

# CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PATIENTS HOSPITALIZED FOR INFLUENZA A (H1N1) IN TUXTLA GUTIÉRREZ; CHIAPAS, MEXICO

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— Abstract—

To evaluate the clinical and epidemiological characteristics of patients hospitalized for influenza A H1N1 in Tuxtla Gutiérrez, Chiapas, Mexico, a cross-sectional study and case series were conducted. It was found that a total of 6,120 samples of people suspected of being infected by the H1N1 influenza virus; 51.5% (3,151) were positive, with the highest percentage of cases in the City of Tuxtla Gutierrez. Of the 1,567 positive cases, (49.7%) were women. The average age of the population studied was  $21.5 \pm 4.5$  years. The most affected group was 30 to 50 years (48.7%), followed by a group of 15 to 29 years (29.5%). Housewives and students (mother and children), were a vulnerable group to get sick; because they presented the highest cases (62%); regarding the risk classification, the most frequent concomitant pathology was diabetes mellitus for 11.5% (n = 9) followed by arterial hypertension with 8% (n = 6) and different respiratory diseases 10.2% (n = 8). Likewise, it was found that cough and general malaise were present in the majority of patients.

### Keywords

*Influenza A (H1N1), epidemiological characteristics, Chiapas.*

Influenza is a newly emerging respiratory communicable disease in human populations, with a rapid increase in incidence and geographic spread. Such an emergency is possible when, over time, infection in animals crosses species barriers due to the transformation of the viral genome, infecting humans (Mc Closkey, Osman, Alimuddin & Heymann, 2014).

Of the four types of influenza viruses A, B, C, and D, types A and B cause seasonal epidemics each year, usually in the winter months; the other two usually cause no or very mild human infection (CDC, 2019). Type A viruses have different bird species as reservoirs and infect pigs, horses, and other mammals, as well as humans; they mutate continuously and rapidly and exhibit a high degree of pathogenicity and virulence (Kumar, Asha, Kahna, Ronsard, Meseke, Sanikas, 2017). Type A viruses are the only ones that can trigger human influenza pandemics, being classified in subtypes from two surface proteins: hemagglutinin and neuraminidase, which give it its infectivity and pathogenicity capacity, being identified 18 subtypes of the first one and 11 of the second one, with multiple combinations, from which 131 have been detected in nature (CDC, 2019).

The A (H1N1) pdm09 virus by its scientific name, which emerged in the spring of 2009 and caused the pandemic, has since been in seasonal circulation around the world; with virtually minimal genetic changes in its antigenicity (CDC, 2010). Currently in circulation in human populations are types A (H1N1) pdm09 and A (H3N2), the latter with more rapid changes genetically and antigenic (CDC, 2019), which represented the majority of cases worldwide (PAHO, 2019). In Mexico since 2009 the same viral subtypes are predominant, for example, the virus A (H3N2) in the 2017-2018 influenza season, or the virus A (H1N1) pdm09 in the recent 2018-2019 season (Department of Health 2019, 5).

According to the WHO report, 18,500 deaths were confirmed by laboratories worldwide between April 2009 and August 2010. This figure would represent a small fraction of the deaths that most likely occurred associated with influenza since the total average estimate of deaths due to A (H1N1) pdm09 by country would have been in the range of 105,700 to 395,600; which by including deaths associated with cardiovascular or respiratory comorbidity would rise to 151,700 to 575,400; most in the young and mature adult population, in the range of 18 to 64 years. More than 51% of the deaths would have occurred in Africa and Southeast Asia; in America and the Western Pacific, the number of deaths associated with influenza A (H1N1) would be 6 times higher in indigenous than in non-indigenous populations. Overall, 0.001% to 0.007% of the world's population would have died during the first year of the virus' circulation between 2009 and 2010, rising to 0.001% to 0.011% when adding the comorbidity associated with influenza

deaths; less or similar to that recorded in other pandemics, except 1918 (Dawood, *et al*, 2012).

In Mexico, between April and May 2009, a preliminary analysis of influenza deaths was conducted by the Department of Health. The epidemic, which officially began in March in the center of the country, had a two-phase behavior in its morbidity curve due to its displacement towards the southeastern states, where Chiapas is located. Although the registration of laboratory-confirmed deaths began in April, it is possible that previously there were other unrecorded deaths, as it was not known that we were facing an epidemic. 79% of mortality was concentrated in those under 30 years of age. The average mortality rate was 1.1 cases per million inhabitants, however, the rate was higher than the average between the ages of 20 and 59, with 1.5 and 1.9 per million, respectively. The fatality rate was 2.2% in this period. Only 17% of the 122 cases studied received hospital care in the first 72 hours and up to 42% died within that time, meaning that the rest of the cases had a delay in the timing of care in addition to the quality of care at the beginning of the epidemic. 58% of the deceased had some comorbidity (Fajardo-Dolci, *et al*, 2009).

In Chiapas, the influenza epidemic began in fact at the end of June 2009 and in July the seriously ill were concentrated in the Hospital Regional de Tuxtla Gutiérrez, which to deal with the severity of the illness only had 6 intensive care beds and some intermediate care beds. No published information was found regarding the behavior of morbidity and mortality of the epidemic in the state, the existing one, refers precisely to the shortcomings and needs in facilities, equipment, and supplies as well as trained personnel and standardized procedures to deal with the situation, which the federation tried to remedy with the acquisition of equipment and training of local staff. Perhaps most serious was the apparent inadequacy of the organization of the health system by state authorities, who failed to assess the risk posed by the epidemic to the Chiapas population (Volkow *et al*, 2011).

The study presented below aims to fill an information gap, describing clinically and epidemiologically the behavior of the epidemic in the state of Chiapas in 2009, from cases hospitalized and confirmed by influenza A (H1N1) pdm09, in the Hospital Regional "Dr. Rafael Pascacio Gamboa" of the Institute of Health of Tuxtla Gutierrez, Chiapas.

## MATERIAL AND METHOD

The population under study consisted of all patients, of any age and both sexes, who were admitted to the regional general hospital, in the city of Tuxtla Gutiérrez, Chiapas; with the confirmed diagnosis of influenza A

H1N1, through the reverse transcription-polymerase chain reaction (RT-PCR) test, from April 24, 2009, to September 21, 2009.

The type of study was a case series. The data were collected from the clinical files of hospitalized patients and the information was complemented with the case studies, for epidemiological notification, with a form from the Single Information System for Epidemiological Surveillance (SUIVE), where it was confirmed the accomplishment of the sample taking, with the method for the detection of virus A (H1N1).

The variables of interest were: sociodemographic, clinical and personal, pathological and non-pathological background, as well as aspects related to treatment. Once the information was collected, a database was created in the statistical program SPSS, version 18. A univariate descriptive analysis was then performed, followed by bivariate analysis.

The inclusion criteria were: to have been admitted to the Hospital General Regional de Tuxtla Gutiérrez, to have an epidemiological study of the case, and to have a confirmed diagnosis of influenza A (H1N1), using the RT-PCR test performed at the State Public Health Laboratory; and the exclusion criteria: to be an outpatient, to have another type of confirmatory test for the disease other than RT-PCR, patients who do not have a clinical record.

## RESULTS

During the study period, 217 patients were hospitalized, of whom 89 (41%) tested positive for H1N1 influenza A through RT-PCR; of these 78 (87.6%) met the inclusion criteria. Table 1 shows that the group from 30 to 59 was the most affected, followed by the group from 15 to 19 years old.

**Table 1**

*Frequency of illness according to age group among hospitalized patients in the study, in the state of Chiapas, Mexico; April 24 to September 21, 2009*

Age group	N	%
14 years and less	1	16.
15 to 29 years	2	29.
30 to 59 years	3	48.
60 years and more	4	5.
Total	7	10

*Source: clinical file from the Hospital General Regional "Dr. Rafael Pascacio Gamboa" of Tuxtla Gutierrez, Chiapas, Institute of Health*

Women made up the majority of the hospitalized patients with 60.3%, (n=47), who were generally housewives. Those affected of reproductive

age represented 72.3% (n= 34) and six of them (12.8%) had an obstetric condition (four with pregnancy and two in postpartum period), the average age of the women was 21.5 years old.

Men constituted 39.7% of the patients (n= 31); the average age was 32 years (range 3 to 70), and their most important activities were as students, 12 (38.7%) and drivers, 5 (16%).

Of the entire series, it was noted that in those over 15 years of age, four (5%) were illiterate, eight (11.5%) had only primary education and 10 (12.8%) had secondary education; however, in 22 patients (28.2%) no schooling was recorded in the file.

Concerning their place of residence, 82% (n=64) belonged to the municipalities that make up the Health Jurisdiction (J.S) No. 1, whose seat is Tuxtla Gutiérrez, of which 46 (71.8%) were residents of the capital city. 15.4% (n=12) were referred from other jurisdictions. Finally, two patients (2.6%) were identified as tourists, coming from Coatzacoalcos (state of Veracruz) and Villahermosa (state of Tabasco).

Regarding the risk classification, 11.5% had diabetes mellitus, the most frequent concomitant pathology, followed by arterial hypertension with 8% (n=6) and different respiratory diseases 10.2% (n=8), among which asthma stood out with 5.1% (n=4); besides others such as pulmonary tuberculosis, COPD, chronic rhinitis, with one case each. When reviewing the non-pathological personal history, living with animals 28.3% and overcrowding 24.4% turned out to be the most frequent conditions.

As shown in table 2, 23 patients presented pathological risks representing 30% and nearly 63% non-pathological, while 27 patients had 3 or more risks.

**Table 2**  
*Distribution of patients according to type and number of risks*

History	n	%
Of pathological risk	23	29.5
Of non-pathological risk	49	62.8
Patients with a maximum of two risks	26	33.3
Patients between 3 and 6 risks	23	29.5
Patients with 7 or more risks	4	5.0

Source: clinical file from the Hospital General Regional "Dr. Rafael Pascacio Gamboa" of Tuxtla Gutierrez, Chiapas, Institute of Health

The average time between the onset of symptoms and the time patients asked for medical attention was 3.7 days, ranging from 0 to 14 days. Of the inpatients, 47 (60.3%), were the same or below the average; the trend was

1 day in 25 patients (32%). The average number of days of hospitalization was four (range 1 to 24).

At the time of hospitalization, a clinical history was taken to identify the initial clinical picture, to gather the typical symptoms or a nosology diagnostic, and it was found that cough and general malaise were present in most patients (table 3).

**Table 3**  
*Percentage distribution of signs and symptoms of cases on admission*

Signs and symptoms	n	%
Cough	71	91.0
Overall sickness	63	80.8
Dyspnea	48	61.5
Fever	43	55.0
Flue	27	34.6
Headache	24	30.8
Throat sore and pain	14	18.0
Chest pain	8	10.3
Cyanosis	5	6.4

Source: clinical file from the Hospital General Regional "Dr. Rafael Pascacio Gamboa" of Tuxtla Gutierrez, Chiapas, Institute of Health

The coughing had an average duration of 3.4 days (a one-day trend in 28 patients; range 1 to 14). The patients who had dyspnea were 48 (61.5%), with an average of 2.3 days. Finally, cyanosis was recorded in five patients (6%); all with one day of evolution.

According to the American College of Chest Physicians Society for Critical Care Medicine Consensus Conference criteria, 40 patients (51.3%) were classified as having systemic inflammation syndrome, of which 35 (87.5%) had at least one disease or history considered to be at risk; including four patients who had a history of chronic respiratory disease.

Excluding those who died; 10 patients (25%) had sepsis as the first cause of complications and five of them (12.5%), went with septic shock, which finally conditioned that two (5%) had acute renal failure. In this group of patients, the average increased to five days (range 0 to 14), to seek care, from the onset of symptoms.

The criterion for admission to the Intensive Care Unit (ICU) was respiratory failure. Of the 40 patients with systemic inflammation syndrome, 20 (50%) were admitted to the ICU, whose average age was 35 years (range 21 to 52). The average number of days at the ICU was 10 (range 6 to 19).

The average number of days these patients sought medical attention from the beginning of the illness was six (range 2 to 14). Of which nine patients (45%), were at or above this average.

For all hospitalized patients, the average number of days between symptom onset and swab sampling for RT-PCR was 4.3 days (range 1 to 15); 63% (n= 49) were equal or below this average; the trend was one day for 22 patients (28%).

Regarding the time of initiation of antiviral therapy, 33 patients (44%) received oseltamivir within the first 48 hours of symptom onset; no deaths were recorded during this period. The first death was recorded on the third day of the onset of symptoms. The average time from the appearance of signs to the beginning of antiviral treatment was 4.3 days (range, 0 to 16), and in 29 patients (38.7%), it began after this average. Then, there was the use of antimicrobials in 20 patients (25.6%).

The number of deaths was 15 patients (19.2%); 10 were women (66.7%), including one pregnant woman and one postpartum woman, as well as 5 men (33.3%). The average age of those who died was 35 (women 32 and men 41). The age range of these patients varied from 23 to 52 years.

Regarding schooling, 10 of the deceased had a basic education (66.7%). There were two with a college degree. One of the 4 illiterate people also died and in 2 cases no record was found. When analyzing the occupation, 9 women were housewives and one was a teacher. Of the men, three were dedicated to construction, one was an architect, and the other two were drivers.

Because of its geographical location: 11 patients (73.3%), belonged to the area of influence of the Health Jurisdiction (J.S.). No. 1 (Tuxtla Gutierrez), two cases from J.S. No. 2 (San Cristobal de las Casas), one case from the Health Jurisdiction. J.S. No. 8, (Tonala), and one of them was a tourist from Villahermosa, Tabasco. By municipality, five patients had their residence in Tuxtla Gutierrez, and three in Jiquipilas, Chiapas.

Regarding the pathological risk history, the most frequent was diabetes mellitus, with five cases (33.3%), followed by obesity with three cases (20%), and of the history of chronic respiratory diseases, asthma was the only one present with only one case.

Of the non-pathological risk background; the most frequent was exposure to animals in seven cases (46.7%), followed by exposure to wood smoke in four cases (26.7%), overcrowding and migration were present in three cases (20%). Alcoholism and smoking were only present in one case for both; however in 5 cases, for each background, no record was found. In summary, eleven patients had three risk factors and one patient had seven.

Coughing was characterized by being purulent and hemoptoic in half of the deceased, 49.9% (n=7). Dyspnea was also present in 14 patients (93%), classified as "severe or very severe" according to the "American Thoracic



Society”, with an average of three days (range 1 to 5). With cyanosis, five patients (33.3%) were treated, all with one day of evolution.

The complications that led them to death were: sepsis in 14 of the cases (93.3%); 12 evolved to septic shock and acute renal failure (85.7%).

The average stay of the 15 deceased who were also admitted to the ICU was nine days (range 0 to 23). The average from the onset of symptoms to seeking medical attention was six days (range 3 to 14), and the average from the onset of symptoms to death was 16 days (range 4 to 26).

It is worth mentioning that the proportion of deaths was significantly higher in people who started treatment after the fourth day, 12 (80%) than in those who started it before, 3 (20%). The case fatality rate during the study period was 4.76/1000 confirmed cases of influenza A (H1N1).

## DISCUSSION

In Mexico, the Department of Health reported to the WHO; between March and April 2009, the occurrence of three outbreaks: in the then Federal District and now Mexico City (854 cases of pneumonia, with 59 deaths), in San Luis Potosi (24 cases with three deaths), and Mexicali (four cases and no deaths). The state of Chiapas began to appear in the statistics until May 6, 2009, in a preliminary report by the Federal Department of Health, which published the first case of death (Department of Health 2009).

As of September 26, 2009 (the period included in this study), Chiapas already had 12% of the cases registered at a national level (INDRE; n= 3561); and as of October, there was a considerable decrease in the number of reported cases, with a difference by mid-July 2010 of only 157 positive cases in 10 months (INDRE; n=3718), which in statistics took the state from first place of confirmed cases to sixth (Salud México, 2010).

In the state, the most affected age group was from 5 to 29 years (65%), and the average age was close to 31 years; a similar result to those registered in Mexico City (López, Solís AM, López V, García Rivas D and Lozano JJ, 2010) in the national statistics (Fajardo *et al*, 2009) and in other countries such as: Brazil (Duarte PAD 2009), Canada (Kumar A *et al*, 2009), Iran (Mehdi, G M *et al*, 2009), and China (The National Influenza A Pandemic (H1N1) 2009)

The age groups considered at risk for IRA (<5 and >65 years) had an overall rate of 5 and 1.5 /10,000 respectively and the hospitalization rate was 4 /100,000; figures similar to those of other studies (Pan American Health Organization [PAHO], 2009), (Ayora, TG 1999), (Virus Investigation Team, 2009), (Libster *et al*, 2010), (Louie JK *et al*, 2009) (Telo Velosa CS, 2009) and (O’Riordan and Sean, 2009). It should be noted that the general strike rate, in the region of Tuxtla Gutierrez was 40/10,000 inhabitants, and the hospitalization rate was 4.5/100 infected.

Housewives and students (mother and child), were a vulnerable group to get sick, they presented the highest cases (62%). However, it is interesting that housewives, mostly, registered during July (n=14) with an average on July 4th; and with the data obtained the mother-student relationship was not found, since the group of students was registered mostly during June (n=19) with an average on June 7th. Also, no complete family groups were identified. This allows us to assume that the mechanism of transmission is the common one; from person to person; and that it followed a pattern similar to that proposed by Cauchemez S. and collaborators (2009); whose index states that transmission in homes where two people live is 29%, and in homes where six people live is 9%.

Concerning pathological and non-pathological clinical history, obesity and diabetes mellitus were the most significant concomitant diseases in the affected population Louie JK *et al* (2009), Jain S. *et al* (2009), Pérez Padilla *et al* (2010), although there is a very important bias since 25% of this data was not recorded in the file. Something important to note is that it does not agree with other studies that show up to 60% incidence of these diseases (Louie, JK *et al*, 2009) (Perez, Padilla, *et al*, 2010). However, it corresponds to the proportion of the population with diabetes (Mexican Diabetes Federation, 2010), (INSP, 2007), but not to people with hypertension (INSP, 2007), (Velázquez, Monroy O, *et al*, 2002) results similar to those presented by Singapore (Cutler, JL *et al*, 2010) which only identifies 13% of similar pathologies.

Likely, the population did not interpret the influenza A (H1N1) pandemic as implying a high risk of illness and death, since the time ranges for seeking medical care were very wide, which was especially observed in patients who died (Pérez R., de la Rosa D., Ponce de León S, 2009).

Cyanosis and dyspnea were the most significant clinical aspects on admission with the risk of death, this condition is manifested because 63% of the deceased had oximetry less than or equal to 75% of oxygen saturation.

The proportion of pregnant or postpartum patients who became ill, compared to the 2008 birth rate (153,738) according to INEGI data, was 0.5 per 10,000 births; it is minimal to be considered a risk ratio for women with an obstetric condition and differs from other studies conducted in the United States, where the rate of pregnant women infected with the Influenza A (H1N1) virus is four times higher than the general population (Louie JK, Acosta M, Jamieson DJ, Honein MA, California Pandemic (H1N1) Working Group, 2010).

Considering the analysis of the average time between the beginning of the illness and the moment of requesting medical attention; a fundamental aspect in the difference between life and death, was the taking of the antiviral medication. It could be established that patients who took it after four days

had a higher risk of dying (Caffaratti, M and Briñón, M.C. 2004). This time had an average of almost 60% delay (average of 7 days, range of 3 to 18), concerning the group of those who did not die. The case fatality in the study period is similar to that expressed by the *Committee of the WHO consultation on clinical aspects of pandemic (H1N1) 2009 influenza 2010*.

Some limitations were observed in this study, especially in the primary sources. There were multiple changes in the reporting formats of the clinical record, leading to a deficiency in data management; this was most likely a consequence of not considering an epidemic in the State's epidemiological surveillance program, due to an apparent historical lack of seasonal influenza in the State; despite being a notifiable disease according to the regulations of the Subsecretaria de Prevención y Control de Enfermedades, and the Directorate of Epidemiology, based on NOM-017-SSA2-1994, for epidemiological surveillance of the Department of Health (Department of Health, 1999).

In 50% of the files, a complete medical history was not found, and to obtain socio-demographic and background data, it was necessary to resort to different medical and social work notes, among others. For the generalization of these findings, we must be cautious, since the cases in the study represent a small proportion of the reality of cases that occurred during the epidemic and that required hospitalization. The second limitation of the study is that it was a study of hospitalized cases, so the epidemiological characteristics cannot be estimated exactly, since it is not a study based on the general population.

Within the limitations of the study, we can point out that its findings cannot be generalized to a larger population, for the following reasons: the cases come from a single hospital, so many other cases may not be part of the study; it is not a community-based study, so the epidemiological measures obtained may have some bias; finally, the geographical dispersion of the infection was not taken into account, and could have an important impact on morbidity.

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