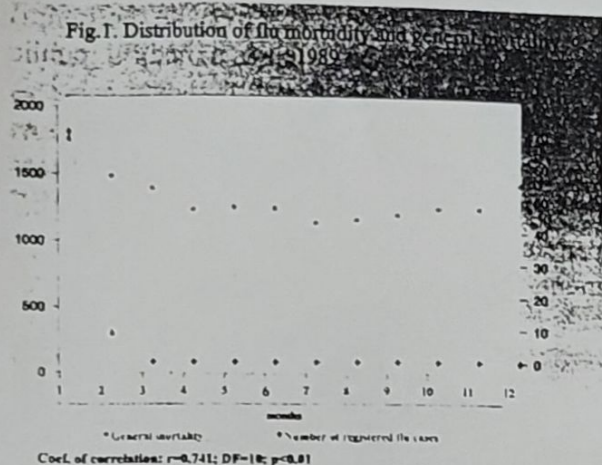


Figure 3. Distribution of flu morbidity and general mortality (absolute numbers) - 1997

maximum reported cases in January (46.7%), February (22.3%) and March (22.2%). During these three months 92.2% of all influenza cases in Macedonia have been registered. Highest positive correlation between influenza morbidity and general mortality in the last 21 years has been registered in January and April and it has been best illustrated on the following two figures (Fig. 4 and 5).

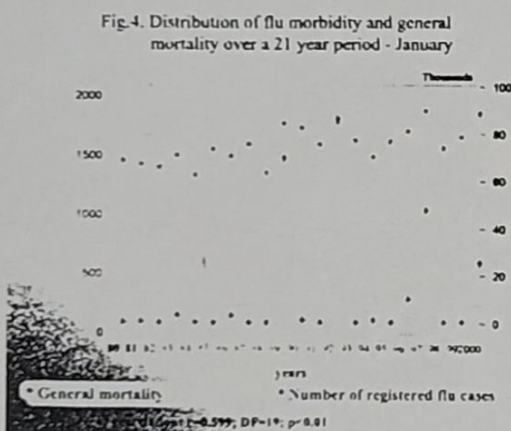


Figure 4. Distribution of flu morbidity and general mortality (absolute numbers) over a 21 year period-January

Highest percentage of diseased people are found in age group 7-19 years (36.5%), followed by 20-59 years (31.8%) and 0-6 years (25.3%), with lowest incidence in patients older than 60 years (6.4%). During epidemics in 1997, 1999 and 2000 we have utmost reported influenza cases, as well as highest general mortality in Macedonia, oldest age group, 60 and above is present with 12.7%, 10.5% and 12.0%, respectively, which presents significant rise considering the average presentation and is considered key cause for the same. There has been firm positive correlation between number of reported

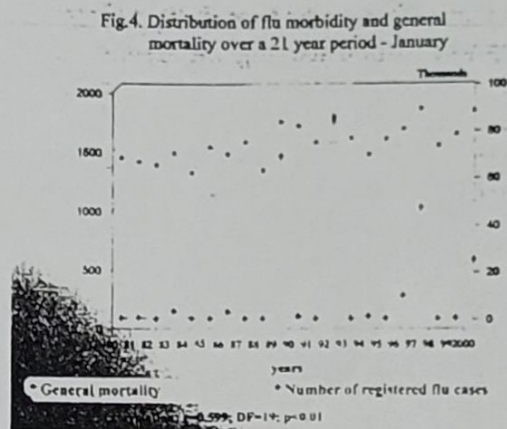


Figure 5. Distribution of flu morbidity and general mortality (absolute numbers) over a 21 year period-April

cases with influenza and overall general mortality in Macedonia. Highest specific morbidity according age groups has been registered in 0-6 years age group (46.819/100.000), followed by 7-19 years (34.877/100.000), 20-59 years (14.460/100.000), and the oldest age group of people, 60 years and above (14.644/100.000). In the same period of time (1980-2001) evaluation has been made on the number of hospitalized patients with respiratory tract infections at the Clinic for infectious diseases in Skopje, mainly hospitalized patients with influenza/pneumonia diagnosis. Positive correlation has been established between the number of reported influenza cases in Macedonia and the number of hospitalized patients with respiratory tract infections at the Clinic. The number of inpatients during above mentioned winter months and years, correlated with influenza season (december/march) and there has been an increased number of reported cases as well, much higher in relation to other years out of influenza epidemics, being as high as up to 26.9%. During the first three months in the years when the highest number of reported flu cases in Macedonia was registered, number of hospitalized patients compared with non-epidemic years was highest as well, as was the percent of inpatients with respiratory tract infections, particularly with pneumonia/influenza, being as high as 78.2% in 1992.

It has been shown that in circumstances when severity of one influenza epidemics is estimated, analysis of hospitalized patients related to influenza is more sensitive index than is the general mortality. Analysis in this study has been restricted on hospitalized patients where

pneumonia, influenza or bronchitis were primary diagnosis when leaving the Clinic. As is well known, other cases with diseases like chronic respiratory and congestive heart failure can also increase by several times during influenza season. This is one more reason why there is need for larger analysis, where primary goal would be estimation of overall impact of influ-

enza on hospitalizations. Given its enormous current and future potential as a medical, public health, and economic threat, it should come as no surprise that influenza is among the most highly ranked targets for further development of new options for prevention and control, particularly such, targeted for vaccine development.

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