Influenza A pandemics: Clinical and organizational aspects: The experience in Chile

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Recently, the World Health Organization declared a pandemic mediated by the novel A H1N1 influenza virus. Soon after the first report from Mexico, the disease arrived in Chile, where it spread quickly from south to north, mimicking cold weather progression through the country. Between May and September 2009, 366,624 cases of H1N1 were reported; 12,248 were confirmed by real-time reverse-transcription polymerase chain reaction and 1562 were hospitalized. One hundred thirty-two deaths were attributable to the infection, creating a death rate of 0.78 per 100,000 inhabitants. Common comorbidities were present in 59%, including obesity, chronic obstructive pulmonary disease, hypertension, type II diabetes, and congestive heart failure. Nine percent were pregnant. Severe disease developed early; the median time to admittance was 5 days, and the most common clinical manifestations were cough, fever, dyspnea, and myalgia. Mean acute physiology and chronic health evaluation II and sequential organ failure assessment scores were 14 and 5, respectively. Highlighted laboratory data were lactate dehydrogenase and creatine kinase elevation, leukocytosis in 50%, elevated creatinine in a 25%, and thrombocytopenia in 20%. Severe respiratory failure requiring high-frequency oscillatory ventilation and extracorporeal membrane oxygenation as sophisticated modes of respiratory support was seen in 17%. Acute renal failure occurred in 25% of the intensive care unit patients, with death rates near 50%. Health systems reinforced outpatient guards with extra staff and extension of the duty schedules. Antivirals were supplied free for medically diagnosed cases. Admissions for severe cases were prioritized, reconverting hospital beds into advanced care ones; a central coordination station rationed their assignment. Recommendations for small hospitals include adding ventilators, using videoconferences, providing tutorial activity from experts, developing guidelines for disease management, and outlining criteria for transport. (Crit Care Med 2010; 38[Suppl.]:S000–S000)

Key Words: influenza; avian flu; pandemic; pneumonia; complications; treatment.

MATERIALS AND METHODS

Epidemiologic and Clinical Aspects

The epidemiologic characteristics of all confirmed cases between May 17 and September 23 in Chile were centralized by the Ministry of Health (4). Case criteria were the presence of temperature >38°C, cough, myalgia, headache, and sore throat. Cases were confirmed by a specific real-time reverse-transcription polymerase chain reaction at the Institute of Public Health and some private health centers in Chile.

During the winter, a marked increase of cases of respiratory disease was reported by the epidemiologic surveillance system (Fig. 1). A total of 366,624 cases of pH1N1 were reported through September 23, and 12,248 of those cases were confirmed. The clinical spectrum of the disease caused by new pH1N1 virus infection ranged from a nonfebrile, mild upper-respiratory tract illness to severe or fatal pneumonia. Most cases have been benign and uncomplicated, behaving as typical influenza-like illness with spontaneous recovery after 3 to 5 days.

However, in all patients hospitalized with a diagnosis of suspected severe human influenza infection and/or pneumonia, World Health Or-
Clinical Features

Recently, we performed a retrospective analysis (5) of all patients admitted to a critical care beds of 11 national health centers (National Institute of Thorax, Hospital del Salvador, Hospital de Valdivia, Hospital de Coquimbo, Hospital San Borja-Arriaran, Hospital Militar de Santiago, Hospital de la Fuerza Aérea, Hospital de Puerto Montt, Hospital de Osorno, Clínica Indisa, and Clínica Santa María), between June 1 and August 30, 2009. In all cases the diagnosis was confirmed by World Health Organization for human pH1N1 virus. We evaluated demographic, clinical, and laboratory findings, number of patients using mechanical ventilation (MV), prone position, high-frequency oscillatory ventilation (HFOV), and extracorporeal membrane oxygenation (ECMO), as well as mortality in the ICU.

We analyzed a total of 75 adult patients admitted to 11 ICU in 11 hospitals in Chile. The median age was 45 yrs (range, 16–77 yrs). Forty-five patients (59%) were male. All patients were Chilean residents. Forty-four had preexisting medical conditions, including obesity (median body mass index, 38 ± 26 kg/m²) in 34 patients (45%), arterial hypertension in 12 patients (16%), asthma in 13 (18%), chronic obstructive pulmonary disease in 10 (13%), non-type 1 diabetes mellitus in three, and chronic congestive heart failure in two. Only eight of the patients had undergone seasonal influenza vaccination in 2008 to 2009; seven of them survived. Our series included seven pregnant women, including one who entered labor because of the seriousness of the respiratory failure (5).

The median time elapsed between the onset of symptoms and admission to the hospital was 5 days (range, 1–15 days). The main symptoms were cough, fever, with temperatures >38°C (100.4°F), dyspnea, and myalgias (Table 1). In this series, 75% of the admitted patients required MV; in four cases, noninvasive ventilation was sufficient for treatment. Prone position ventilation, HFO, and ECMO were used in 18 (24%), eight (10.6%), and five (6%) cases, respectively. ICU mortality was 26%. Survival was seen in 75% of those treated with HFO and in 40% of those treated by ECMO. At admission, 27% (21 patients) had acute renal failure, seven of whom required hemodialysis. Ten (50%) patients who had acute renal failure died. The gastrointestinal symptoms (nausea, vomiting, and/or diarrhea) occurred in <11% of patients (5), which is less than the incidence of 38% reported in the US (6).

The median acute physiology and chronic health evaluation II (APACHE II) score was 14 (range, 1–35), and the median sequential organ failure assessment (SOFA) score was 5 (range, 0–15); both were higher in those who died, indicating more severe abnormalities in those patients than in those who survived (Table 2) (5).

Laboratory

At the time of admission, all 66 (88%) tested patients had elevated lactate dehydrogenase levels. Fifteen cases (20%) had increased creatine kinase levels, exceeding 1000 IU/L (range, 1065–7582) in eight cases (10.6%). In 27 (36%) there was leukocytosis >10,000/mm³, and 21 patients (28%) had thrombocytopenia at admission. Fourteen cases (18.6%) had elevated creatinine levels (1.5–8.5 mg/dL) (5).

Microbiology

Bacterial coinfections were documented in seven cases on admission (four had Streptococcus pneumoniae and three had Staphylococcus aureus). In five patients, pleural empyema developed, and the etiology was identified (bacteremic penicillin-sensitive S. pneumoniae) in one patient (5).

Imaging

All patients except one had radiologically confirmed pneumonia showing bilateral patchy alveolar opacities (predominantly basal). Interstitial opacities affected three of the four lung quadrants in 45 patients. A
provided by triage policies designed for
cially in the evening hours. This staff was
reinforced with extra personnel, espe-
viate health system. 516 were referred to the pri-
and 471 were referred to the public health
management system were performed; referrals coordinated by this central bed
From May 11 through August 8, 987 re-
ferrals to an available health
determined the management of the pa-
ients with different degrees of severity. The elective outpatient care system’s
schedule was extended to evening hours and weekend days.
Basic acute care beds, mainly from the
surgery and gynecology departments,
were converted into respiratory care beds,
along with an interruption of elec-
tive general surgery, orthopedic, and gy-
necologic procedures. This mechanism
allowed the conversion of 50% of extra
beds, with an increase from 4261 to 6481
beds for acute disease. In the same way, 25% of the intermediate care beds were
converted into intensive care beds (Table 2). Finally, a rate of one intensive care bed for
every 20,000 inhabitants was achieved for adult care, and one bed for
every 30,000 inhabitants was achieved for pediatric care. At the same time, 20% of
the professional staff was absent from
work because of respiratory disease, with
most of the cases being mild and self-
limited. No case of severe pneumonia was
reported among them. This whole sce-

dario required reassignment and hiring of
extra nursing, physical therapy, and
medical staff for the care of pH1N1 pa-
tients. All of them were monitored by
experienced critical care staff.
As for medical education, conceptual
support, and guidelines, the Health Min-
istry assigned a group of respiratory, in-
tensive care, and infectious disease spe-
cialists entrusted to compile the
guidelines for management of pH1N1
cases, which were available through the
Internet for users around the country (8).
Daily videoconferences were held by ex-
erts in respiratory and intensive care,
leading daily analysis and discussion of
cases countrywide. Also, we had tutorial
and support activities distributed for the
needs in the provinces, by direct visit,
mail, or telephone, to assist in sharing and
advising in decision-making. Private
system, military, and university hospitals
and their professional staffs were settled
“online” as backup of the public system
using the same criteria.
Critical care beds and ventilators were
main limiting resources for adequate
management of our patients, so 150 new
MV devices were purchased by the public
system and were distributed throughout
the country (Table 3). This number was
limited by the number of devices available
for sale in the country during the severest
phase of the pandemic. Following the same
policy and needs, the private system also
purchased equipment. The exact quantity is
unknown by the authors.
Advanced critical support for acute lung injury—ARDS patients was resumed.
Eleven of the 150 new ventilators were
HFOV machines, which were distributed throughout the country according to the
technical complexity of each center and
the complexity of care needs. Eventually,
17 HFOV machines were available. ECMO
was available for 10 patients at a time.
Interhospital transport of critically ill
cases, with trips up to 1500 km, were
required for severe cases needing ad-
vanced modes of therapy, mainly respira-
tory, surgical, and renal support (9–12).
These transports were not available in
small and peripheral hospitals. We no-
ticed that many of these cases suddenly
became severe, making them ineligible
for management with transport ventila-
tors. We considered patients eligible for
air medical transport provided they had
an oxygen saturation of \( \geq 90\% \) while un-
dergoing testing on transport ventilator
in volume- or pressure-control modes, an
inspired oxygen fraction up to 1, positive
end-expiratory pressure \( \leq 15 \) cm of water,
eventual pneumothoraces were drained, and
were hemodynamically stable with
two or less vasoactive drugs. The trans-
pot of patients needing HFOV or ECMO
used to be technically impossible, even
after hours working at the bedside with
the ventilatory, sedation, and relaxation
parameters. Our recommendation is to
consider the early referral of the most
severe cases, because that referral may
not be possible later in the evolution.

![Figure 2. Daily calls to centralized administration of critical beds in the metropolitan area of Santiago, Chile, between April 14 and July 25, 2009.](image-url)
Table 3. Acquisition of new equipment for mechanical ventilation for public health services during the pandemic outbreak in Chile

<table>
<thead>
<tr>
<th>Regional Health Services</th>
<th>Conventional Ventilators, N</th>
<th>HFO Ventilators, N</th>
<th>Noninvasive Ventilators, N</th>
<th>Transport Ventilators, N</th>
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<tr>
<td>Total</td>
<td>84</td>
<td>11</td>
<td>51</td>
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HFO, high-frequency oscillatory.

<sup>a</sup>The acquisition of noninvasive ventilators was aimed for management of seasonal respiratory disease different from pH1N1.

Instructions were disseminated to provide antivirals widely, free from cost, to the cases properly diagnosed, certified, and registered by physicians. Nearly 1,000,000 doses were acquired (and 662,428 treatments administered by September 20) and distributed to outpatient and emergency care systems, including private, university, and military institutions.

**Lessons Learned About the Clinical Management of Severe Pneumonia in Human Infection With New Influenza A Virus: Advanced Respiratory Support**

Treatment of ARDS associated with the pH1N1 virus infection should be based on published evidence-based guidelines for sepsis-associated ARDS. Lung-protective MV strategies were used (13). Although noninvasive ventilation was discouraged because of the risk of spreading viruses, some centers made limited use of noninvasive ventilation, with clinical success in properly isolated cases, and with the staff using adequate means for protection. When invasive ventilators with noninvasive ventilation software and closed masks were used, these limitations were considered to be not that restrictive.

The 17% of patients with severe respiratory failure supported by HFOV or ECMO needed prolonged support, up to 21 days in our series. Whereas this course seemed disappointing initially, eventually we learned that it did not necessarily predict a poor outcome.

Despite the initial improvement of oxygenation in our series, three in five patients (60%) died and one survived with severe sequelae. We believe that implementation of this complex technique should be reserved for well-trained and experienced centers.

HFOV had a lower mortality in our series (two of eight patients) and, despite being virtually unknown technology in our country, it could be implemented quickly in different regions. We reserve it as an early rescue strategy for patients with oxygenation index >15 or P/F<sub>O2</sub>.7 with positive end-expiratory pressure >15 cm H<sub>2</sub>O.

**Hemodynamic Support**

On admission, a restrictive fluid strategy was attempted (14) for the management of patients with acute respiratory failure secondary to pH1N1, provided they were not experiencing hypoperfusion or a state of shock, before the connection to MV. Centers provided with PICCO technology (Pulsion Medical Systems, Munich, Germany) to measure extravascular lung water reported it was increased from the onset of respiratory failure, reflecting impaired permeability. Once respiratory failure and MV are established, the strategy consists of supplying the least volume input compatible with maintaining hemodynamics and renal perfusion. Care must be taken in the interpretation of elevated pulmonary artery catheter figures in patients requiring high airway pressures.

**CONCLUSIONS**

The pH1N1 in our country, located in the southern hemisphere, was associated with winter, generating an increase in demand for medical care and numerous hospitalizations for severe cases. This situation necessitated the development of strategies to optimize the use of scarce medical resources in the highly demanding time of winter. We communicate the lessons that we learned about the clinical presentation and treatment of a new form of influenza.

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