Original Article

Influenza vaccination of individuals over the age of 60: impact on hospital admissions and deaths from respiratory and circulatory diseases in Fortaleza, Brazil*

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ABSTRACT

Objective: The objective of this study was to evaluate the impact of influenza vaccination on hospital admissions and deaths from respiratory and circulatory diseases in the city of Fortaleza, located in the state of Ceará, Brazil. **Methods:** Brazilian Health Ministry data regarding deaths from respiratory and circulatory diseases occurring between 1995 and 2001, as well as hospital admissions related to such diseases between 1995 among 2003, in both cases limited to residents of Fortaleza above the age of 60 years, were analyzed. **Results:** There were 29,867 admissions for respiratory disease. Between 1995 and 1998, the mean number of annual admissions was 3067.3 (standard deviation, 365.8). Between 1999 and 2003, the average was 3519 (standard deviation, 195.6). When adjusted for the increase in population, the difference between the two periods was less than significant. From 1998 to 1999, there was no significant reduction in the number of admissions from circulatory disease ($p > 0.641$). Nor was there a significant reduction from 1998 to 2000 ($p < 0.5$) or from 1998 to 2003 ($p > 0.72$), although there were significant reductions in 2000 ($p < 0.002$) and 2001 ($p < 0.0014$). There was a significant reduction in the number of deaths and in overall mortality rates during 1999, 2000 and 2001 in relation to 1998 ($p < 0.05$), with no difference between 2000 and 2001. The monthly distribution of admissions was not altered as a result of the vaccinations. **Conclusion:** Our data show that vaccination of the elderly did not achieve the desired results. This suggests that seasonality studies are needed in order to identify the ideal time of year for such vaccinations.

Keywords: Influenza; Vaccination; Respiratory tract infection; Death certificates; Length of stay

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INTRODUCTION

Due to its high degree of antigenic variability, influenza is one of the infectious diseases that most concerns health authorities. Such concern is centered around the possibility that a single infected individual could transmit influenza to multiple susceptible individuals, thereby leading to epidemics, or even pandemics, which are typically abrupt, peaking in two to three weeks and persisting for eight weeks.[1] Infants up to 23 months of age and individuals over 60 years of age are among the populations that are the most vulnerable to complications and death from influenza.[2] Individuals with primary or secondary immunological deficiencies, heart disease or lung disease are also considered highly vulnerable and are prime candidates for vaccination against influenza. Health professionals who treat patients with respiratory diseases or work in nursing homes, as well as individuals who work with birds or pigs are also more vulnerable to the acquisition of the infection.

The vaccination of elderly individuals against influenza reduces the risk of hospital admission for heart disease by up to 19%, for cerebrovascular diseases by up to 23%, and for influenza or pneumonia by up to 32%, as well as reducing death from all causes by up to 50%.[2] The vaccine administrated in Brazil is composed of two strains of influenza A (H3N2 and H1N1) and one strain of influenza B.[3] The viral strains isolated from patients in the southern hemisphere, including those in greatest circulation and isolated in Brazil, are part of the composition of the vaccine administrated in the country. The production, packaging and distribution of the vaccine requires approximately six months, and administration requires an extra one to two months.[4] The protective antibodies are detected one to two weeks after the administration of the vaccine, and antibody titers peak at four to six weeks after administration, ideally coinciding with the maximum viral load.[3]

Until 2003, the state of Ceará was not a participant in the Sistema de Vigilância da Influenza (Influenza Awareness System), then in effect in twelve states of the five regions of Brazil. This system has various objectives, including tracking the many circulating strains of the influenza virus and monitoring influenza-related morbidity and mortality, as well as evaluating the impact of the vaccine.[5] In 2002, this system identified a flu syndrome treatment peak between weeks 29 and 40 in the southern and southeastern regions, and the influenza B virus was isolated. Between weeks 15 and 19 of 2003, another flu syndrome treatment peak was detected, related to outbreaks in the central-west and northern regions, and the influenza A (H1N2) virus was isolated.[3] In the city of Fortaleza (Ceará), etiological studies of children with acute respiratory diseases in which viruses were isolated have been carried out. In the period from August of 1984 to August of 1986, a community-based study was conducted involving 175 children below the age of five and presenting acute respiratory diseases, among which 5.9% of the viruses isolated were influenza. The isolation of the influenza virus coincided with the rainy season. Influenza viruses were isolated in the periods: February to April of 1985; February to April of 1986, October to November of 1984; and October to November of 1985.[6] In a hospital-based study of children, conducted from January of 2001 to June of 2003, the influenza virus was identified in 27.65% of the isolates. This calls attention to the fact that isolates of the influenza virus and the respiratory syncytial virus were only found between the months of January and June, whereas adenovirus and parainfluenza virus type 3 can be seen at any time of the year.[7-8]

Due to the growth of the elderly population and its vulnerability, the Brazilian Ministério da Saúde (Ministry of Health) introduced influenza vaccination for those over the age of 65 in 1999 for those over the age of 60 in the year 2000. Brazil has met the goal, set by the Ministry of Health, of vaccinating 70% of these individuals.[9] In Fortaleza, campaigns to vaccinate the elderly begin between the 7th and the 23rd of April and continue until May. The citywide campaign has reached an ever-increasing proportion of the target population, growing from 80% in 1999 to 92% in 2003.[10] The pneumococcal vaccine is not included in the vaccines administered en masse to the elderly during the campaigns in Fortaleza, being reserved for the institutionalized elderly.

The objective of this study was to evaluate the impact of influenza vaccination on rates of hospitalization for respiratory and cardiovascular diseases, as well as on mortality rates among those over the age of 60.

METHODS

Fortaleza presents little variation in temperature over the course of the year. Between 1995 and 2000,

the absolute maximum temperature registered was 33°C, and the absolute minimum was 21°C. The principal climatic variation is the rainy season, which occurs at the beginning of the year, lasting for three to five months, in general from February to June.[11]

The hospitalization records of Fortaleza residents over the age of 60 were reviewed, limited to the 1995-2003 period.[12] In addition, the files of the Sistema de Informação de Mortalidade (Mortality Database)[13], made available by the Ministry of Health via the Departamento de Informação e Informática do Sistema Único de Saúde (DATASUS, Unified Health Care System Department of Information and Information Science), were searched for the 1995-2001 period. With this data source, it is possible to build tables based on the year of occurrence, city, gender, age, diagnosis, etc., using the Tabnet program, which is also made available. Hospital admissions and deaths were classified according to the International Classification of Diseases, Ninth Revision (ICD-9) for the 1995-1997 period and according to the International Classification of Diseases, Tenth Revision (ICD-10) for the 1998-2001 period. The data obtained from hospitalization records were used as numerators in the calculation of coefficients of hospital admission, and those obtained from the Mortality Database were used as numerators in the calculation of coefficients of mortality.

To calculate the coefficients of hospital admission and mortality (by age bracket and by cause), the population used was that estimated by the Instituto Brasileiro de Geografia e Estatística (Brazilian Institute of Geography and Statistics) and released by the Ministry of Health.[14]

The statistical analyses were made with the Epi Info program, version 6.04, using the chi-square test.[15]

RESULTS

Between 1995 and 2003, 29,867 individuals over the age of 60 were hospitalized for diseases of the respiratory system, with an annual mean of 3318.6 admissions and standard deviation (SD) of 355.6. Between 1995 and 1998, the annual mean was 3067.3 (SD: 365.8), compared with 3519.6 (SD: 195.6) between 1999 and 2003. The monthly mean was 2488.9 (SD: 411.5), being 1022.4 (SD: 145.2) between 1995 and 1998 (ranging from 858 in November to 1321 in April), and 1466.5 (SD: 195.6) between 1999 and 2003. In terms of absolute numbers, there was a reduction in the number of admissions in the post-vaccination period only when compared with 1995.

Adjusting the number of admissions in relation to the population and using 1998 as a reference, no significant reduction was observed between the coefficients of hospital admission prior to and following the initiation of the vaccination program, nor was there any such difference for diseases of the respiratory system in general, flu or pneumonia ($p > 0.05$) (Figure 1). In a year-to-year comparison, we observed a reduction

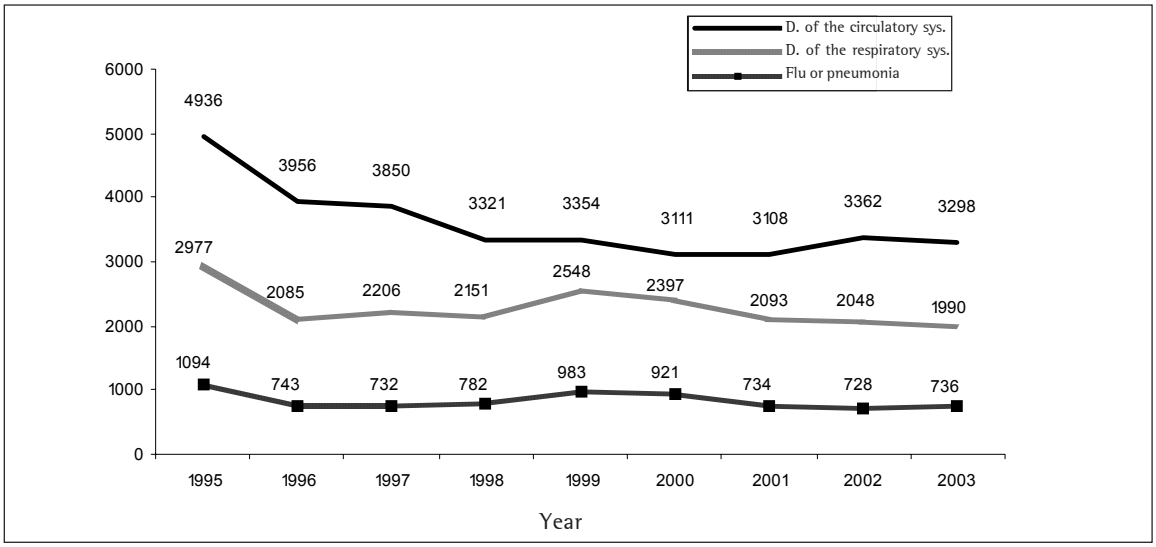

Figure 1 - Admissions/1000 inhabitants over the age of 60 for diseases (D.) of the respiratory system (sys.) and for flu/pneumonia in Fortaleza, Ceará, 1995-2003

TABLE 1

Coefficient of admissions per year through the authorized hospital admissions system for circulatory system diseases, cerebrovascular system diseases, coronary ischemia, respiratory diseases, pneumonia/flu and chronic obstructive pulmonary disease in individuals over the age of 60 in Fortaleza, Ceará, 1995-2003

Year	Circulatory System	p in relation to the year before	Cerebrovascular disease	p in relation to the year before	Coronary ischemia	p in relation to the year before	Respiratory System	p in relation to the year before	Pneumonia and flu	p in relation to the year before	COPD	p in relation to the year before
1995	4936.2		930.7		864.4		2977.0		1094.0		982.9	
1996	3955.9	0.0000	801.2	0.0000	649.9	0.0000	2085.1	0.0000	742.7	0.0000	749.5	0.0000
1997	3849.9	0.0240	815.8	0.0252	668.2	0.1121	2205.6	0.3025	732.0	0.4483	814.3	0.0000
1998	3321.1	0.0000	688.2	0.0000	594.5	0.0000	2151.1	0.1357	782.0	0.3748	534.9	0.0000
1999	3354.0	0.6794	757.8	0.0000	567.7	0.0133	2547.7	0.0000	982.9	0.0000	594.7	0.0000
2000	3111.1	0.0000	717.1	0.0008	533.6	0.0011	2397.2	0.0000	920.5	0.0000	627.8	0.0028
2001	3107.9	0.4237	695.9	0.0755	522.7	0.2901	2092.6	0.0000	733.8	0.0000	631.6	0.7357
2002	3361.8	0.0134	914.5	0.0000	650.8	0.000	2047.6	0.2220	727.9	0.6380	677.9	0.0000
2003	3297.5	0.1516	716.7	0.0000	719.7	0.0000	1990.2	0.1552	735.7	0.9188	608.3	0.0000

Between 1996 and 2000, there was reduction in the rates of hospital admissions for circulatory system diseases, cerebrovascular disease, coronary ischemia, respiratory system diseases, pneumonia/flu and COPD ($p<0.0000$).

between 1995 and 1996, an increase in 1997, stabilization in 1998, new growth in 1999, a reduction in 2000, a reduction in 2001, stabilization in 2002 and continued stabilization in 2003 (Table 1). If we compare only those years in which there were population counts (1996) or censuses (2000), there was a reduction in the number of admissions ($p < 0.00001$).

Taking 1998 as a reference year, there was no reduction in the coefficients of hospital admission for diseases of the circulatory system in 1999 ($p > 0.641$), although there were reductions in 2000 ($p < 0.002$) and 2001 ($p < 0.0014$), returning to 1998 levels in 2002 ($p > 0.5$) and 2003 ($p > 0.72$). In addition, no difference was found between 2000 and 2001 ($p > 0.95$) (Figure 1). There was a tendency toward a decrease from 1995 to 2000, shifting toward an increase by 2003 (Table 1).

Comparing the 1995-1998 period with the 1999-2003 period, the distribution curves of the total number of cases per month adjusted for population were virtually identical, with no difference between the groups of months preceding the initiation of the vaccination program and those of the months following ($p > 0.05$) (Figure 2).

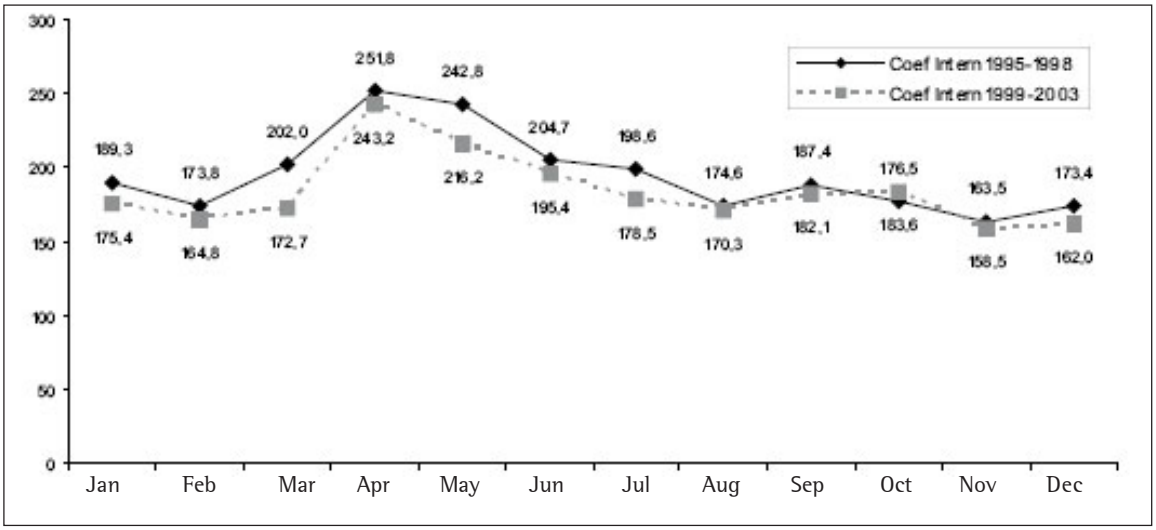

Figure 2 - Incidence de admissions for diseases of the respiratory system, by month, in the 1995-1998 and 1999-2003 periods in Fortaleza, Ceará

TABLE 2

Morbidity and mortality from diseases of the respiratory and circulatory systems, together with deaths and overall mortality rates among individuals over the age of 60, by year, in Fortaleza, Ceará, 1995-2001

Event	1995	1996	1997	1998	1999	2000	2001
Diseases of the circulatory system	1.963	1.892	1.917	1.990	1.997	1.767	1.745
Diseases of the respiratory system	497	524	626	708	835	662	642
Deaths from all causes	5.165	2.416	2.543	2.698	2.832	2.429	2.387
Deaths from respiratory system diseases	4.1	4.0	4.6	5.1	5.9	4.1	3.9
Deaths from circulatory system diseases	16.3	14.4	14.2	14.5	14.2	11.0	10.7
Overall mortality	42.8	38.4	40.7	41.6	43.6	34.3	36.3

*Number of deaths among individuals over the age of 60/100,000 inhabitants per year

There was a significant reduction ($p < 0.05$) in the number of deaths (Table 2) and in the overall mortality rate among individuals over the age of 60 in the years 1999, 2000 and 2001 in relation to 1998. Comparing 2000 and 2001, there was an increase in the overall mortality rate ($p < 0.004$). Mortality from respiratory diseases increased from 1998 to 1999 ($p < 0.005$) and decreased in 2000 and 2001 ($p < 0.0001$). Between 2000 and 2001, there was no significant reduction ($p > 0.36$). From 1998 to 1999, there was no significant difference in mortality from diseases of the circulatory system ($p = 0.34$), although mortality from such diseases was lower than the 1998 level in 2000 and 2001 ($p < 0.0001$). There was no significant difference between 2000 and 2001 ($p = 0.34$) (Figure 3).

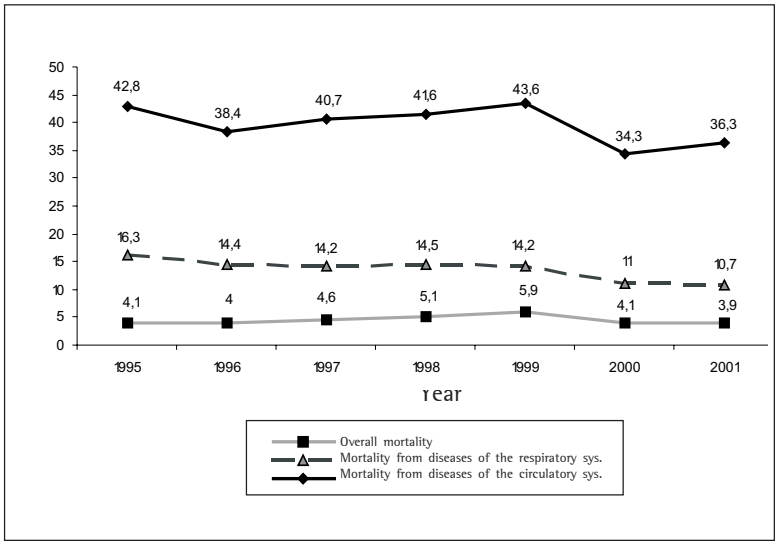

Figure 3 - Overall mortality from diseases of the respiratory system (sys.) and from diseases of the respiratory system (sys.), by year, in Fortaleza, Ceará, 1995-2001

DISCUSSION

The present study had several limitations: only approximately 70% of the population of Fortaleza is fully served by the Unified Health Care System, the remaining 30% subscribing to private health care plans; the number of admissions under the Unified Health Care System is restricted by the number of beds available and by the requirement that all admissions be authorized, which can result in repressed demand for hospital admission; the cause of hospital admission was based on the stated principal diagnosis, defined as being the motivation for admission (there may have been subsequent, undocumented, changes in diagnosis).[6]

In Fortaleza, the population of individuals over the age of 60 presented abrupt increases in 1996, when it grew by approximately 10,000, thereafter growing by approximately 3000/year until 1999, when it grew by approximately 20,000, returning to the 3000/year rate in 2001. These increases coincided with the recounting of the population that occurred in 1996 and with the census of 2000. It is possible that the reduction in the mortality rate would not have occurred if the growth of the population had been more homogeneous. When the discrepancies were lower (between 2000 and 2001), no reduction in the mortality rate was seen. The same rationale can be applied in relation to the coefficients of hospital admission.

Influenza epidemics occur predominantly in winter in regions where this season brings cold weather, together with the peak of acute respiratory diseases and their complications.[2] In Fortaleza, the period during which the treatment of acute respiratory diseases peaks is between March and June.[16] The highest numbers of admissions are seen in March and April. If this period coincides with the greatest

circulation of the influenza virus, the second half of February would be the ideal period in which to administer the vaccine since it should be given at least two weeks before the arrival of the virus.[3] Administering the vaccine between April and May would reduce its effectiveness since, at the peak of the epidemic, the elderly would not have built up a protective quantity of antibodies.

In the city of São Paulo (state of São Paulo), a reduction in the number de episodes consistent with flu was seen in elderly individuals having received the vaccine in comparison with those not having received it. However, there were no significant differences in the overall hospitalization rates, in the rates of hospital admission for respiratory diseases, or in the overall use of antibiotics in the treatment of respiratory diseases.[17]

In the city of Maceió (state of Alagoas), the influenza virus was isolated with greater frequency in the oropharynx and nasopharynx of children treated at the two surveillance clinics in July, September, October and December. If the distribution of the influenza virus in Fortaleza presented seasonality similar to that seen in Maceió, one would expect greater effectiveness of the vaccination program.[18] There were no reports of the influenza virus being isolated in elderly individuals in Fortaleza. However, there were reports of the influenza virus being isolated in the nasopharynx of children, exclusively in the first semester (February to June) in the period from January of 2001 to June of 2003.[7-8]

In the final analysis, taking into consideration the fact that the vaccine against influenza administered to the elderly had the objective of reducing the risk of serious illness or death from influenza complications, it was not possible, from the data analyzed, to assess the effectiveness of such vaccination in the elderly population of Fortaleza. It is possible that infection occurred prior to the administration of the vaccine, or that another viral subtype was introduced, as occurred in the state of Pará. Studies of the seasonality of the influenza virus in Fortaleza should be conducted in order to re-evaluate the timing of the vaccination campaign.

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