

Patterns of Influenza Infections Among Different Risk Groups in Brazil

Nancy Bellei, Emerson Carraro, Ana Perosa and Celso Granato

Clinical Virology Laboratory, Infectious Diseases Unit, Medicine Department, São Paulo Federal University; São Paulo, SP, Brazil

Influenza virus infections are associated with high morbidity and mortality. Influenza activity varies worldwide, and regional detection is influenced by geographic conditions, demographic and patient-risk factors. We assessed influenza activity and patterns of seasonality during three consecutive years (2001-2003) in three risk groups in São Paulo city. Four-hundred-twelve outpatients with acute respiratory infection were subjected to epidemiological, clinical and laboratory investigations; these included community population (N=140), health-care workers (N=203), and renal-transplanted patients (N=69). Nasal wash samples were tested by direct fluorescent assay for influenza, parainfluenza, adenovirus, and respiratory syncytial virus. Overall Influenza positivity was 21%, and a progressive decline was observed in all groups over time. Influenza A and B co-circulated at the same time in 2001 and 2002, but not in 2003. Low influenza-vaccination rates (19%) were reported by health-care workers. Unexpected low levels of etiological agents were detected in renal-transplanted patients, and infected cases were less symptomatic than immunocompetent patients. Based on this study, we conclude that health-care worker-immunization programs should be implemented and the clinical patterns of infected influenza patients should be used as a guide for better case-definition criteria for adequate influenza surveillance, particularly for renal-transplant patients.

Key-Words: Influenza, risk groups, respiratory viral infection.

Influenza activity varies over time, with different patterns observed around the world, particularly when comparing the northern and southern hemispheres. Brazilian regional influenza seasonality is marked by high diversity due to geographic conditions [1].

Influenza-related complications are more frequent among some risk groups, such as the elderly, patients with chronic diseases and immunosuppressed patients. Influenza immunization is highly recommended for these risk groups, as well as for their healthcare providers [2]. Healthcare workers have increased risk of acquiring influenza during known outbreaks, since they are exposed to the community population as well as to hospitalized patients. There have been reports of rates varying from 11-59% during nosocomial-influenza outbreaks [3].

Influenza can have a profound effect on the clinical course of immunosuppressed patients, especially transplanted patients [4]. Consequently, an accurate diagnostic assay is required. There are few studies assessing influenza diagnosis in immunocompromised patients.

Clinical case definitions of influenza-like illness (ILI) are used by physicians for the surveillance of acute-respiratory infections that are suggestive of influenza orient sample collection and virological analyses for the detection of outbreaks; however, various factors, such as previous drug use, previous immunizations and immunocompetence can affect clinical presentation of viral disease [5].

There is little information about influenza disease among different risk groups, such as healthcare workers and immunocompromised patients in Brazil. We examined influenza activity and seasonality patterns during three consecutive years in various risk groups in São Paulo.

Materials and Methods

Population

The study period began June 2001 and was concluded September 2003. Subjects were adults who were attended by general-practice physicians among community population patients registered by the Medical Department Outpatient Office, healthcare workers (HCW) from São Paulo Hospital, and renal-transplanted patients registered at the Outpatient Office of the Nephrology Division of São Paulo Federal University.

Inclusion Criteria

Adults (>18 years) were considered eligible after evaluation by a physician if they presented with any acute respiratory infection (ARI) of possible viral etiology. Influenza-like-illness (ILI) was considered when the patient reported fever with at least one respiratory symptom (cough, sore throat, or nasal congestion) and at least one constitutional symptom (headache, malaise, myalgia, sweat or chills, or fatigue).

Sample Collection

Each patient had one nasal wash sample collected and was interviewed by an investigator. Samples were immediately sent to the virology laboratory for assays. Fresh samples were aliquoted; two aliquots were frozen at -70°C for further analysis (viral isolation and PCR) and the other centrifuged for DFA.

Direct fluorescence assay (DFA): after centrifugation, the cell pellet was fixed in two slides and DFA was performed to detect influenza virus A and B, parainfluenza (PIV) 1, 2 and 3,

Received on 12 February 2007; revised 10 July 2007.

Address for correspondence: Dr. Nancy Bellei. E-mail: nbellei@uol.com.br. Phone/fax: 55(11)50815394. Rua Pedro de Toledo, 781, andar 15. Vila Clementino, São Paulo – SP, Brazil. Zip code: 04039-032.

The Brazilian Journal of Infectious Diseases 2007;11(4):399-402.
© 2007 by The Brazilian Journal of Infectious Diseases and Contexto Publishing. All rights reserved.

adenovirus and respiratory syncytial virus (RSV), in a two step procedure, according to manufacturer's instructions (Light Diagnostics Simulfluor® Respiratory Screen and Panel, Chemicon – Canada).

Epidemiological and Clinical Data

The patients were interviewed by our researchers; information included demographic data, household children contact, place of work, type of patient assistance (direct or indirect contact), history of symptoms, clinical presentation, comorbidities, smoking, and influenza vaccination status.

Results

Subjects

From 2001 to 2003, a total of 412 subjects were included as follows: 140 subjects from the community population, 203 health-care workers and 69 renal-transplant patients; 63% were female, with a mean age of 34 years (18-83 years). Baseline characteristics, epidemiological and health status are shown in Table 1.

Etiology Results

Among 412 DFA tests, 21% resulted positive for influenza A or B. Frequencies of other viral etiology were: 2.5% RSV, 0.25% PIV-1, 0.25% PIV-2, 0.5% PIV-3, and no adenovirus. Samples were collected between 1 and 21 days after onset of symptoms (mean three days), with 83.7% of the samples taken within five days. Samples from more than five symptomatic days were taken frequently (45.6%) from renal-transplant patients.

Influenza Results

Figure 1 shows influenza-positive cases over the study period. We obtained different peak activity frequencies of ARI for each year. Positivities in 2001, 2002, and 2003 were 42%, 18%, and 13%, respectively. Influenza A and B co-circulated at the same time in 2001 and 2002, with alternate predominance of types, but not in 2003, when influenza B was not found.

Comparisons Among Distinct Populations

Laboratory-confirmed rates of influenza for each group were: 38.6% for the community population, 13.3% for HCW and 5.8% for renal-transplanted patients. Community population, health-care workers and renal-transplant peak rates were compared during the 2002 epidemic season (Figure 2). We found a 54% peak rate of positive tests in the community population, 11% in healthcare workers, and 20% in renal-transplant patients.

Clinical Data

Table 2 shows clinical data among ARI cases regarding flu symptoms in the different groups. Fever was reported by 93% of laboratory-confirmed influenza patients and among 57% of the influenza-negative patients. Myalgia, headache and chills

varied from 69%-89%. General symptoms and sore throat were less commonly reported among influenza-positive renal-transplant patients (25%-50%).

Risk Factors

Analysis of exposure risk according to the pattern of patient care or contact with children indicated 48.3% direct contact with patients and 38.1% with preschool children at health service facilities or in the household. In univariate analysis, no association was detected among patients with influenza infection.

Influenza Vaccine

The overall rate of immunization was low, since no patient from the community population or among the renal-transplanted patients had been vaccinated, and only 19% of HCWs had been immunized.

Discussion

To our knowledge, this is the first study assessing clinical, epidemiological and virological aspects of respiratory viral infections among different risk groups of adult populations in Brazil. Viral laboratory analysis assessed an etiology in 24.5% of the cases, using a direct fluorescence assay. This method is the most widely used in laboratories in Brazil. We have found that molecular methods reach 60% viral etiology detection, including other viruses. However, comparison of both methods did not lead to increased detection of influenza [6]. Indeed, during the study period there was low influenza activity in São Paulo city, as reported by official health surveillance [7]. Low prevalence was also obtained for other viruses, but these are usually more common among children [8].

Monthly incidence of influenza cases correlated with expected seasonality, in the southeast, which usually starts in April and ends in September [1]. Annual peak rate differences may be explained by population immunity, poor antigenic match with the vaccine strain, and frequent climate alterations during the winter in São Paulo. Influenza-virus types found during the study period correlated well with those of the influenza isolates from official surveillance in this region of the country, with a prevalence of influenza A in 2001 and 2003, and influenza B in 2002 [7]. Reappearance of Influenza B Victoria-lineage was replaced by the Yamagata-lineage during 2002, which diverged from the recommended seasonal vaccine, and was more prevalent than influenza type A [9].

We documented a decrease in influenza activity in all groups. In comparing 2002 influenza peak rates, the community populations had the highest rates; they reflect overall influenza activity in an unvaccinated population. HCWs are usually at higher risk for influenza, but even though they had a low immunization rate (19%), this group had a lower infection rate than for the general community because of vaccination

Table 1. Characteristics and health status of 412 subjects investigated for influenza

Characteristics	Cases	%	Variation
Median age (years)	34		18-83
Female sex	260	63.1	
Community population	140	34.0	
Health care worker	203	49.3	
Renal transplantation	69	16.7	
Exposure to children (<5 years)	143	38.1	
Patient contact	98	48.3*	
No comorbidities	230	55.8	
Rhinitis/sinusitis	92	22.3	
Asthma and/or Lung diseases	34	8.2	
Diabetes mellitus and/or hypothyroidism	15	3.6	
Hypertension/cardiovascular	89	21.6	
Anemia	1	0.2	

* Patient contact referred to 203 HCWs.

Figure 1. Laboratory-confirmed influenza cases among acute respiratory infection cases by month, 2001- 2003.

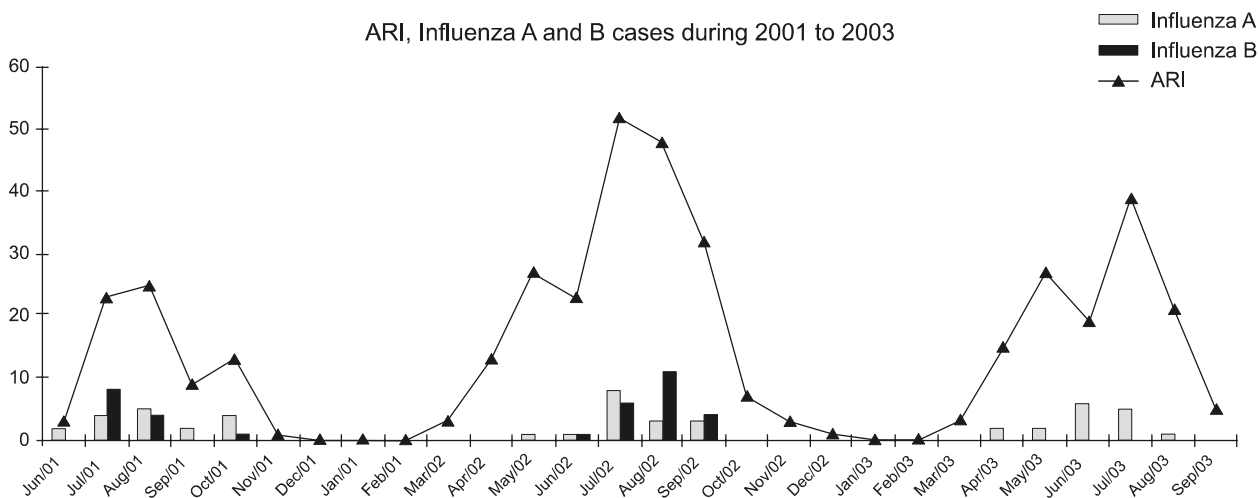
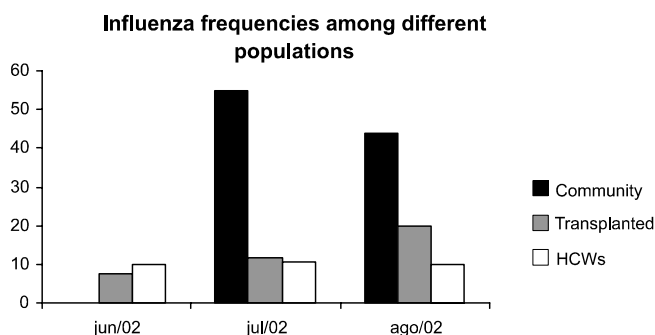


Figure 2. Influenza activity among different populations in 2002. HCW = healthcare workers.



protection. Unexpectedly, the renal-transplant-patient group had a low infection rate, even though they were immunosuppressed and had not been vaccinated. We hypothesize that the use of steroids and others immunosuppressors reduced clinical expression, such as fever and general symptoms. In addition, they may often have asymptomatic infections that our protocol could have missed. A follow-up of hospitalized patients that examined this issue was made on bone-marrow-transplant patients in another study [10].

Differentiating influenza virus from the other respiratory viruses is of prime importance, because the influenza virus is associated with higher morbidity and mortality, it is potentially preventable by vaccination, and it can be managed with specific antivirals. Influenza

Table 2. Clinical data regarding flu symptoms in different risk groups (%)

	Community		HCW		Transplanted	
	Pos	Neg	Pos	Neg	Pos	Neg
Fever	98	74	84	61	75	21
Cough	89	82	76	77	100	79
Nasal Congestion	78	77	72	90	75	87
Sore throat	51	69	56	64	25	37
Headache	91	75	84	79	25	53
Myalgia	82	64	84	74	25	39
Chills	65	48	80	54	50	24

infections cause an extremely-varied clinical syndrome, which makes case definition for ILI variable in different parts of the world [5]. Our unusual findings, of a lower rate of sore throats (50%) and frequent coryza (70%), compared to international-published studies about laboratory-confirmed influenza syndromes should be considered for influenza-like illness in Brazilian surveillance strategies. ILI definitions frequently include sore throat and do not include coryza. In addition, some reports have indicated coryza to have negative predictive value for predicting influenza infections [11].

We hypothesized that there would be an occupational risk of influenza acquisition among our under-vaccinated HCWs. However we did not find a significant difference among workers with direct contact with patients. This could be explained by low influenza activity during the study period.

In conclusion, influenza activity varies among different seasons and according to risk group. Healthcare workers immunization programs should be implemented, although our study, conducted during low activity periods, did not show a relevant occupational risk. Clinical patterns of infected influenza patients should help guide better case definition criteria for adequate influenza surveillance, particularly for renal-transplant patients.

References

1. Forleo-Neto E., Halker E., Santos V.J., et al. Influenza Rev Soc Bras Med Trop **2003**;36(2):267-74.
2. CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practice (ACIP). MMWR Morbid Mortal Wkly Rep **2003**;52(RR-8):1-36.
3. Salgado C.D., Farr B.M., Hall K.K., Hayden F.G. Influenza in the acute hospital setting. Lancet Infect Dis **2002**;2(3):145-55.
4. Ison M.G., Hayden F.G. Viral infections in immunocompromised patients: what's new with respiratory viruses? Curr Opin Infect Dis **2002**;15(4):355-67.
5. Aguilera J.F., Paget W.J., Mosnier A., et al. Heterogeneous case definitions used for the surveillance of influenza in Europe. Eur J Epidemiol **2003**;18(8):751-4.
6. Bellei N., Carraro E., Perosa A.H.S., et al. Influenza and Rhinovirus infections among health-care workers. Respirology **2006**;12(1):100-3.
7. Paiva T.M., Ishida M.A., Carvalhanas T.R.M.P., Barbosa H.A. Influenza: desafio de saúde pública. Boletim Epidemiológico Paulista **2004**;1(7):14-17.
8. Meissner H.C. Reducing the impact of viral respiratory infections in children. Pediatr Clin North Am **2005**;52(3):695-710.
9. Motta F.C., Siqueira M.M., Lugon A.K., et al. The reappearance of Victoria lineage influenza B virus in Brazil, antigenic and molecular analysis. J Clin Virol **2006**;36(3):208-14.
10. Machado C.M., Cardoso M.R., da Rocha I.F., et al. The benefit of influenza vaccination after bone marrow transplantation. Bone Marrow Transplant **2005**;36(10):897-900.
11. Call S.A., Vollenweider M.A., Hornung C.A., et al. Does this patient have influenza? JAMA **2005**;293(8):987-97.